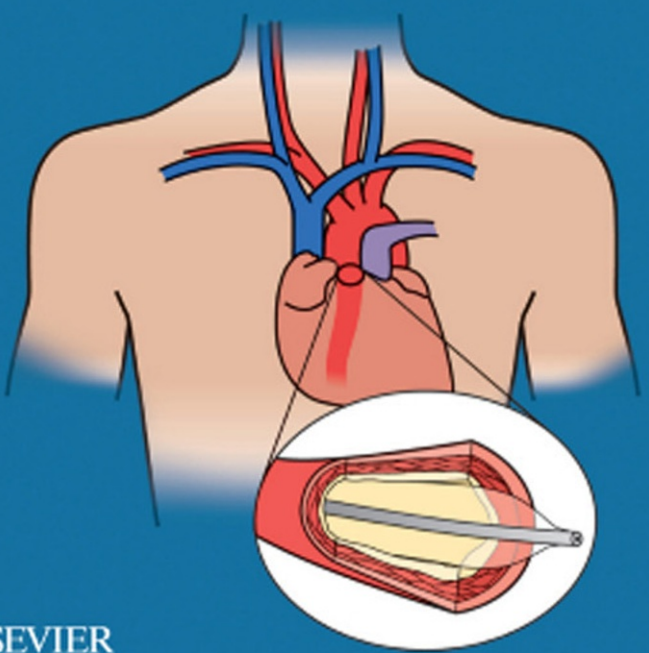
3RD EDITION

Interventional Cardiac Catheterization Handbook

Morton J. Kern



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THE INTERVENTIONAL CARDIAC CATHETERIZATION HANDBOOK

Edited by

Morton J. Kern, *MD, FSCAI, FACC, FAHA*
Chief
Department of Cardiology
Long Beach Veterans Administration Health Care System
Long Beach, California;
Professor of Medicine and Associate Chief, Cardiology
University of California, Irvine
Orange, California

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1600 John F Kennedy Blvd.
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To my friends who work in the cath labs around the world - this one is for you.
and
To Margaret and Anna Rose, for putting all dear things in proper perspective. Thank you.

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Contributors

Wail Al Kashkari, MD
Interventional Fellow
Rush Center for Congenital and Structural Heart Disease
Rush University Medical Center
Chicago, Illinois

Ryan Berg, MD, FACC
Assistant Professor of Medicine
Associate Program Director
Cardiology
UCSF Fresno
Fresno, California

John A. Bittl, MD
Interventional Cardiologist
Munroe Heart and Vascular Institute
Munroe Regional Medical Center
Ocala, Florida

Christine Cabiling, BS
Senior Product Manager
Marketing
Edwards Lifesciences
Irvine, California

Qi Ling Cao, MD
Research Faculty
Rush Center for Congenital and Structural Heart Disease
Rush University Medical Center
Chicago, Illinois

Ahmad Edris, MD
Fellow
Cardiovascular Disease
Department of Cardiology
University of California
Irvine School of Medicine
Irvine, California

Ted Feldman, MD, FESC, FACC, FSCAI
Professor of Medicine
Northwestern University
Feinberg School of Medicine
Chicago, Illinois;
Director
Cardiac Catheterization Laboratory
Evanston Hospital
Evanston, Illinois

Connie N. Hess, MD
Fellow
Cardiology
Division of Cardiology
Duke University Medical Center
Durham, North Carolina

Ziyad M. Hijazi, MD, MPH, FSCAI, FACC, FAAP
Professor of Pediatrics and Internal Medicine
James A. Hunter, MD, University Chair;
Director
Rush Center for Congenital and Structural Heart Disease
Rush University Medical Center
Chicago, Illinois

John M. Hodgson, MD
Department of Cardiology
Geisinger Health System
Wilkes-Barre, Pennsylvania

Morton J. Kern, MD, FSCAI, FACC, FAHA
Chief
Department of Cardiology
Long Beach Veterans Administration Health Care System
Long Beach, California;
Professor of Medicine and Associate Chief, Cardiology
University of California, Irvine
Orange, California

Michael S. Kim, MD
University of Washington School of Medicine
Seattle, Washington

Andrew J. Klein, MD
Associate Professor of Medicine
Cardiology
John Cochran VA Medical Center
Saint Louis University School of Medicine
St. Louis, Missouri

Mitchell W. Krucoff, MD, FACC, FAHA, FSCAI
Professor
Medicine/Cardiology
Duke University Medical Center;
Director
Cardiovascular Devices Unit
Duke Clinical Research Institute
Durham, North Carolina

Michael S. Lee, MD, FACC, FSCAI
Assistant Professor
Medicine
UCLA Medical Center
Los Angeles, California

Michael J. Lim, MD, FACC, FSCAI
Director
Division of Cardiology and J. Gerard Mudd
Cardiac Catheterization Laboratory
Department of Internal Medicine
Saint Louis University
St. Louis, Missouri

Mohammad Marashdeh, MD
Interventional Cardiologist
Saint Clair Regional Medical Center
Morehead, Kentucky

Igor F. Palacios, MD
Director of Interventional Cardiology and Structural Heart Disease Interventions
Massachusetts General Hospital
Harvard Medical School
Boston, Massachusetts

Charles M. Parise, MD
Chief Fellow
Division of Cardiology
University of California, Irvine
Orange, California

Pranav M. Patel, MD
Interim Chief and Associate Professor
Cardiology;
Director
Cardiac Catheterization Laboratory
Cardiology
University of California, Irvine
Orange, California

Sunil V. Rao, MD
Associate Professor of Medicine
Cardiology
Duke University Medical Center
Durham, North Carolina;
Director
Cardiac Catheterization Laboratories
Durham VA Medical Center
Durham, North Carolina

Jonathan A. Rapp, MD
Assisting Staff
Department of Cardiology
Ochsner Medical Center
New Orleans, Louisiana

Michael H. Salinger, MD
Assistant Clinical Professor of Medicine
Section of Cardiology
University of Chicago School of Medicine
Chicago, Illinois;
Director
Interventional Cardiology
NorthShore University HealthSystem
Evanston, Illinois

Arnold H. Seto, MD, MPA
Assistant Clinical Professor
Cardiology
University of California, Irvine
Orange, California;
Assistant Clinical Professor
Cardiology
Long Beach VA Medical Center
Long Beach, California

Nauman Siddiqi, MD
Cardiology Fellow
University of California, Irvine
Orange, California

Kimberly A. Skelding, MD, FACC, FAHA, FSCAI
Associate
Interventional Cardiology, Geisinger Medical Center;
Director of Cardiovascular Genomics and Cardiovascular Research
Geisinger Center for Health Research
Danville, Pennsylvania

Paul Sorajja, MD
Associate Professor of Medicine
Cardiovascular Diseases
Mayo Clinic
Rochester, Minnesota

William M. Suh, MD
Assistant Clinical Professor
Department of Medicine
Ronald Reagan UCLA Medical Center
Los Angeles, California

Barry F. Uretsky, MD
Clinical Professor of Medicine
Internal Medicine
University of Arkansas for Medical Sciences
Little Rock, Arkansas;
Director
Interventional Cardiology
Cardiology
Central Arkansas Veterans Health System
Little Rock, Arkansas

Christopher J. White, MD, FSCAI, FACC, FAHA, FESC
Professor of Medicine and System Chair for Cardiovascular Diseases
The Ochsner Clinical School
University of Queensland;
Medical Director
John Ochsner Heart and Vascular Institute
Ochsner Medical Center
New Orleans, Louisiana

Todd K. Zynda, DO
Fellow
Cardiovascular Disease
University of California, Irvine
Orange, California

Preface

The discipline of interventional cardiology, an American Board of Internal Medicine–certified subspecialty since 1999, requires an understanding and application of extensive specialty information and skills. Success in interventional cardiology requires the mastery of complex cognitive information coupled with the in-lab, minute-by-minute application of techniques used to implant coronary and peripheral stents, repair vascular injury and structural heart defects, and manage critically ill patients, at times simultaneously. The interventional physician and his or her team should have a complete understanding of the indications and practice guidelines for percutaneous coronary intervention (PCI), coronary bypass graft surgery, and medical therapy for coronary, peripheral arterial, and structural heart disease. Specifically the physician and team should know:

- The chance of a successful procedure
- The benefit/risk to the patient if the procedure is successful/unsuccessful
- The occurrence and management of various complications

These facts must also be integrated into judgments for a specific patient given a large variety of factors related to the comorbidities and underlying medical cardiac and noncardiac conditions.

In this third edition of *The Interventional Cardiac Catheterization Handbook,* we have tried to provide the critical information to those beginning their journey into interventional cardiology. Of course this material is an extension of techniques and methods described for diagnostic catheterization and specially related techniques in *The Cardiac Catheterization Handbook,* fifth edition. Excellence in intervention begins with excellence in diagnostic catheterization. The ICCH third edition is a handbook and by design cannot include every aspect of the universe of interventional cardiology. Such detail is provided in larger reference textbooks in the field.

The ICCH third edition is new in several ways. Beyond a redesigned format with full color images, making the reading and diagrams easier and more instructional, the contents have been brought as up to date as possible given the nature of printed books. Many of the basic chapters discuss what PCI does and how to achieve best access, and angiographic images now reflect the modern approach with both third-generation drug-eluting stents as the principal tool to open arteries and radial access highlighted to emphasize the increased safety of this method. Angiographic views for intervention, use of different contrast media, and identification of patients at high risk are fundamental reading for all students and physicians meeting the minimum knowledge requirements.

In contrast to the prior editions, more focused and specific chapters now emphasize the unique nature of several well-recognized and well-studied angiographic subsets undergoing complex PCI such as bifurcation lesions, left main stenosis, chronic total occlusions, saphenous vein graft interventions, complications, and peripheral vascular

disease. Each chapter concentrates on the question at hand in a concise and hopefully useful presentation by one of the experts in the field.

The chapter on complications by Dr. Lim highlights the fact that no area of cardiology has a greater need for online decision making than PCI. To minimize the unanticipated complications, the planning and execution of PCI require an in-depth understanding of the options, limitations, and alternative methods of proceeding if the initial approach fails.

It is impossible for reading alone to substitute for the experience needed to learn and handle different types of guiding catheters, guidewires, balloon catheters, stents, intravascular ultrasound imaging, and a host of FDA-approved non-balloon interventional devices. However, an initial acquaintance with descriptions of the equipment's physical and material properties and the handling characteristics of intravascular devices will be an important starting point.

The most critical step in performing an intervention begins well before introducing a stent. That step is ensuring that the correct procedure will be performed for the correct indications. Intravascular ultrasound and translesional physiology, specifically fractional flow reserve (FFR), must be used appropriately and frequently to select which lesions do and do not require treatment and must be part of the complete interventional cardiologist's practice.There may come a time when the physician's competency and reimbursement will require a more concrete demonstration of ischemia for patients in whom no prior stress testing or out-of-lab evidence of ischemia is present.

I thank my colleagues and cardiology fellows in training who contributed their valuable time, knowledge, and effort to make this book possible. I again thank my wife, Margaret, and daughter, Anna Rose, whose love and support give me purpose. Finally, this book would have no value were it not for the overwhelming desire of the cath lab physicians, nurses, techs, and fellows to help their patients through what at times may be a life or death procedure. I am humbled and at the same buoyed by our mutual goals to care for our patients through better knowledge in the cath lab.

Morton J. Kern
Long Beach, California
March 2012

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Basics of Percutaneous Coronary Interventions

MORTON J. KERN

On September 16, 1977, Andreas Grüntzig performed the first human percutaneous transluminal coronary angioplasty in Zurich, Switzerland. Until then, coronary artery bypass surgery was the only alternative to medicine for the treatment of coronary artery disease. Over the past 35 years, PTCA has evolved into more sophisticated techniques involving predominantly stenting and is now called percutaneous coronary intervention (PCI). PCI is one of the most successful methods of coronary revascularization with more than 1,500,000 procedures done in the United States alone. PCI is the treatment of choice for discrete single- and double-vessel coronary lesions and plays an important role in complex revascularization in patients with multivessel coronary artery disease, including left main narrowings with and without depressed left ventricular function. Techniques and technology used in PCI extend into the treatment of peripheral arterial disease. Further evolution of PCI into the treatment of structural heart disease (valves, septal defects, etc.) is emerging as a separate discipline within interventional cardiology.

PCI encompasses various coronary techniques, such as balloons, stents, cutters, lasers, grinders, suckers, filters, and other tools. The term *percutaneous transluminal coronary angioplasty* (PTCA) is used when describing techniques and outcomes related to use of the original balloon inflation technique first used by Grüntzig.

This chapter is the extension of the PCI chapter from *The Cardiac Catheterization Handbook*, fifth edition, and presents the basic method and mechanisms of balloon angioplasty and stenting as an introduction to the practice of interventional cardiology. The various techniques of PCI can be placed into niche applications for specific devices (Table 1-1).

Overview of the Basic PCI Method

PCI was derived from the basic procedures used for diagnostic cardiac catheterization and coronary angiography. PCI begins with vascular access by means of the same techniques for the insertion of an arterial sheath through the arm (radial artery) or leg with Seldinger's method (needle and guidewire). In contrast to diagnostic catheters, specialized large-lumen "guiding" catheters engage the coronary artery in the same manner but are designed to provide stabilization or backup for delivery of PCI equipment.

Steps in the PCI Procedure

The steps in the PCI procedure are shown in Figure 1-1. First, a guiding catheter is seated in the coronary ostium. A thin, steerable guidewire is introduced into the guide catheter and then into the coronary artery and positioned across the stenosis into the distal aspect of the artery.

Table 1-1

Niche Applications of PCI Devices

Special Lesion Type	Stent	Cutting Bal	Rotablator	Thrombus Aspiration
Type A	+++	+	±	—
Complex	++	++	+	—
Ostial	++	++	+	—
Diffuse	+	+	++	—
Total occlusion	++	+	—	—
Calcified bifurcation	±	++	+++	—
SVG focal	+++	±	±	—
SVG diffuse	+	±	—	—
SVG thrombotic	±	—	—	++
Complication	+++	—	±	±
Acute occlusion	±	—	—	±
Thrombosis	+	—	—	+++
Perforation	@	—	—	—

+++highly applicable; ++somewhat helpful; +applicable; ±marginal depending on status; —not applicable; @covered stent
PCI, percutaneous coronary intervention; SVG, saphenous vein graft.

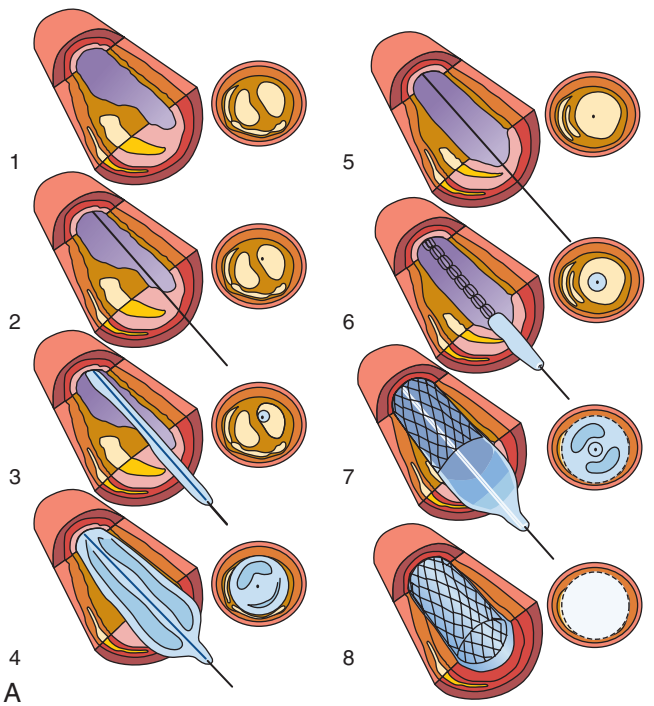

Figure 1-1A,B **A,** How angioplasty and stenting works. *1*, The artery is filled with atherosclerotic material, compromising the lumen. A cross-section of the artery is shown on the right side. *2*, A guidewire is positioned past the stenosis through the lumen. *3*, A balloon catheter is advanced over the guidewire. *4*, The balloon is inflated. *5*, The balloon is deflated and withdrawn. *6*, The balloon catheter is exchanged for a stent (on a balloon). *7*, The stent is expanded. *8*, The expanded stent remains in place after the deflated balloon is withdrawn.

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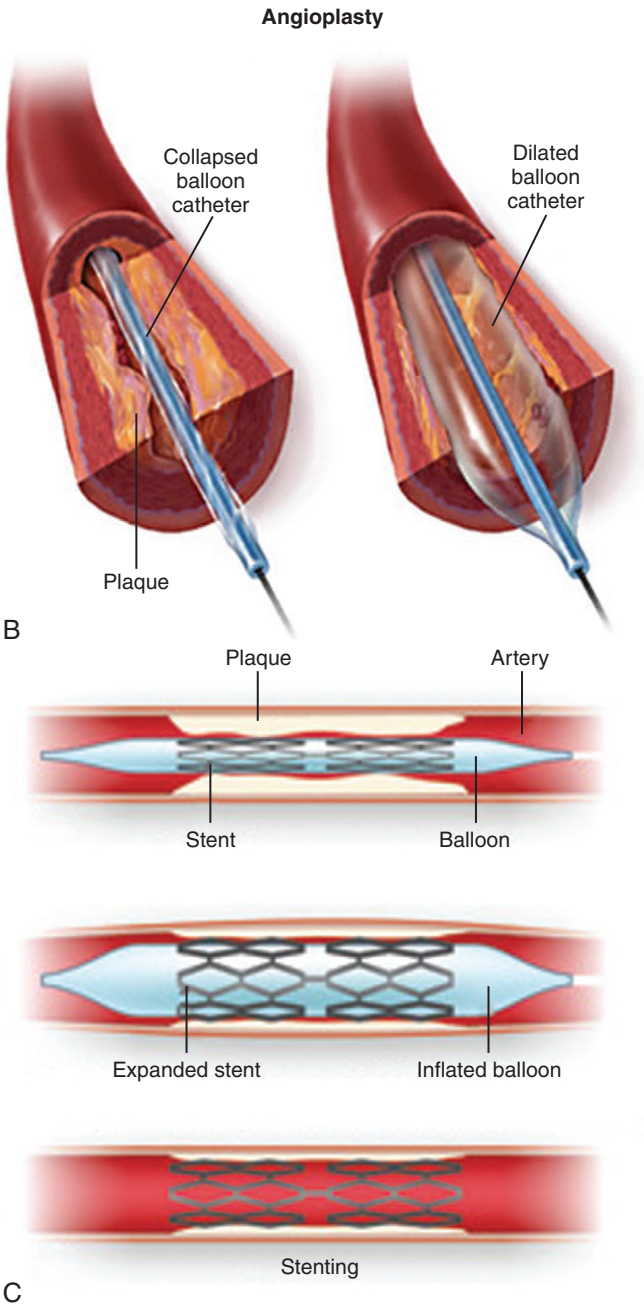

Figure 1-1, cont'd **B**, Drawing of angioplasty balloon before (*left*) and during inflation (*right*). **C**, Diagrams of stent expansion. *Top*, Crimped stent delivered to lesion; *middle*, balloon-expanded stent implanted in lesion; *bottom*, after balloon deflation and withdrawal, stent is seen implanted in artery wall with widely patent lumen.

A very small angioplasty balloon catheter is placed on the guidewire, inserted through the guiding catheter, and is positioned in the artery across the stenotic area by tracking it over the guidewire. Once correctly placed within the narrowed area to be treated, the balloon on the PCI catheter is inflated several times for brief periods (10–60 seconds). The inflation and deflation of the balloon expand the stenosis and restore blood flow to an area of the heart previously deprived by the stenosed artery.

Table 1-2

Definitions of PCI Success

Percutaneous coronary intervention (PCI) success may be defined by angiographic, procedural, and clinical criteria.

Angiographic Success

- Angiographic success in a stented artery is a minimum stenosis diameter reduction to <20%.

Procedural Success

- A successful PCI should achieve angiographic success without in-hospital major clinical complications (e.g., death, myocardial infarction [MI], emergency coronary artery bypass surgery) during hospitalization. MI is often defined as the development of Q waves in addition to elevation of troponins three times the upper limit of the laboratory's normal value. Cardiac troponin T and I as measurements of myocardial necrosis are more sensitive and specific than CK-MB. Enzyme elevation in the absence of new Q waves is counted as MI, peri-procedural. There is no consensus on what level of troponin alone is clinically important enough to change major management following the interventional procedure.

Clinical Success

- A clinically successful PCI is an anatomical and procedural success with relief of signs and/or symptoms of myocardial ischemia after recovery from the procedure. The long-term clinical success requires that the patient have persistent relief of signs and symptoms of myocardial ischemia for more than 6 months. Restenosis is the principal cause of lack of long-term clinical success when short-term clinical success has been achieved.

After the balloon expands the stenotic area, the balloon catheter is exchanged for a stent-carrying balloon catheter. The stent is a metal scaffold, mounted in a compressed form on another balloon catheter, and delivered in the same manner as the first balloon catheter was delivered. The stent is deployed by inflation of the balloon as was performed for dilating the stenosis. The stent should be carefully positioned. It is inflated with the same pressure gauge syringe (8–16 atm pressure) for 10 to 20 seconds. A full opening of the stent with complete strut apposition to the vessel wall is important for good short- and long-term results.

After the stent struts have been expanded and implanted into the artery wall, the balloon is deflated, and the delivery catheter and guidewire are removed. Intravascular ultrasound (IVUS) imaging is often used to confirm appropriate vessel-stent matching and full stent strut apposition (contact without space against the wall). After IVUS and final angiography have been performed, the guide catheter is removed. The femoral or radial arterial sheath is removed, and hemostasis is obtained in the laboratory. The patient is then transferred to a recovery area and then to the patient's room. If no complications occur, the patient is discharged the next morning. The patient usually returns to work shortly (<2 days) thereafter. The definitions of a successful PCI procedure are summarized in Table 1-2.

Mechanisms of Angioplasty and Stenting

1. Disruption of plaque and the arterial wall

   The inflated balloon exerts pressure against the plaque and the arterial wall, causing fracturing and splitting. Concentric (round or circumferential) lesions fracture and split at the thinnest and weakest points. Eccentric lesions split at the junction of the plaque and the normal arterial wall. Dissection or separation of the plaque from the vessel wall releases the restraining effect caused by the lesion and results in a larger lumen. This is the major mechanism of balloon angioplasty.

2. Loss of elastic recoil

   Balloon dilatation causes stretching and thinning of the medial wall. Stretching causes the vessel wall to temporarily lose its elastic (recoil) properties. The degree of elastic recoil is affected by the balloon/artery size ratio. Almost all vessels have some elastic recoil. The major initial benefit of stenting is the elimination of elastic recoil, maintaining a large lumen over time.

3. Redistribution and compression of plaque components

   During angioplasty, balloon pressure causes denudation of the vessel wall lining (endothelial) cells and the extrusion or pushing out of plaque components. There may be some molding and extrusion longitudinally of the softer lipid material, but this effect accounts for a very small part of the overall effect.

Indications for PCI

Guidelines and recommendations for the performance of PCI are provided in extensive detail in the updated (2009) PCI guidelines written by the American Heart Association (AHA), the American College of Cardiology (ACC), and the Society for Cardiovascular Angiography and Interventions (SCAI). Specific anatomical and clinical features for each patient should be considered for the likelihood of success, failure, and risk of complications with vessel closure, morbidity, mortality, and restenosis. Restenosis and incomplete revascularization must also be weighed against the outcome anticipated for coronary artery bypass graft (CABG) surgery.

In general, PCI is indicted for patients with the following:

- Stable angina pectoris unrelieved by optimal medical therapy with objective evidence of ischemia (abnormal stress test or abnormal stress thallium) and a coronary lesion in a vessel supplying a large area of myocardium
- Unstable angina
- Acute myocardial infarction
- Angina pectoris after CABG surgery
- Symptomatic restenosis after previous PCI
- Relative contraindications to PCI
- Unsuitable coronary anatomy (e.g., multiple severe complex lesions or diffuse distal disease)
- High-risk coronary anatomy in which closure of vessel would result in death

Contraindications to PCI

- Bleeding diathesis (low platelet count, peptic ulcer disease, coagulopathy, etc.)
- Patient noncompliance with procedure and post-PCI instructions and inability to take dual antiplatelet therapy (acetylsalicylic acid [ASA], Plavix, etc.)
- Multiple PCI restenoses

Note: Some patients with contraindications may have PCI as their only alternative to revascularization.

Complications of PCI (see also Chapter 4)

For most elective procedures:

1. Death (0.1%)
2. Myocardial infarction (1%–3%)
3. Emergency CABG surgery (0.5%–2%)

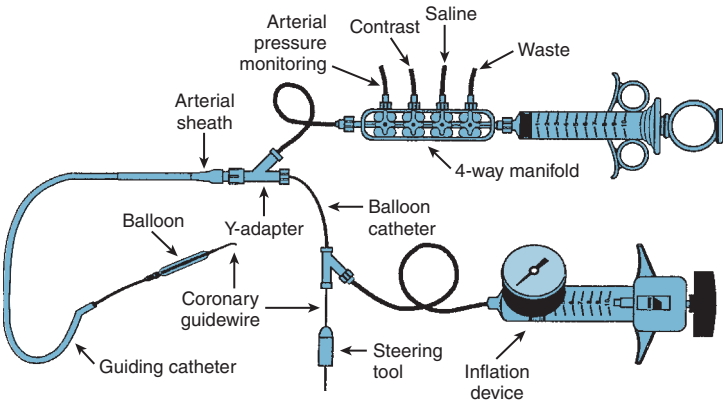

Figure 1-2 Diagram of components of percutaneous coronary intervention equipment. (Adapted from Safian RD, Freed MS, eds. *The manual of interventional cardiology,* 3rd ed. Birmingham, MI: Physicians' Press, 2001.)

All complications that can occur during diagnostic cardiac catheterizations can also occur during PCI: access-site bleeding, especially with larger sheaths and prolonged anticoagulation (1:250 patients); contrast-medium reactions; cerebrovascular accident; myocardial infarction; and vascular injury (e.g., pseudoaneurysm of femoral artery)

- Restenosis (see Chapter 7).

Note: Restenosis at the site of PCI occurs in approximately 10% of patients and may lead to recurrence of anginal symptoms. Typically, restenosis occurs most frequently within the initial 12 months after PCI. This biologic effect is not considered a complication but rather a clinical part of angioplasty.

PCI Equipment

The most commonly used PCI equipment consists of four basic elements: a guiding catheter, a balloon catheter, a coronary guidewire, and a stent (Fig. 1-2 and Table 1-3 list approximate costs of such equipment).

There are three major operational challenges with PCI: (1) placing the guide catheter in a stable position, (2) negotiating tortuous vessel segments with the guidewire, and (3) delivering the stent through

Table 1-3

Approximate Costs of Coronary Angioplasty Equipment

Equipment	Cost ($US)
Balloon dilatation catheter	300 OTW/250 Rx
Guiding catheter	65
Guidewire	80
Exchange guidewire (300 cm)	120
Indeflator	55
Y connector	31
Sheath introducer	8
Torque tool	18
Nonballoon devices	
Stent (noncoated)	1300
Stent (drug-eluting)	2300
Rotablator	1330
IABP	840

IABP, intra-aortic balloon pump; OTW, over-the-wire; Rx, rapid exchange.

tortuous segments. To complete the PCI, the operator must control the three principal movable components (guide catheter, balloon catheter, and guidewire) simultaneously.

Guiding Catheter

A special large-lumen catheter is used to deliver the coronary balloon catheter and other interventional devices to the vessel that contains the lesion to be dilated. The features of the guide catheter noted in Figure 1-3 differentiate it from diagnostic catheters.

Functions

A guiding catheter serves three major functions during angioplasty:

1. Balloon/stent catheter delivery and guidance
2. Backup support for balloon/stent advancement
3. Pressure monitoring and contrast injections

Balloon Catheter Delivery and Guidance. To deliver the balloon catheter to the coronary artery over the guidewire, the guiding catheter should be seated with the tip parallel to the long axis of the artery (coaxial) at its origin. Coaxial alignment permits safer transmission of force needed to advance the balloon across a stenosis. This act may require guide catheter repositioning or occasionally deep seating into the artery.

Adequate contrast injection through the guide catheter is critical to position the balloon/stent and depends on the size of the guide catheter lumen with the angioplasty device in place. A guiding catheter must be large enough to permit adequate contrast administration with the PCI catheter in place to opacify the target vessel and visualize the lesion. Large, nonballoon PCI devices (Rotablator, thrombus aspiration catheters, etc.) in small guide catheters may not allow adequate vessel visualization during angiography. This problem has been overcome with large-lumen, small guide catheters and contrast media power injectors in some laboratories.

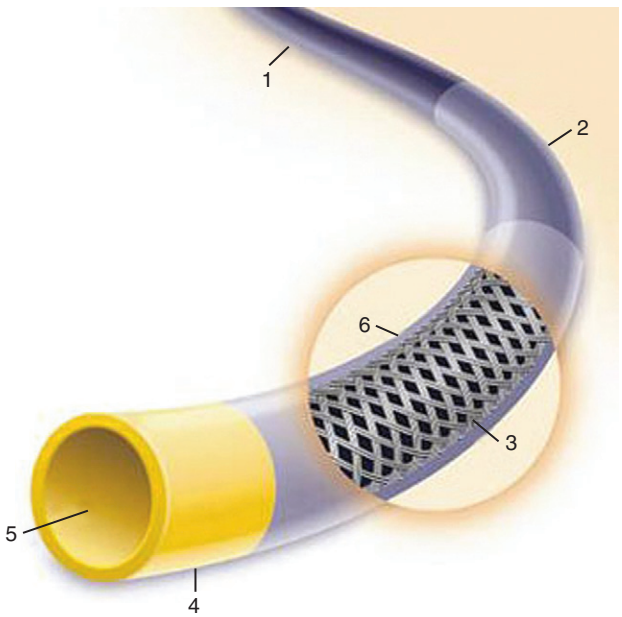

Figure 1-3 Illustration of a guiding catheter shows (*1*) stiffer body, (*2*) variable softer primary curve, (*3*) wire braiding, (*4*) atraumatic tip, (*5*) large lumen (optional radiopaque marker), (*6*) lubrious coating. (Courtesy Boston Scientific, Inc.)

Operators should select a guide catheter with a lumen diameter large enough to allow enough contrast flow around the PCI device to permit clear angiographic imaging of the lesion. As balloon and PCI catheters have become smaller, the size of internal diameter of the guiding catheter has become less important for achieving adequate visualization. A large guide catheter lumen, however, is critical to facilitate easy passage of double balloon/stent systems for complex or bifurcation lesions.

Backup Support for Balloon Catheter and Stent Advancement. Support or "backup" for stent advancement is achieved after seating (cannulation) the guide catheter in the coronary ostium. The guiding catheter provides a platform from which one can push the stent over the guidewire through the artery and across the stenosis.

Inadequate backup support will result in failure to cross a lesion and an unsuccessful procedure. Backup support requires a combination of correct coaxial (in-line with the artery ostium) alignment and the ability to provide carefully controlled advancement (deep seating) of the guiding catheter into the coronary ostium.

The improved quality and size of currently used stents have reduced the need for robust backup support in most situations. For more complex and technically difficult lesions, the choice of an appropriate guiding catheter for extra support and lesion visualization remains essential (see Chapter 3). When there is insufficient backup in crossing a very tight stenosis, the guiding catheter will disengage from the coronary ostium and back out into the aortic root. When pressure is applied to the stent catheter during attempts to cross the lesion, repositioning the guide catheter in a stepwise fashion while the stent is advanced may overcome this loss of support. However, aggressive intubation of the coronary ostium may damage the vessel, stopping the procedure prematurely, or may require additional stenting for an ostial dissection.

Deep seating of the guide catheter is achieved by manipulating the guide catheter over the balloon catheter shaft, past the aortocoronary ostium, and farther into the vessel. This maneuver is used to obtain increased backup support for crossing difficult lesions and is typically a last resort maneuver because of the increased chance of guide catheter–induced dissection of the left main or proximal vessel.

Pressure Monitoring. The guiding catheter measures aortic pressure during the case. Pressure wave damping may occur during coronary artery engagement if there is plaque in the coronary ostium. In addition, pressure measured through the guide catheter proximal to the stenotic area can be compared with distal transstenotic pressure measured with a pressure sensor guidewire for assessment of hemodynamic lesion significance before and after PCI. Some catheters have side holes near the tip to permit perfusion into the artery when the catheter is deeply seated and obstructing flow.

Characteristics

Compared with the diagnostic catheters, the guiding catheters have thinner walls, larger lumens, and stiffer shafts (Fig. 1-3). A large catheter lumen is achieved at the expense of catheter wall thickness and thus may result in decreased catheter wall strength, less torque control, or catheter kinking. The guiding catheters are generally stiffer to provide backup support during the PCI catheter advancement into the coronary artery and, therefore, respond differently to manipulation than diagnostic catheters. The guiding catheter tip is not tapered. Pressure-wave damping upon engaging the coronary ostium is seen more often than with similar-sized diagnostic angiographic catheters. Some guide catheters have relatively shorter and more flexible tips to decrease catheter-induced trauma.

Guiding catheters with small side holes near the tip permit blood to enter the coronary artery when the ostium is blocked by the guide catheter. Side holes are used when the guide catheter either partially or

totally occludes blood flow into the coronary artery. The guide catheter coronary occlusion is noted by the change in the arterial pressure waveform to one of "damping." Catheter side holes reduce ischemia when the guiding catheter is seated in a small artery. However, side holes may lead to inadequate artery visualization from loss of contrast media exiting the catheter before entering the artery. Although side holes may provide reliable aortic pressure, coronary flow can still be compromised during the angioplasty procedure. The guide catheter and side holes act as a "second stenosis" at the coronary ostium.

Small shaft diameter guide catheters (e.g., 6F) are the most frequently used size of guiding catheter. The use of small-diameter guide catheters results in fewer femoral vascular complications and allows earlier ambulation of patients. Small-size (<5F) guide catheters do not allow for the use of some stents. Guide catheters sized 7F or 8F are used for complex procedures involving larger PCI devices or two stents for treatment of bifurcation lesions. Use of 6F (or, in some patients, 7F) guide catheters from the radial artery approach may become the favored access because of the markedly reduced vascular complications associated with radial PCI procedures.

Balloon Dilatation Catheter Systems

Types

There are three types of PCI balloon catheters (Fig. 1-4):

1. Over-the-wire (OTW)
2. Monorail
3. Fixed-wire

The OTW and monorail balloons, but not fixed-wire balloons, are also used to deliver stents that are mounted by the manufacturer on a specific balloon. The advantages and limitations are summarized in Table 1-4.

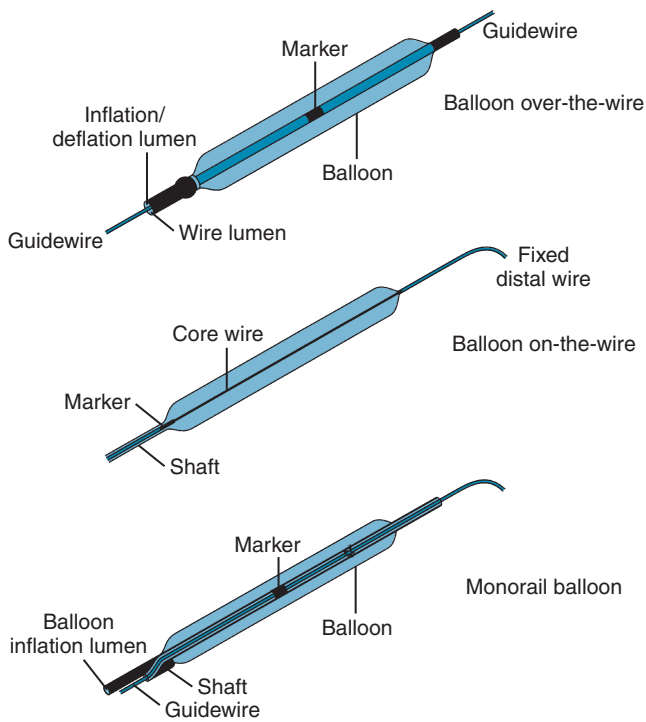

Figure 1-4 Three common types of coronary balloon angioplasty catheter design. (Adapted from Freed MS, Grines C, eds. *New manual of interventional cardiology.* Birmingham, MI: Physicians' Press, 1992: 29.)

Table 1-4

Advantages and Limitations of Angioplasty Balloon Types

Advantages	Limitations
Over the wire	
Distal wire position Distal port available for pressure measurement or contrast media injection Accepts multiple guidewires	Two experienced personnel required Larger profile
Rapid exchange	
Distal wire position Enhanced visualization Low-profile balloons Single-operator system	Exchanging balloons at hemostatic valve may be technically demanding
Fixed wire	
Enhanced visualization Single-operator system Use with small guiding catheters system Low-profile balloons	Lack of through lumen Inability to recross lesion without removing

Modified from Kern MJ, ed. *The cardiac catheterization handbook,* 2nd ed. St Louis, MO: Mosby, 1995.

OTW Angioplasty Balloon Catheters. Historically, the OTW balloon was the first introduced and has remained popular in a few centers. A standard OTW angioplasty balloon catheter has a central lumen throughout the length of the catheter for the guidewire and another, separate lumen for balloon inflation (Fig. 1-5). These balloons are approximately 145 to 155 cm long and are designed to be used with guidewires of various dimensions (0.010–0.014 inches). The major OTW advantage is the ability to maintain distal artery access with the balloon beyond the lesion while one guidewire is exchanged for another. The OTW system tracks very well because the whole balloon length has a wire lumen. It permits long guidewire exchanges, and because of the through lumen, it allows for delivery contrast and drugs distally in an artery. To exchange PCI catheters, the balloon is advanced over the wire to a distal position. The standard short (145-cm) wire is then removed from the balloon. A longer guidewire (300 cm) is then inserted to maintain distal wire position while the balloon catheter is completely withdrawn over the guidewire and another balloon catheter is introduced over the same long guidewire for additional dilatations. OTW catheters can accept multiple guidewires, which allows for exchanging additional devices that may require stronger, stiffer, or specialized guidewires.

Limitations of OTW balloon catheters include a slightly larger diameter than the rapid-exchange (monorail) and fixed-wire catheters and the need for additional personnel to help with long guidewire catheter exchanges.

Rapid-Exchange (Monorail) Balloon Catheters. "Rapid-exchange" or monorail catheters were developed to permit the exchange of angioplasty balloon catheters by a single operator. Rapid-exchange catheters

Figure 1-5 Typical over-the-wire balloon (OTW) catheter. Quantum Maverick OTW. OTW "Quantum" Maverick Balloon. (Courtesy SciMed-Boston Scientific, Boston, MA.)

have only a short (30–40 cm) length of the catheter shaft containing two lumens (Fig. 1-6). One lumen, in the distal 30-cm portion of the catheter shaft, houses the guidewire. The remaining lumen runs the entire length of the catheter and is used for balloon inflation. Because only a limited portion of the balloon requires dual lumens, rapid-exchange catheters are smaller in diameter than are OTW balloon catheters.

Rapid-exchange balloon catheters address certain inherent limitations of OTW catheters. First, OTW balloon exchanges require a long (or extension) guidewire, which is unnecessary for the rapid-exchange balloon. Second, a single operator can use rapid-exchange balloon catheters without the aid of other assistants to maintain distal guidewire position.

Limitations of monorail catheters include the need for more care in manipulation of the guidewire, balloon catheter, and guiding catheter. Excessive blood loss at the rotating hemostatic valve during removal of the balloon catheter (back-out) maneuver may occur, but valved Y connectors have reduced this problem. More caution when moving the balloon is needed. If the monorail balloon is advanced beyond the distal end of the guidewire, the wire may come out of its short lumen, necessitating catheter withdrawal and reassembly of the balloon and guidewire. This is especially true when catheters with relatively short "rail" segments are used. If the balloon catheter requires force to advance beyond a lesion, a loop of guidewire may sometimes form outside the guide catheter in the aorta. This loop is nearly invisible but should be considered if the operator advances the catheter without seeing motion at the balloon tip.

Fixed-Wire Angioplasty Balloon Catheters. The fixed-wire catheter was the first catheter designed by Grüntzig. It has the balloon mounted on a central hollow wire with a distal flexible steering tip. The proximal end of the catheter consists of a single port connected to a thin metal tube (hypotube) used to inflate the balloon. A core wire extends from the hypotube to the end of the distal steerable tip. This assembly is coated with a thin plastic shaft that enhances flexibility. Fixed-wire balloons have only one enclosed lumen for balloon inflation.

In the balloon on-the-wire catheter system, the guidewire cannot be advanced independently of the balloon and the balloon cannot be exchanged without removing the entire system. Because the wire is attached to the distal end of the balloon, there is no central balloon lumen, resulting in a lower total profile than an OTW or monorail system. Its principal advantages relate to its low profile, enabling passage through very tight stenoses, and good contrast visualization of the lesion being dilated around the balloon catheter.

The small shaft size provides excellent coronary visualization. Because the balloon is mounted on the distal guidewire, the device was designed to be used by a single operator. Fixed-wire balloon catheters are particularly useful for distal lesions, subtotal stenoses, and lesions located in tortuous vasculature.

The limitations of fixed-wire catheters include lack of stent capability and the loss of the inherent safety advantage of OTW and rapid-exchange systems because there is no movable wire available to exchange for a stent if a dissection occurs. To exchange this catheter for another, the operator either must remove the entire system and recross the stenosis or dissection anew or, while leaving the fixed-wire balloon in place, advance another guidewire next to it to secure distal position and proceed with

Figure 1-6 Typical rapid-exchange or monorail balloon catheter. Maverick 2 Monorail. Monorail balloon catheter. (Courtesy SciMed-Boston Scientific, Boston, MA.)

stenting in the usual fashion. A dissected lesion may not permit recrossing with a guidewire or advancing another balloon catheter.

Characteristics

The plastic material of the balloon determines its compliance (defined as the amount of expansion or diameter size for given amount of pressure) and strength. Compliance is the main differentiating feature among balloon catheters. Inflation of a compliant balloon above factory-determined average mean pressure (also called nominal or a set pressure for a known balloon size) will lead to further expansion of the balloon size approximately 10% to 20% over the predicted diameter. Noncompliant balloons, on the other hand, remain very close to their rated diameter even when inflated several atmospheres above nominal pressure. The advantages and disadvantages of balloon materials remain controversial. A compliant balloon may produce oversizing, particularly on second and third high-pressure inflations, resulting in dissections. After most stents are deployed, post-deployment high-pressure inflations are performed with low-compliance or noncompliant balloons to implant the stent struts into the vessel wall. Most balloons are also coated with low-friction surface polymers to facilitate lesion crossing.

The mechanical aspects of balloon inflations apply the following fundamental principles:

- Overinflation at balloon ends. According to Laplace's law, wall stress increases with radius. At a given pressure, a larger balloon undergoes more wall stress than a smaller balloon, promoting balloon rupture. The arterial segment next to the lesion has a larger luminal radius than the lesion. Thus artery sites adjacent to the lesion may be traumatized. At high pressures, balloons weaken over time. The balloon burst pressure may be decreased during subsequent inflations of the same balloon. When inflating a balloon above the rated burst pressure, operators should consider limiting the number and duration of inflations.
- Balloon diameters always increase with increasing pressure. Even noncompliant balloons will grow in diameter (usually by <10% over nominal) with high pressure. Compliant balloons may increase by more than 20%. The balloon diameter–pressure relation is usually linear, reflecting the compliance characteristics. Figure 1-7 shows the balloon during inflation and a graph for pressure versus diameter.
- Balloons do not return to their original dimensions after deflation. At any given pressure, the balloon diameter during a subsequent inflation will be larger than during the first inflation. When dilating two lesions with a compliant balloon, cardiologists should consider approaching the narrower lesion first.

Selection

The selection of a balloon catheter is highly subjective and less critical in the current era of stents. The balloon size is selected to achieve a 1:1 size match with the vessel. Balloon-to-artery ratios of more than 1.2:1 are associated with increased complications. Longer balloons (30–40 mm) are useful for dilating long and diffuse narrowings. Short (10–15 mm) balloons are used for stent re-expansion to avoid stretching the vessel wall outside the stent.

The balloon size is determined with the distal arterial reference segment diameter as gauged by the size of the guiding catheter (e.g., 7F guide = 2.31 mm, 8F = 2.64 mm, 9F = 2.97 mm, 11F = 3.63 mm). Visual estimation of artery diameter is less accurate than quantitative angiographic and IVUS imaging approaches, but it is the method used by most interventionalists. From IVUS studies, most stents selected by visual sizing are 0.5 mm smaller than true vessel dimensions.

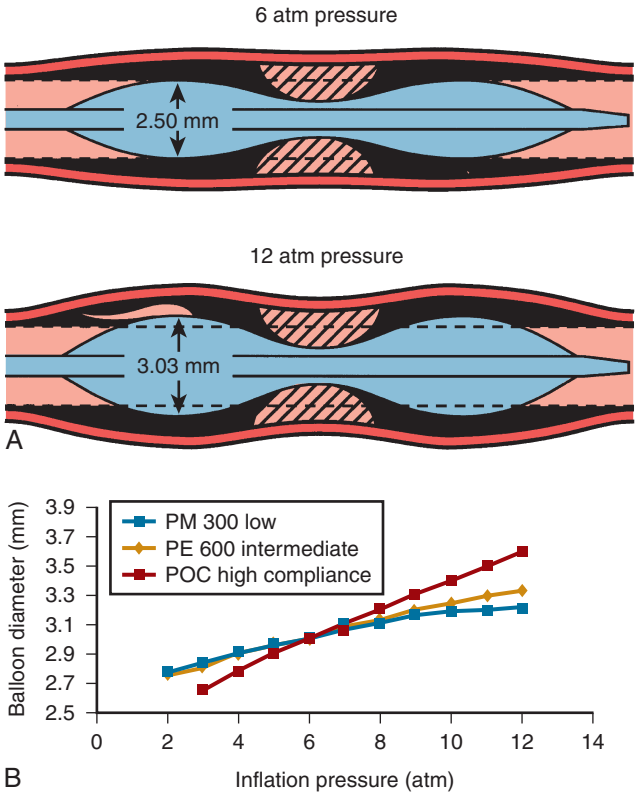

Figure 1-7 **A,** Balloon size changes proposed to occur during increasing inflation pressure when compliant balloon material is used. (From *Clinical issues in angioplasty balloon material: a review of the literature regarding polyethylene terephthalate (PET),* USCI Division of C.R. Bard, Inc.) **B,** Diameter–pressure relationships of three balloon materials. All three balloons have a nominal size of 3.0 mm at 6 atm. (From Raymenants E, Bhandari S, Desmet W, *et al.* The impact of balloon material and lesion characteristics on the incidence of angiographic and clinical complications of coronary angioplasty. *Cathet Cardiovasc Diagn* 1994;32:303–309.)

Important technical considerations for selecting PCI systems include catheter profile, trackability, pushability, and ease of exchange. The size of a deflated catheter has been emphasized in catheter selection. Stent profiles are now very small (profile size of 0.035 and 0.033 inches). There appears to be no practical difference among equipment sizes. *Stent profile* is not the only factor in facilitating a stent to cross a lesion.

Trackability is the ability to advance the stent through the vessel to reach the lesion and is a function of friction related to both the guidewire and the delivery catheter. Although stent systems are marketed based on their ability to track and conform to the vessel, trackability is difficult to measure in an objective manner. For a balloon to track, it must be able to transfer force through the shaft of the balloon catheter (a feature referred to as *pushability*). There may be little difference in the pushability of the majority of the available systems. Resistance to balloon catheter forward motion may occur as a result of guidewire–balloon friction, balloon–guide catheter friction, or balloon–artery friction.

Ease of device exchange is a strong consideration. The monorail catheter system is the quickest and easiest to exchange. The standard OTW balloon requires the placement of a long guidewire, or the attachment of an exchange system to the end of the guidewire, or a guidewire trapping system. A rapid-exchange system reduces x-ray exposure time because fluoroscopy is not required if the wire is fixed during catheter removal.

Balloon Inflation Strategies

Stenosis resolution occurs when the balloon pressure eliminates the balloon indentation caused by the stenosis (called the *waist*). Unstable or thrombotic lesions are generally soft and, compared with chronic, stable lesions, are associated with a lower balloon inflation pressure. Most coronary lesions respond to inflation pressures of less than 10 atm. Calcific or fibrotic lesions may require higher inflation pressure (12-17 atm) to eliminate the balloon waist. Because stenting after PTCA is now routine, issues regarding optimal balloon inflation strategies are relatively unimportant. Balloon inflations are generally brief (<60 seconds). The balloon should be inflated long enough to permit elastic tissue to relax or stretch. However, in lesions not receiving a stent, high pressures in compliant balloons may produce an oversized balloon-to-artery ratio, associated with an increased incidence of dissection and complications. Low-pressure inflations may reduce complications. Most procedures start with low pressures, but operators often feel compelled to use higher pressures to achieve satisfactory angiographic results.

PCI Guidewires

PCI guidewires are small-caliber (0.010–0.018 inch) steerable wires, advanced into the coronary artery or its branches beyond the lesion to be dilated. A J-tip of varying degree, usually shaped by the operator, allows steering across side branches through tortuous artery curves.

Guidewires are made with an inner core wire and an outer spring tip. The shorter the distance is between the end of the central core and the spring tip, the stiffer and more maneuverable the wire will be. Differences in core construction affect guidewire handling. When a guidewire is selected, important considerations include diameter, coating, torque control, flexibility, malleability, radiopacity, and trackability. The diameter for the most commonly used coronary guidewire is 0.014 inch, although diameters from 0.010 to 0.018 inch are available. Large-diameter guidewires have better torque and backup support, while small-diameter wires are more maneuverable. Custom tip shaping will help steer the guidewire.

Characteristics

The selection and placement of a guidewire distal to the stenosis depend on the clinical situation and the operator's experience and skills. The following terms are applied to angioplasty guidewires.

Stiffness of the guidewire determines specific performance. Soft wires are safer and easier to advance through tortuous artery branches. Stiff wires torque better and are often useful for crossing difficult or total chronic occlusions. Extra-stiff guidewires provide better support for intracoronary stent placement in highly tortuous arteries.

Steerability is defined as the ability to turn and advance the wire through tortuous segments and side branches by rotation of the wire. Steerability is an important feature of a guidewire.

Flexibility is determined by the distance from the end of the central core to the distal spring tip of the wire and is important in avoiding vascular trauma when crossing and recrossing lesions.

Malleability is the ability to shape the spring tip and maintain a desired tip shape. Repeated attempts with different wire tip configurations may be required to cross distal stenoses. The manufacturer preforms some guidewire tip shapes. Guidewire tip shaping is accomplished by bending the wire between the thumb and index finger, rolling the guidewire tip over a needle, or bending the wire tip at the end of an introducer tool. In general, the length of the distal bend in a large vessel should approximate half the usual diameter of the vessel (about 2 mm). A larger bend may be needed to reach a takeoff. When the wire is steered into an abruptly angled branch, a double 45-degree bend is often helpful (Table 1-5).

Table 1-5

Guidewire Tip Curves That Can Facilitate Difficult Anatomic Problems During PTCA

No. of Angulations	Configuration of the Tip	Location of the Lesion	Characteristics of the Coronary Anatomy	Rationale
Single 	Angle is mild or moderate. RD is smaller than the diameters of the LMCA (tip is similar to commercial J curves).	Proximal RCA, Cx, or LAD.	Vessels are straight, takeoff of the branches is shallow, difference in diameter of the LMCA and a narrowed branch is not marked.	Lesions are easily reached with only minimal manipulations.
Double 	Proximal and distal angles are mild or moderate. Total RD approximates the diameter of the LMCA. Distal RD is similar to the diameter of the narrowed branch.	Proximal or mid RCA, LAD, and Cx.	Vessels are mildly tortuous; branches take off with mild to moderate angles; difference between the diameter of the LMCA and diameter of the narrowed branch is not marked.	Proximal angle adds RD to improve entry into the branches of the large proximal vessels; distal angulation allows easier manipulations in the smaller narrowed distal branches.
	Shallow distal angle. Proximal angle is steeper; total RD is unchanged from the above.	Proximal, mid, or distal RCA, Cx, and LAD.	Tight stenoses; trifurcation or two opposing branches originating from the same segment (e.g., septal and diagonal branches of the LAD) lesions more easily.	The shallow distal angle with small RD has tendency to remain centrally located, avoid side branches and traverse.
	Steep distal angle, with short arm and small reaching distance. Proximal RD is unchanged.	Distally, primarily in the obtuse marginal or diagonal arteries.	Vessels have sharp bends and kinks; narrowed branches have sharp angles; the difference in diameter of the LMCA and the narrowed branch is very marked (e.g., the diagonal branch taking off sharply and subsequently curving resembling a small letter “h”).	Steep distal angle is required to enter the side branches at the proper angle and improves advancement of the wire around a steep curve.

Continued

Table 1-5—cont'd

Guidewire Tip Curves That Can Facilitate Difficult Anatomic Problems During PTCA—cont'd

No. of Angulations	Configuration of the Tip	Location of the Lesion	Characteristics of the Coronary Anatomy	Rationale
	Long proximal arm required.		Use if the LMCA has large diameter and the LAD or Cx has a sharper angle of origin (more common with Cx).	Longer proximal arm adds RD, thus improving entry into the large proximal vessels (LAD or Cx).
	Very long proximal arm. Distal arm is shallow.	Severe stenosis of the proximal Cx (rarely LAD).	The vessel has a takeoff of 90 degrees or more from the LMCA with subsequent posterior curve; the lesion is severe, located immediately distal to the bend.	The very long proximal arm permits the distal angle to function "independently," facilitating the vertical entry into the lesion.
	Both arms are long. Total RD is large but usually smaller than the diameter of the large vessels.		Large vessels—e.g., severely arteriosclerotic abdominal aorta or iliac arteries.	Large RD is required to enter eccentrically located lumen, often from the aneurysmal areas.
Triple or multiple 	Angles are moderate. Distal arm is shorter; total RD is large.	Mid or distal in all major vessels.	The difference in diameter of the LMCA and a narrowed branch is very marked; the LAD or Cx originate steeply.	Transition from the long to short arm and advancement of the wire around a sharp angle of the proximal vessel are smoother.

From Voda J. Angled tip of the steerable guidewire and its usefulness in percutaneous transluminal PTCA. *Cathet Cardiovasc Diagn* 1987;13:204–210.
Cx, cirucumflex; LAD, left anterior descending; LMCA, left main coronary artery; PTCA, percutaneous transluminal coronary angioplasty; RCA, right coronary artery; RD, reaching distance.

Radiopacity, Marker Bands, and Special Coatings

Visualization of the guidewire is provided by a radiopaque coating usually applied only to the distal part of the wire. The limited radiopaque segment permits lesion visualization without obscuring useful angiographic detail, such as small dissections. Calibrated radiopaque marker bands are used to gauge lesion length. Angioplasty balloons usually have two markers, one at each end of the balloon. Small balloons, for example, 1.5 mm diameter, have one central marker. These markers may be confused for markers on some guidewires.

Various wire coatings increase ease of wire movement within the balloon catheter and artery. Some coated plastic tipped wires, especially with hydrophilic tips, have a higher likelihood to perforate.

Exchange and Extension Guidewires

An exchange guidewire is similar to those mentioned previously, except that its length is 280 to 300 cm. This long wire replaces the initial 140-cm wire when an exchange of the balloon catheter is necessary (e.g., upsizing balloon or insertion of stent). Alternatively, a 120- to 145-cm extension wire can be connected to a companion 145-cm guidewire, thus creating a long exchange guidewire to allow balloon catheter exchanges.

Accessory Equipment (Fig. 1-8)

Adjustable Hemostasis and Rotating Y-Connector Valve

The Y connector is attached to the guide catheter to permit introduction of a PCI catheter into the guide while allowing contrast injection through the guide catheter. The end of the Y connector has a rotating hub and a valve. The valve minimizes back bleeding from the guide catheter while the PCI catheter is inserted or removed. The Y connector also permits pressure monitoring through the guiding catheter, regardless of PCI catheter position.

Balloon Inflation Devices

A disposable syringe device is used to inflate the balloon on the PCI catheter. A pressure gauge display indicates the precise inflation pressure in atmospheres (atm or torr) or pounds per square inch (psi).

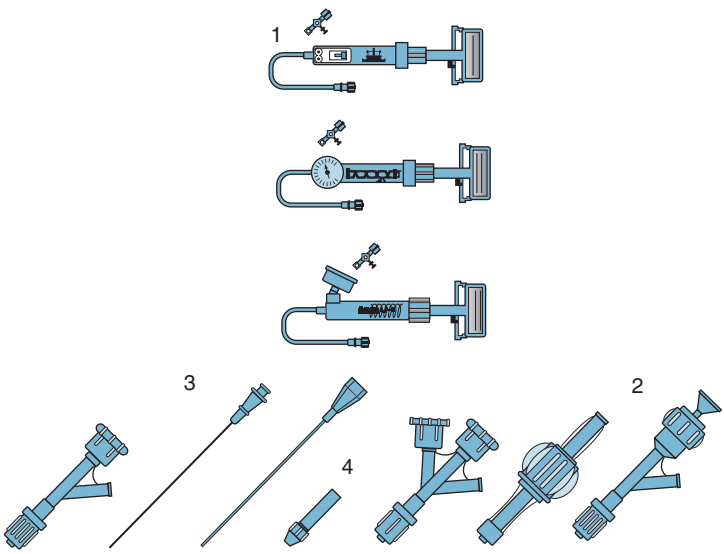

Figure 1-8 Ancillary equipment, Y connectors, inflation devices. (1) Indeflators, (2) Y connectors, (3) needle wire introducers, (4) torque tool. *Courtesy of Merit Medical Inc.*

Typically, the balloon is inflated with sufficient pressure (4–12 atm) to fully expand the stenosis indentation (*dumbbell* or *waist*) of the partially inflated balloon. Occasionally, some calcified or highly fibrotic lesions require very high inflation pressures (>14 atm) to expand and eliminate the "dumbbell" appearance of the balloon. Overinflation of the balloon increases the risk of artery dissection.

Guidewire Torque (Tool) Device and Guidewire Introducer

A small, cylindrical pin vise clamp slides over the end of a guidewire and permits the operator to perform fine steering manipulations of the guidewire. A guidewire introducer is a thin, needle-like tube with a tapered conical opening on one end which helps the operator insert the guidewire through Y connector valve or into a balloon catheter.

Stents

Stents reduce abrupt vessel closure from dissections and coronary restenosis. The implantation of coronary stents has superseded traditional balloon angioplasty and is the most widely practiced procedure of PCI. The multitude of stent designs has arisen because of patent design issues, improved scaffolding mechanisms, and unique coatings. Most of the advances in stent design have been to increase deliverability. Stent delivery depends on both stent flexibility and profile, which must be designed without sacrificing radial strength and scaffolding length. Characteristics of an ideal stent are listed in Table 1-6.

Types

Stents are classified based on their mechanism of expansion. Two types of stents are in common use: balloon expandable and self-expanding. Nearly all commonly used coronary stents are balloon expandable. Some stents for saphenous vein graft and peripheral vascular disease stenting are self-expanding. Stents are designed with a mesh structure, coil, slotted tube ring, multicellular design, or unique custom design.

Composition. Stents vary in their composition and may be made of stainless steel, cobalt-based alloy, tantalum, titanium, or nitinol. Drug-eluting stents have drug-impregnated coatings or biodegradable coatings and/or other types of drug delivery systems. Biodegradable stents are currently in clinical trials.

Dimensions and Designs. For native coronary arteries, expanded stent diameters range from 2.5 to 5 mm. Stent lengths vary from 8 to 33 mm. For saphenous vein grafts, larger stent diameters (>5 mm) are available. Specialized stents are specifically designed for particular problems. For

Table 1-6

Ideal Stent Characteristics
• Biocompatible
• Conformity to tortuosity
• Flexibility
• High radial strength
• Low metallic surface area
• Low profile
• Radiopaque
• Secure delivery system
• Side branch access
• Thromboresistant
• Trackability

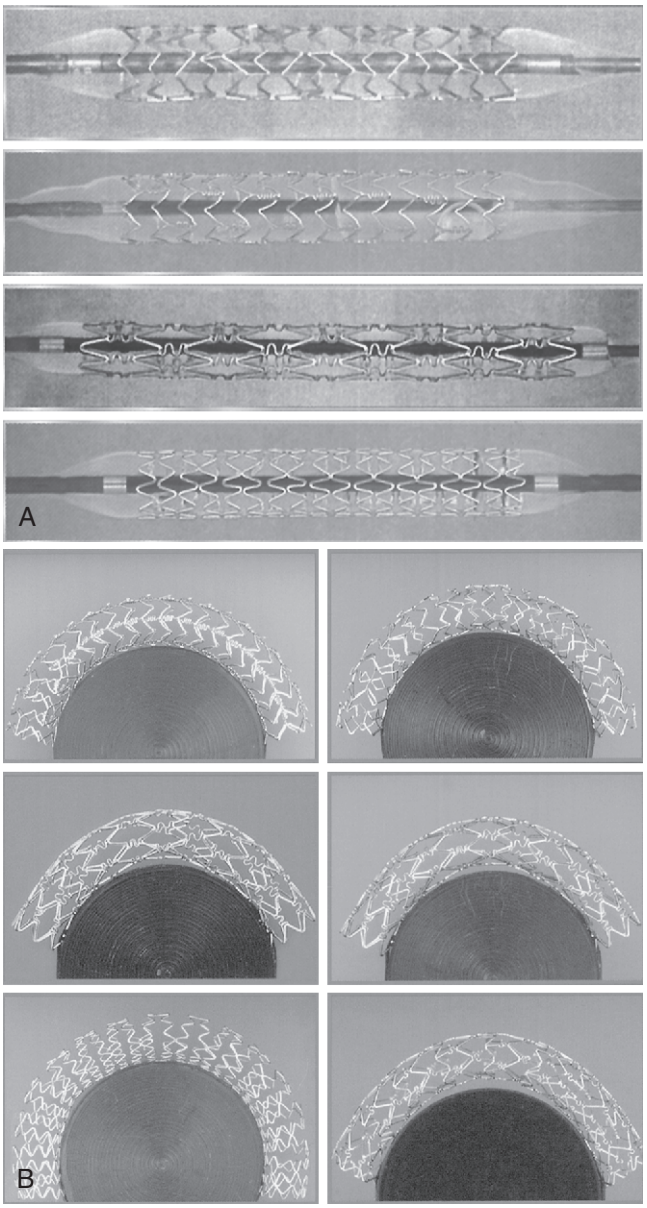

Figure 1-9 Currently available coronary stents. **A,** Straight stent inflations. **B,** Stents on curved segments.

example, a unique stent covered with polytetrafluoroethylene (PTFE) has been designed for coronary perforation or rupture and can be used to cover aneurysms. Dedicated bifurcated stents are in development.

Each stent has specific characteristics that differentiate their selection for clinical use. Figure 1-9 shows several currently available stents. Table 1-7 lists stent types, characteristics, and specialized features of material and cell configuration. Figure 1-10, A, depicts different polymer metallic stents. Figure 1-10, B, is an example of stent placement in right coronary angioplasty (RCA).

Contraindications

Relative contraindications to stenting can be determined based on patient and anatomical factors.

Table 1-7

Stent Types and Their Characteristics

Stent Type	Description	Examples
Drug-eluting stent	A stent that slowly releases a drug to block cell proliferation and/or restenosis	Cypher (J&J/Cordis) Taxus (Boston Scientific) Xience V (Abbott Vascular) Endeavor (Medtronic)
Bare metal stent, stainless steel	A vascular thin metal wire or mesh stent without a coating, typically first-generation technology	Bx Velocity (J&J/Cordis) Express2 (Medtronic) Millennium Matrix (Sahajanand Medical Technologies)
Bare metal stent, CoCr	A vascular thin metal wire or mesh without a coating, typically next-generation technology	Driver (Medtronic) Multi-Link Vision (Abbott Vascular) Corronnium (Sahajanand Medical Technologies)
Absorbable stent	Completely biodegradable, bioabsorbable stent, typically polymer or magnesium, sometimes coated with antirestenotic agent	AMS (Biotronik) ABSORB trial (Abbott Vascular) REVA/RESORB trial (REVA medical)
Bioactive stent	A stent that reacts with the body's natural processes to achieve an antirestenotic effect	Genous (OrbusNeich) Titan2 BAS (Hexacath)
Radioactive stent	Stent with a radiation-emitting coating	(Name undisclosed) (MoBeta, Inc.)
Drug-eluting balloon	Angioplasty balloon that, after deflation, leaves behind an antirestenotic drug	SeQuent Please (B. Braun Melsungen) DIOR (EuroCor) Elutax (Aachen Resonance)

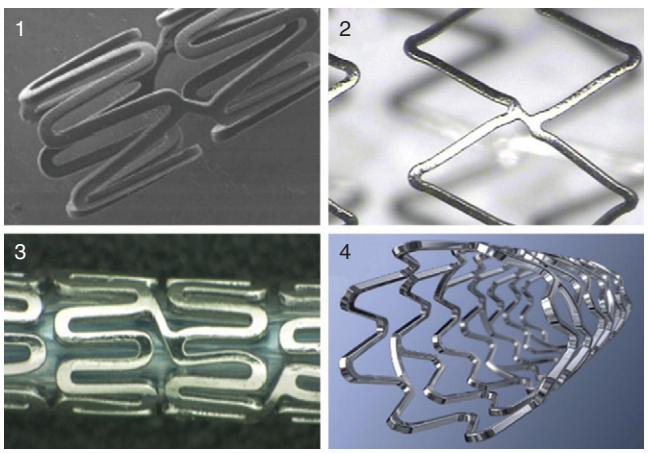

Figure 1-10 **A,** Examples of new durable polymer metallic stents. The cobalt chromium Elixir DESyne novolimus-eluting stent crimped (*1*) and expanded (*2*) The platinum chromium everolimus-eluting Element stent crimped (*3*) and expanded (*4*) (Images 3 and 4 are courtesy of Boston Scientific. From Garg, S, *et al. J Am Coll Cardiol* 2010;56:S43–S78.).

Continued

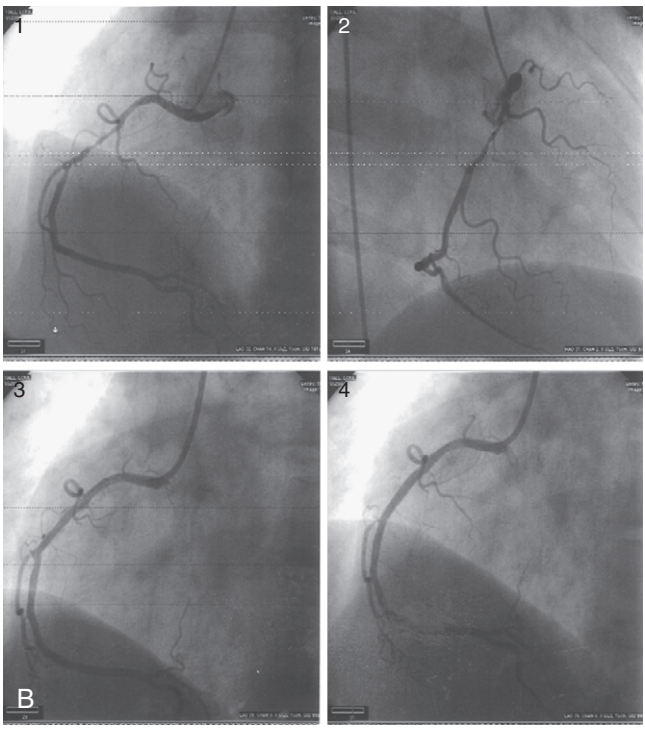

Figure 1-10, cont'd **B,** Stent placement in right coronary angioplasty. (*1*) Cineangiographic frames of right coronary artery before PCI with a stenosis in the proximal segment (left anterior oblique view). (*2*) Right coronary artery (RCA) in right anterior oblique view. (*3*) RCA after balloon angioplasty. (*4*) RCA after stent placement. Note compression of plaque into ostium of RV marginal branch.

Patient Factors

- Gastrointestinal bleeding that prevents 4 to 5 hours of anticoagulation during or following the stent procedure
- Inability to take dual antiplatelet therapy (e.g., ASA and a thiopyridine-like clopidogrel)
- Conditions prone to hemorrhage; intracranial hemorrhage, recent surgery, or bleeding diathesis

Anatomical Factors

- Small vessels, less than 2.5 mm
- Vessels with poor distal runoff or severe diffuse disease
- Vessels supplying poorly functional or nonfunctional myocardium
- Heavily calcified vessels

Complex Stenting

Stenting for patients with complex anatomy should be carefully considered. Any of the following characteristics are considered at higher risk for complications and are discussed in detail in Chapters 8 and 9:

- Long lesions requiring more than one stent per lesion
- Small coronary artery reference vessel diameters (<2.5 mm)
- Significant thrombus at the lesion site
- Lesions in saphenous vein grafts, the left main coronary artery, ostial locations, or bifurcation lesions
- Restenotic lesions

- Diffuse disease or poor outflow distal to the identified lesion
- Very tortuous vessels in the region of the obstruction or proximal to the lesion
- Unprotected left main stenosis
- Complex coronary artery disease (CAD) with significant impairment of left ventricular function

Over the past decade the indications for stenting have expanded, demonstrating a favorable outcome in nearly every anatomical subset studied. These subsets include native coronaries that are 3.0 mm or less in diameter, stenotic vein grafts, restenotic lesions after nonstent interventions, chronic total occlusions, acute myocardial infarction, bifurcation lesions, ostial lesions, unprotected left main stenting, multivessel stenting. Potentially favorable but as yet unproven situations for stenting include small vessels, long lesions, and diffuse disease.

Delivery Technique

Delivery of a stent to the lesion is usually performed after initial balloon angioplasty. A preliminary balloon dilation provides the operator with information on the difficulty of negotiating the artery and crossing the lesion as well as helping to select the correct stent size. After the stenosis is opened, the increased blood flow produces flow-mediated vasodilation, and on second look angiography, the vessel diameter is often larger than when seen before dilation. Stenting without predilation is called *direct stenting*. Although this method saves a small amount of time, the advantage is minimal.

Stent implantation technique differs from balloon angioplasty technique in two respects: (1) selecting the correct stent diameter and length is more critical than balloon sizing because a stent becomes a permanent implant and undersized stents are associated with poor long-term results, and (2) stent delivery to the stenosis can be more difficult than advancing a balloon catheter because of vessel calcification, tortuosity, angulation, and lesion length. These conditions are not generally problems for balloon catheters, but they can be significant problems for stents and must be considered beforehand. Stent delivery can be performed equally well from the femoral or radial approach with 6 F sheaths and guide catheters. If double balloons or stents are anticipated for bifurcation lesions or for Rotablator, 7F or 8F systems should be used.

Before stent implantation, predilation with a balloon that is slightly undersized relative to the reference vessel diameter is a safe strategy that gives the operator useful information such as the pressure needed to expand the lesion. Using a slightly undersized balloon also leaves an indication of the lesion so the stent can be optimally positioned. Predilation also allows for the vessel to be fully re-pressurized with restored flow, which often produces vasodilation. It is not uncommon to find a vessel enlarged after balloon dilation. This enlargement results in the operator selecting a larger stent than would have been chosen initially.

Alternatively, an operator may choose to go directly to stenting without balloon predilation. Although this method is usually successful, stents cannot always be delivered to the lesion site because of tortuosity or calcifications. In these cases, exchange for a balloon catheter, predilation, and/or exchange for a stiff guidewire may be needed. It is disconcerting to the operator to place a stent directly in a lesion only to find that the stent cannot be fully expanded because of heavy calcification. Undersized stents may be selected because of unappreciated flow-mediated vasodilation.

Guiding Catheter and Guidewire Selection. Coaxial guiding catheter support is even more important for effective stent delivery. Correct guide catheter selection is especially important when stent implantation is performed in an angulated circumflex or the verticle orientation of a

"shepherd's crook" right coronary artery, tortuous vessels, distal lesions, or vessels with long complex dissections. Stenting for lesions in these vessels often require use of stronger backup guides than standard right and left Judkins. Many operators prefer EBU, Q, Voda, or Amplatz, or similar wide-curve configurations. Stent delivery into some saphenous vein graft conduits, especially to the circumflex or left anterior descending artery, may require a multipurpose guiding catheter support. Although large-lumen (>6 F) guides provide better contrast delivery and visualization of the target site, power injection of contrast facilitates visualization and reduces the procedure time and contrast load with guide catheters of less than 6F.

Routine stent implantation procedures can be easily performed with regular support guidewires. Extra-support or extra-stiff guidewires (0.014 inch) provide a good "rail" when stent implantation is undertaken in lesions with extreme angulation or tortuosity and for lesions with long dissections. The extra-support guidewire assists both guiding catheter stability and stent delivery. Although helpful in stent delivery in tortuous vessels, extra-support guidewires can sometimes fold the intima of the vessel, causing pseudo lesions, or precipitate vessel spasm. A strategy of exchanging back to a floppy-tipped wire after stent delivery may prevent these effects. Using two wires to straighten vessels, called the *buddy wire technique*, is also helpful.

Stent Implantation and Expansion

After having positioned the stent, the operator should recheck the position relative to the side branches and landmarks of the target lesion. It is important to remember that the stent is a permanent implant and time should be taken to place it correctly, thus avoiding additional and unnecessary stents. It is also important that the stent covers the entire length of the dissection or lesion without leaving any inflow and outflow obstruction.

Stent expansion should be performed under fluoroscopy to judge whether it is fully expanded and to ensure that its diameter matches the proximal and distal reference coronary artery diameter(s). Optimal implantation requires that the stent struts be in full contact with (also known as *apposition*) the arterial wall. If the stent is not symmetrically expanded, a larger balloon (up to 4 mm) or a high-inflation pressure (>14 atm) may be used. Ideally, the final stent diameter should match that of the referenced vessel. All efforts should be taken to ensure that the stent is not underdilated. IVUS imaging is the only method of guaranteeing this.

General Notes for Stent Deployment

1. When multiple lesions are stented, the distal lesion should be treated initially, followed by the proximal lesion. Stenting in this order obviates the need to recross the proximal stent with the distal stent and reduces the chances of stent delivery failure or loss of stent when an undeployed stent is pulled back for whatever reason.
2. When recrossing a recently implanted stent, ensure that the guidewire traverses the stent and does not go between the stent and the vessel wall, which may result in inadvertent dislodgement of the stent during further balloon/stent passage.
3. If there is stent inflow or outflow obstruction or residual distal vessel narrowing, a freshly prepared balloon catheter can be advanced into and through the stented area for further dilatations. Re-wrapping previously used balloons should also be considered.
4. Eliminate any inflow or outflow narrowing by additional balloon inflations or stent implantation (especially if the stent margin has a dissection).

5. An acceptable angiographic result is a residual narrowing of less than 10% by visual estimate, but a truly optimal result must be confirmed by IVUS.
6. Vasospasm may occur during the procedure when high inflation pressures are used for stent optimization. Vasospasm is self-limiting, nearly always resolves with time or intracoronary nitroglycerin, and has not been associated with any unfavorable clinical events. Extraordinarily high-pressure inflations (>16 atm) are generally unnecessary and have been associated with stent overexpansion and higher in-stent restenosis rates.

Optimizing Stent Implantation. The concept of stent optimization is to expand the stent to the maximal extent that it is safe without vessel injury. Optimal stent expansion is determined by the ratio of the stent lumen cross-sectional area (CSA) relative to the vessel CSA at the stent site and also relative to the reference lumen CSA. The essential steps of the stent optimization technique are the following:

1. Evaluate the dimensions of reference vessel and implanted stent by IVUS.
2. Select an appropriately sized, noncompliant balloon based on IVUS target vessel diameter at the stent site.
3. Perform high-pressure balloon dilatation of the stent (usually >12 atm) or dilation with a larger balloon.

IVUS Optimization Based on the Reference Lumen. Successful stent expansion is achieved when (1) there is no significant difference between the lumen diameters of the stent and the reference site (particularly the distal reference), and (2) there is complete apposition of the stent to the vessel wall. For small vessels, the IVUS criterion of achieving a final stent lumen CSA larger than the distal reference lumen CSA is strongly recommended. In larger (>2.5 mm) vessels, a final stent lumen CSA greater than the distal reference CSA is acceptable with optimal stent apposition. This is accepted because the reference sites in large vessels commonly have less disease in the reference segments than do the small vessels. This also makes a final stent lumen larger than the distal CSA more difficult to achieve in large vessels than in small vessels. Typically, a final stent lumen CSA of 80% of the distal reference vessel is accepted.

IVUS Optimization Based on the Reference Vessel Area. Using criteria based only on IVUS vessel area has the inherent flaw of not incorporating stent expansion relative to the reference lumen CSA. The use of a criterion of 50% of the average vessel area would leave a significant number of patients with a stent that was underexpanded compared with the distal reference lumen. The use of a criterion of 60% of the average would position the final stent lumen between the CSAs of the proximal and distal reference lumens (Fig. 1-11). The use of reference vessel criteria has the disadvantage of requiring multiple additional measurements, in contrast to using the reference lumen criterion, which requires only a few.

IVUS Optimization Based on Final Balloon Size. A simplified guideline for assessing final stent lumen uses the balloon chosen for final stent optimization. The interventionalist usually selects an appropriate-sized balloon based on visual estimation of the diameter of the reference vessel. The minimum CSA of the stent lumen should be more than 70% of the calculated CSA of the balloon selected, based on the angiogram. This simplified criterion provides a safety buffer in small vessels, where the risk of stent thrombosis is higher, and is less strict for larger vessels, where the risk of stent thrombosis is reduced.

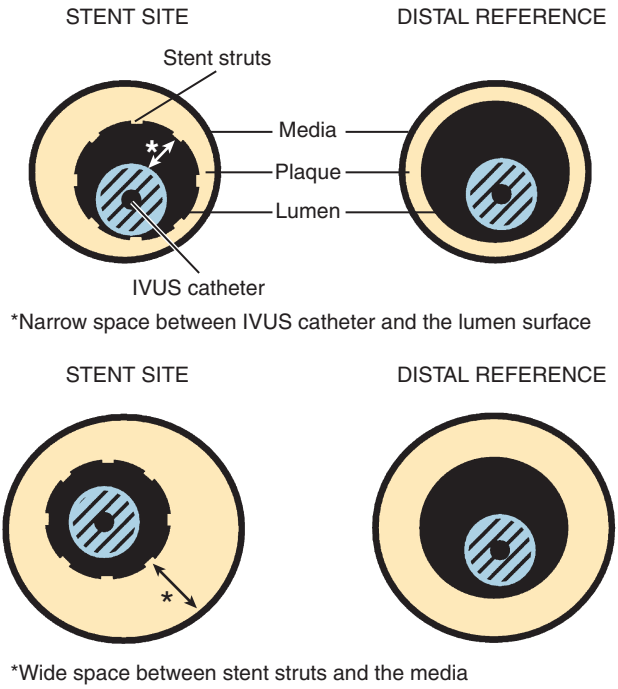

Figure 1-11 IVUS assessment of stent deployment Top, asymmetric deployment in small vessel. Bottom, asymmetric deployment can be improved in large vessel. *distance to wall.

Stent Expansion Strategies

There are two methods of optimizing stent expansion and improving the CSA of the stent lumen: (1) high pressure and (2) a larger diameter balloon. When an oversized balloon is used, there is an increased likelihood of coronary vessel rupture or dissection. Using high pressure with a balloon that is appropriately sized to the vessel allows stent expansion to occur within the natural confines of the vessel. To avoid complications, the ratio of the balloon to the angiographic reference vessel should be approximately 1.0. If a balloon/vessel ratio is more than 1.0, a short, noncompliant balloon with medium pressure (12–16 atm) is preferable. When a balloon larger than the angiographic vessel diameter is used for final stent optimization, it should never be larger than the distal IVUS minimum vessel diameter (measured media to media). When there is a large differential between the size of the proximal and distal vessels, as may occur in the left anterior descending artery before and after the second diagonal, careful balloon selection is important. In general, using slightly lower pressure in the distal part of the stent segment and a higher pressure for the proximal portion of the stent is all that is necessary. Care should be taken not to dilate beyond the distal edge of the stent with an oversized balloon. Occasionally, if there is significant vessel tapering, dilation with two balloons of different diameters should be considered.

Noncompliant balloons are preferable to compliant balloons for final dilations for several reasons. Noncompliant balloons will expand and dilate uniformly, even in focal areas of resistant lesions, and they are more likely to maintain a uniform diameter even at high pressures. Thus noncompliant balloons allow for optimal stent expansion without overexpansion of the balloon in adjacent unstented segments, which contributes to dissection. In addition, experience with IVUS has shown that 25% of stents have improved stent expansion with an increase in pressure from 15 to 18 atm or more.

Asymmetrical Stent Expansion. Stent expansion should be symmetrical in soft plaques. Very hard plaques (fibrotic or calcified), seen in approximately 20% to 30% of lesions, are not easily compressed by the balloon/stent, resulting in asymmetrical stent expansion into the normal arc of the vessel. In lesions with a significant arc (= 270 degrees) of dense or hard fibrocalcific disease, asymmetrical stent expansion occurs with a minimum to maximum lumen diameter ratio (symmetry index) of less than 0.7. In such lesions, further inflation leads to focal overstretching in the less diseased arc of the vessel. The symmetry index can worsen after further dilation, especially if an oversized balloon is used (Fig. 1-12). Using a balloon that is 0.25 to 0.5 mm smaller than the size of the vessel, and very high pressures (>18 ATM), may improve the symmetry index but will not necessarily increase the CSA of the lumen at the stent site.

Asymmetrical overexpansion is associated with a risk of vessel rupture. The risk is highest if a larger balloon is used. If the stent lumen CSA is acceptable relative to the distal lumen CSA and the stent is well apposed, efforts to make stent symmetry perfect should be avoided.

Incomplete Stent Expansion. Adequate stent expansion is dependent on the plaque burden. Optimal stent expansion in lesions with 50% to 70% diameter stenosis or lesions with a spiral dissection can be easily accomplished because there is not much atheroma. In lesions with more than 90% diameter stenosis, optimal stenting is more difficult to achieve and is associated with a higher percentage of asymmetrical stent expansion. Incomplete stent expansion (i.e., when the stent struts do not contact the intimal surface) can occur, particularly in ectatic vessels (at poststenotic dilation or aneurysm sites) and in the ostial left anterior descending artery (LAD), where the operator is cautious about performing a high-pressure balloon inflation in the left main trunk (Fig. 1-13). In the latter case, dilation of the ostial lesion with only the shoulder of the balloon does not provide sufficient expansion force to implant the stent fully. Table 1-6 suggests ways to redeploy stent after initial failure to expand.

Dissection at the Stent Margin. Stent dilations sometimes cause a plaque fracture or dissection at the edge of the stent and vessel, which requires additional stents to stabilize the newly produced dissection (Fig. 1-14). Plaque fracture may result from misplacement of the balloon post dilation, especially if the balloon is clearly oversized relative to the angiographic vessel size. Plaque fracture can also occur even when the balloon is positioned within the stented segment, especially

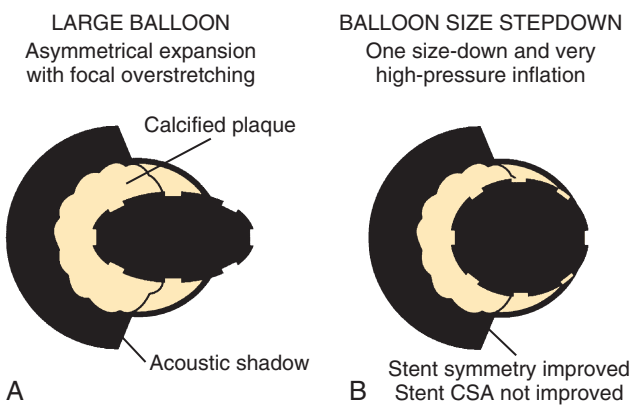

Figure 1-12 Balloon inflation strategy based on intravascular ultrasound imaging after stent placement. **A,** Asymmetrical stent expansion may require larger balloon. **B,** Stent symmetry is improved but cross-sectional area is not increased; use smaller balloon at very high inflation pressure.

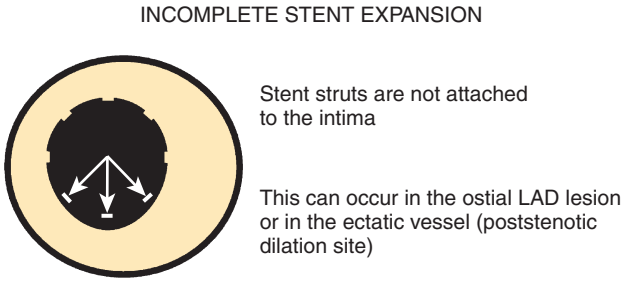

Figure 1-13 Intravascular ultrasound image of incomplete stent expansion.

in calcific lesions or vessels. In more elastic or soft lesions, this is less likely to occur, but it can be seen at the stent margins when the stents are deployed on bend lesions.

Plaque Prolapse. Plaque prolapse through stent struts may occur in 5% of coil-type stent implantation. Although the coiled stents have advantages in flexibility, the stent structure provides less complete radial support to the vessel wall. Further dilation does not improve the stent lumen CSA. An additional stent within the primary stent is necessary.

Managing Complications During Stent Delivery and Implantation

The complex nature of the procedure predisposes to unique complications and technical challenges. Complications of stenting implantation can be broken into several major categories.

Delivery Failure

Failure to deliver the stent is most often due to:

1. Suboptimal guide catheter support
2. Failure to predilate a significant coronary lesion
3. Unsuspected proximal tortuosity or calcification of the vessel with unanticipated vessel rigidity and acute angulation
4. Unsuspected obstruction proximal to the target lesion
5. Failure of adequate guidewire support

For these reasons, predilatation has advantages for stent delivery in most circumstances. A pre-deployment balloon that tracks easily to the lesion dilates the lesion simply, provides evidence of good guide catheter support, and bodes well for the delivery of the stent to the lesion. On the other hand, difficulties with advancing the balloon, guide catheter instability, and difficulty in dilating through tortuous segments herald the onset of stent delivery problems.

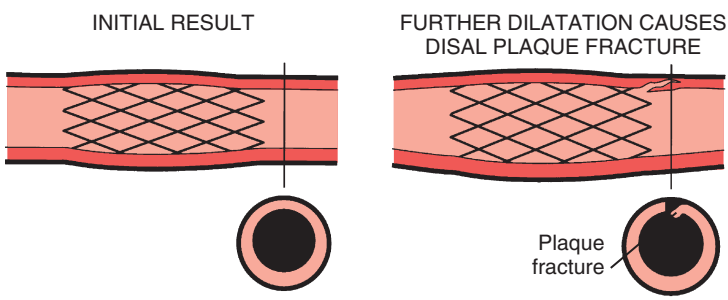

Figure 1-14 Overexpansion of stent may cause distal dissection.

In arteries that are highly tortuous and have multiple bends and folds, guidewire selection is an important factor in stent delivery success. Extra-support guidewires may not be ideal for initially crossing lesions, producing folds and pseudo stenosis, and conventional guidewires that are softer may permit delivery of the stent system without encountering the pseudo stenosis (Table 1-8).

Table 1-8

Technical Manipulations When a Stent Fails to Advance

General

- Best technical manipulation: Secure a more stable guide position or, if possible, the guide can be deep-seated safely. A potential late complication is ostial stenosis due to endothelial trauma.
- Constant forward pressure is exerted on the stent catheter while pulling the wire back to decrease friction inside the stent catheter lumen and to straighten the stent catheter.
- Additional proximal segment dilation or plaque removal facilitates stent advancement.

Wire Manipulations

- Advance a second stiffer wire to straighten the artery (the buddy wire technique). This stiff wire can cause wire bias.
- Advance the stent on the second stiffer buddy wire. Occasionally stents may advance more easily over a softer wire.
- Shape the wire along the curve of the artery to lessen wire bias so there is less friction or resistance at the outer curve of the vessel and the path of the wire is more coaxial with the path of the vessel.
- Use a "Wiggle" wire.

Stent Manipulations

- If the problem is due to tortuosity of the proximal segment, change the stent to a shorter one.
- Select a different type of stent with better flexibility.
- Gently bend the stent to conform it along the curve of the artery.
- Guide manipulations.
- Change to a guide with a different curve, to achieve better backup, and more coaxial to allow less friction at the ostium.
- Use a larger or smaller guide to achieve better backup.

Techniques Facilitating Recrossing of a Stented Area by a Balloon or Another Stent

General

- Best technical manipulation: Steer the wire into a different direction, or to a different branch to lessen wire bias and increase more wire centering.
- Rotate the balloon catheter while advancing it and let the catheter enter the stent by itself through its rotational energy (like torquing the Judkins right catheter).

Guidewire Manipulations

- Bend the wire and place the bent segment near the ostium of the stent to be crossed to position the wire more at the center of the entrance of the stented segment and to decrease wire bias.
- Insert a second stiffer wire to straighten the vessel.
- Change the current wire to a stiffer one.

Balloon/Stent Manipulations

- Use a shorter balloon or stent.
- Use a more flexible balloon or stent.
- Use a fixed-wire balloon to cross the stent.
- Use a fixed-wire balloon to track alongside a buddy wire.
- Mount a stent on a balloon with the tip partially inflated.
- If only the balloon needs to enter the stented segment, inflate the balloon with 1 to 2 atm so the balloon centers the wire in the lumen and facilitates the crossing of the wire and balloon.

Modified from Nguyen T, Douglas JS Jr, Hieu NL, *et al.* Basic stenting. *J Interv Cardiol* 2002;15:237–241.

Expansion Failure or "Persistent" Stent Narrowing

The inability to fully expand the stent or have an appearance of narrowing after implantation may be due to:

1. Tissue prolapse through cell sites
2. Calcification or rigid vessels
3. Dissection at stent margins
4. Unsuspected thrombus formation within or adjacent to the stent, which may appear as narrowings related to stent implantation

During the balloon inflation phase of stent implantation, full expansion of the balloon should always be observed. If an indentation persists, higher balloon inflation pressures or a larger, short balloon should be used. Failure of full stent expansion is usually the result of an inadequate predilatation approach. In cases where stent deployment appears suboptimal, IVUS imaging will confirm the mechanism of persistent narrowing due to tissue prolapse, incomplete apposition, heavy calcification, or, in some cases, thrombus.

Loss of Access to the Stent

1. Loss of guidewire access to a stent may result in a complication, especially if the stent has been inadequately expanded or when new lesions have been produced distal or proximal to the implanted stent. Recrossing a recently deployed stent is facilitated by using a soft guidewire with an exaggerated tip loop to prolapse through the stent. Care should always be taken so that the wire does not enter under a stent strut between the strut and the arterial wall. Once the guidewire has crossed the stent, a second problem may be encountered of inability to advance a balloon for high-pressure post-stent deployment.
2. Recrossing stents with balloons may be difficult when the proximal border of the stent is on a tortuous vessel segment, forcing the tip of the dilatation balloon into the vessel wall where it is blocked by the stent struts. Several approaches can be used to overcome this problem. The guide catheter can be repositioned in a more coaxial manner. A stiffer guidewire can be advanced to reshape the curve of the artery. The balloon can be withdrawn slightly, rotated, and readvanced during inspiration or coughing (the balloon's profile should be as low as possible). Several operators have recommended putting a curve onto a stiff part of the guidewire and using it to advance across a tortuous segment proximal to a stent and placing a curve on the balloon by forming it with the finger and using a technique similar to that of putting a gentle curve on a guidewire. Table 1-8 summarizes several technical manipulations that may be used to recross a deployed stent. Table 1-5 lists unique guidewire tip shapes that will help in difficult PCI situations.

Malpositioned or Embolized Stent

Several techniques for recovery of embolized stents have been proposed. These include loop snares, basket retrieval devices, biliary forceps, biopsy forceps, and other specifically designed retrieval systems.

Artery Perforation

Consider using a covered stent (see Chapter 4).

Stent-Related Dissection, Thrombosis, and Ischemia

The following factors are associated with an increased risk of stent thrombosis and ischemia:

1. Inadequate stent expansion
2. Dissection, not covered by the stent
3. Poor distal runoff or infarct in related vessel
4. Presence of thrombus
5. Subtherapeutic anticoagulation
6. Vessels less than 2.5 mm in diameter

Subacute thrombotic occlusion is rare within the first week after implantation but may happen during the week following discharge if the patient is not faithfully taking the prescribed dual antiplatelet therapy. Risk factors for subacute occlusion are previously noted. The risk of subacute thrombosis is increased when multiple overlapping stents are used. Subacute occlusion is treated with repeat balloon dilatations and continuation antiplatelet agents.

Ruptured or Tethered Balloon

Loss of inflation pressure during expansion of the stent can indicate balloon perforation. A ruptured balloon must be exchanged for a new one. If balloon rupture occurs after the ends of the stent are flared and anchored in the artery wall, the balloon can be deflated, rotated two or three times inside the stent, and gently pulled back inside the sheath and removed. A new balloon catheter is introduced through the sheath and positioned inside the partially expanded stent. Inflation of the new balloon catheter then completes the expansion and deployment of the stent. Alternatively, a rapid high-pressure inflation can deploy the partially opened balloon/stent enough to fully expand the stent and withdraw the balloon. A tethered balloon may be caught on the edge of the stent. The ends of the stent may not have been expanded and anchored securely in the arterial wall. The balloon should be deflated, advanced slightly to the stent edge, rotated, and gently withdrawn.

Safety of Magnetic Resonance Imaging After Stent Implantation

A magnetic resonance imaging (MRI) scan should not be performed until the implanted stent has begun to be endothelialized (>4 weeks). The risk of migration of the stent under a strong magnetic field is small, given the implant method. The stent may cause artifacts in MRI scans because of distortion of the magnetic field. In some patients this is not an issue because many stents may be nonferromagnetic.

Stent Implantation Before Noncardiac Surgery

Catastrophic outcomes have been reported for stenting after noncardiac surgery. Kaluza *et al.* (2000) noted that patients who underwent coronary stent placement less than 6 weeks before noncardiac surgery requiring general anesthesia had a high incidence of myocardial infarction, bleeding, and death. Among 40 consecutive patients, there were 7 myocardial infarctions, 11 major bleeding episodes, and 8 deaths; 4 patients died after undergoing surgery 1 day after stenting. Stent thrombosis accounted for most of the fatal events, with the time between stenting and surgery as the main determinant of the outcome. It is recommended that elective noncardiac surgery be postponed for 2 to 4 weeks after coronary stenting, which should permit completion of the

mandatory antiplatelet regimen and start of endothelialization, reducing the risk of stent thrombosis and bleeding complications.

Pre-PCI Workup

Noninvasive testing for ischemia provides the objective basis from which to proceed with PCI in stable patients. Several types of stress tests are available. The most common are (1) exercise stress with or without perfusion imaging or echo left ventricular (LV) wall motion as indicated; (2) pharmacologic stress study (e.g., dipyridamole); and (3) two-dimensional echo cardiogram (as indicated for assessment of LV function or valvular heart disease).

In the absence of objective evidence of ischemia, invasive assessment of the ischemic potential of a stenosis can be obtained during coronary angiography measuring translesional physiology for pressure-derived fractional flow reserve (FFR) determination.

Pre-PCI Preparation—Holding Area

- Patient preparation (intravenous access, meds, consent)
- Patient and family teaching (procedure, results, complications)
- Cardiothoracic surgeon consultation, particularly for high-risk, multivessel disease, or decreased LV function
- Appropriate laboratory data (type and cross-match, complete blood cell and platelet counts, prothrombin time [PT], partial thromboplastin time [PTT], electrolytes, blood urea nitrogen [BUN], creatinine)

Patient Preparation in Catheterization Suite

- Electrocardiogram ([ECG]; inferior and anterior wall leads): 12-lead (radiolucent) ECG.
- One or two IV lines.
- Skin-prepare both inguinal areas or wrist for radial artery (venous access for temporary pacing no longer routine; consider for high-risk patient, acute myocardial infarction, left bundle branch block requiring RCA PCI; Rotablator or thrombus aspiration device).
- Aspirin (325 mg PO); failure to administer aspirin before PCI is associated with a two to three times higher acute complication rate.
- Plavix (600 mg PO, best 24 hours beforehand); best outcomes are associated with Plavix preloading.
- Continue patient's routine antihypertensive medications.
- Heparin 40 to 70 U/kg bolus (or 40 U/kg bolus if GPIIb/IIIa blocker used). Target activated clotting time (ACT) more than 200 seconds. Heparin is critical for PCI, despite controversies regarding dosing and unpredictable therapeutic responses. Higher levels of anticoagulation are roughly correlated with fewer complications during coronary angioplasty, albeit at the expense of increased bleeding complications at higher heparin doses. Weight-adjusted heparin provides a clinically superior anticoagulation method over fixed heparin dosing.
- Consider glycoprotein IIb/IIIa blockers.
- Premedication (e.g., fentanyl [25–50 mg IV] and Versed [1-2 mg IV]).

Postprocedure Angiograms and Hemostasis

- Remove guidewire for final images after additional intracoronary nitroglycerin. Angiography with guidewire in place may disguise intimal flap or dissection.
- Femoral angiography before vascular closure device selection (perform right anterior oblique view for right femoral artery and left anterior oblique for left femoral artery). Alternatively, if not suitable for closure device, secure arterial and venous sheaths in place.

Remove in 4 hours when ACT less than 150 seconds. These considerations do not apply to radial artery access.

- No postprocedure heparin infusions unless there are highly unusual circumstances.

Postprocedure Care—Recovery Area

Nurses should begin patient teaching on hospital course and bleeding problems, late complications, and restenosis. The PCI team notifies departments, intensive care (or other appropriate patient care area), operating room, and surgical team on stand down. Postprocedure laboratory and ECG results are obtained.

Postprocedure Care—Step Down Area

After PCI, chest pain may occur in as many as 50% of patients. ECG evidence of ischemia identifies those at significant risk of acute vessel closure. When angina pectoris or ischemic ECG changes occur after PCI, the decision to proceed with further interventional procedures, CABG surgery, or medical therapy should be individualized, based on factors such as hemodynamic stability, amount of myocardium at risk, and the likelihood that the treatment will be successful. Following PCI, the hospital care team should monitor the patient for recurrent myocardial ischemia, puncture site hemostasis, and contrast-induced renal failure.

Post-PCI Care—Medications

- Order aspirin (325 mg orally daily).
- Give clopidogrel (600 mg loading dose and 75 mg/day orally, at least 4 weeks after stenting with a bare metal stent and 12 months with a drug-eluting stent).
- Initiate statin drugs if not already prescribed.
- Restart or initiate antihypertensive or antianginal medications depending on the patient's clinical needs.
- Resume prior medications for other conditions (e.g., GERD).

Appropriate secondary atherosclerosis prevention programs should be started involving adherence to recommended medical therapies and behavior modifications to reduce morbidity and mortality from coronary heart disease.

Patients with renal dysfunction and diabetes should be monitored for contrast-induced nephropathy. In addition, those patients receiving higher contrast loads or a second contrast load within 72 hours should have their renal function assessed. Whenever possible, nephrotoxic drugs (certain antibiotics, nonsteroidal anti-inflammatory agents, and cyclosporin) and metformin (especially in those with preexisting renal dysfunction) should be withheld for 24 to 48 hours after PCI.

After discharge, the patient then returns to activities of daily living within 1 or 2 days. Factors preventing rapid return to work include access site complications and persistent symptoms. A functional (ischemic testing) evaluation for patients with multivessel coronary angioplasty or incomplete revascularization after angioplasty will indicate the limitations, if any, on work status.

CAD Risk-Factor Modification

All patients should be instructed about risk-factor modification and medical therapies for secondary atherosclerosis prevention before leaving the hospital. The interventional cardiologist should emphasize these measures directly to the patient and family. Failure to do so suggests that secondary prevention therapies are not important. The interventional cardiologist should contact the primary care physician regarding the secondary prevention therapies initiated and those to be maintained, including aspirin therapy, hypertensive control, diabetic management, aggressive control of serum lipids to a target low-density lipoprotein

goal of less than 100 mg/dL following AHA guidelines, abstinence from tobacco use, weight control, regular exercise, and ACE inhibitor therapy as recommended in the AHA/ACC consensus statement on secondary prevention.

Follow-up Schedule and Stress Testing

- Access site is checked on first office visit, 2 to 4 weeks following PCI.
- Stress testing is neither routinely nor annually performed after PCI, unless symptoms appear.
- If symptoms or signs of ischemia are present early after PCI, coronary angiography is repeated.

There is no indication for annual exercise testing in asymptomatic patients. AHA and ACC practice guidelines recommend selective evaluation in patients considered to be at particularly high risk (e.g., patients with decreased LV function, multivessel coronary artery disease, proximal left anterior descending disease, previous sudden death, diabetes mellitus, hazardous occupations, and suboptimal PCI results). For many reasons, stress imaging is preferred to evaluate symptomatic patients after PCI. If the patient's exertional capacity is significantly limited, coronary angiography may be more expeditious to evaluate symptoms of typical angina. Exercise testing after discharge is helpful for activity counseling and/or exercise training as part of cardiac rehabilitation. Neither exercise testing nor radionuclide imaging is indicated for the routine, periodic monitoring of asymptomatic patients after PCI without specific indications.

Medical Therapy After PCI

Anticoagulant Drugs

Anticoagulant drugs (heparin, enoxaparin) are needed only for the brief intraprocedural period. Unless indicated by unusual circumstances (e.g., continued intracoronary thrombus formation), only bolus heparin without later IV infusions is used. In some labs, low-molecular-weight heparin (enoxaparin) is replacing bolus unfractionated heparin for PCI.

Warfarin is not used for PCI but may be needed for other reasons such as atrial fibrillation or severe LV dysfunction. Orally administered anticoagulants (warfarin) after PCI are no more effective than aspirin for preventing restenosis or abrupt closure.

Antiplatelet Agents

Platelet deposition is partially inhibited by selected antiplatelet regimens (aspirin and clopidogrel, ticlopidine, or prasugrel). Acute re-occlusion is more frequent in patients who have not received aspirin before angioplasty. Late stent thrombosis is also more frequent in patients not receiving clopidogrel.

Antiplatelet agents of the thienopyridine family (clopidogrel, ticlopidine, prasugrel) inhibit platelets by blocking adenosine diphosphate (ADP)–stimulated aggregation and are highly effective for preventing subacute thrombotic occlusion after stenting. A rare associated side effect of ticlopidine, and less so of clopidogrel, is thrombotic thrombocytopenia purpura. Clopidogrel is the currently preferred oral antiplatelet drug. Recommended antiplatelet regimens include aspirin (80–365 mg/day) and clopidogrel (75 mg PO daily).

Prasugrel (also known commercially as Effient) is a third-generation oral thienopyridine which irreversibly antagonizes the platelet A5diphosphate P2Y12 receptor. It can replace Plavix in patients who are nonresponders or who have demonstrated stent thrombosis on therapy. It is not recommended for patients who weigh less than 60 kg, who have had a cerebrovascular accident, or who have any propensity for bleeding. Loading dose is 60 mg PO and daily dose is 10 mg PO.

Given in the intensive care unit or catheterization laboratory only, the intravenous glycoprotein-receptor-blocking platelet drugs, abciximab, tirofiban, and eptifibatide, block the final common pathway of platelet activation of the platelet receptor (called glycoprotein IIb/IIIa) and are highly effective in blocking platelet adhesion (sticking to vessel wall) and aggregation (clumping together). Reduced acute and subacute adverse event rates are reported for all three drugs. All high-risk interventions should consider using abciximab with heparin.

PCI Program Without Surgical Backup

PCI has been performed in laboratories without on-site surgical backup. Criteria for the performance of angioplasty at hospitals without on-site cardiac surgery have been summarized as follows:

1. The operators must be experienced interventionalists who regularly perform elective intervention at a surgical center (75 cases/year). The institution must perform a minimum of 36 primary PCI procedures per year.
2. The nursing and technical catheterization laboratory staff must be experienced in handling acutely ill patients and must be comfortable with interventional equipment. They must have acquired experience in dedicated interventional laboratories at a surgical center. They participate in a 24-hour, 365-day call schedule.
3. The catheterization laboratory itself must be well equipped, with optimal imaging systems, resuscitative equipment, and intra-aortic balloon pump (IABP) support, and must be well stocked with a broad array of interventional equipment.
4. The cardiac care unit nurses must be adept in hemodynamic monitoring and IABP management.
5. The hospital administration must fully support the program and enable the fulfillment of the institutional requirements listed previously.
6. There must be formalized written protocols in place for immediate (within 1 hour) and efficient transfer of patients to the nearest cardiac surgical facility that is reviewed or tested on a regular (quarterly) basis.
7. Primary intervention must be performed routinely as the treatment of choice around the clock for a large proportion of patients with acute myocardial infarction to ensure streamlined care paths and increased case volumes.
8. Case selection for the performance of primary angioplasty must be rigorous. Criteria for the types of lesion appropriate for primary angioplasty and for the selection for transfer for emergency aortocoronary bypass surgery are shown in Table 1-9.
9. There must be an ongoing program of outcomes analysis and formalized periodic case review.
10. Institutions should participate in a 3- to 6-month period of implementation, during which time development of a formalized primary PCI program is instituted that includes establishing standards, training staff, detailed logistic development, and creation of a quality assessment and error management system. (Smith et al. 1993) (See Smith SC Jr, Dove JT, Jacobs AK, *et al.* ACC/AHA guidelines for percutaneous coronary intervention (revision of the 1993 PTCA guidelines)—executive summary: a report of the American College of Cardiology/American Heart Association task force on practice guidelines (Committee to revise the 1993 guidelines for percutaneous transluminal coronary angioplasty) endorsed by the Society for Cardiac Angiography and Interventions. *Circulation* 2001;103:3019–3041.)

Table 1-9

Patient Selection for PCI at Hospitals Without On-Site Cardiac Surgery

Avoid intervention in hemodynamically stable patients with the following:

1. Significant unprotected left main coronary artery narrowing upstream from an acute occlusion in the left coronary system that might be disrupted by the angioplasty catheter
2. Extremely long or angulated infarct-related lesions with TIMI grade 3 flow
3. Infarct-related lesions with TIMI grade 3 flow in stable patients with three-vessel disease
4. Infarct-related lesions of small or secondary vessels
5. Lesions in other than the infarct artery

Transfer for emergency aortocoronary bypass surgery patients

- With high-grade residual left main or multivessel coronary disease and clinical or hemodynamic instability.
- After angioplasty of occluded vessels, preferably with intra-aortic balloon pump support.

Adapted from Wharton TJ Jr, McNamara NS, Fedele FA, *et al.* Primary angioplasty for the treatment of acute myocardial infarction: experience at two community hospitals without cardiac surgery. *J Am Coll Cardiol* 1999;33:1257–1265.
PCI, percutaneous coronary intervention; TIMI, thrombolysis in myocardial infarction.

Training for Coronary Angioplasty

Advances in interventional procedures have maintained high and durable success rates despite increasingly complex procedures. The need for appropriate training and guidelines for the procedure is obvious. Recent guidelines for the assessment and proficiencies of coronary interventional procedures have been summarized in a report from the joint task force from the AHA/ACC (Table 1-10). ABIM board certification in interventional cardiology requires documentation of training

Table 1-10

Considerations for the Assessment and Maintenance of Proficiency in Coronary Interventional Procedures

Institutions

- Quality assessment monitoring of privileges and risk-stratified outcomes
- Support for a quality assurance staff person (e.g., nurse) to monitor complications
- Minimal institutional performance activity of 200 interventions per year with the ideal minimum of 400 interventions per year
- Interventional program director who has a career experience of more than 500 PCI procedures and is board certified by the American Board of Internal Medicine (ABIM) in interventional cardiology
- Facility and equipment requirements to provide high-resolution fluoroscopy and digital video processing
- Experienced support staff to respond to emergencies
- Establishment of a mentoring program for operators who perform fewer than 75 procedures per year by individuals who perform 150 procedures per year

Physicians

- Procedural volume of 75 per year
- Continuation of privileges based on outcome benchmark rates with consideration of not granting privileges to operators who exceed adjusted case-mix benchmark complication rates for a 2-year period
- Ongoing quality assessment comparing results with current benchmarks, with risk stratification of complication rates
- Board certification by ABIM in interventional cardiology

From Hirshfeld JW, Elllis SG, Faxon DP. Recommendations for the assessment and maintenance of proficiency in coronary interventional procedures: statement of the American College of Cardiology. *J Am Coll Cardiol* 1998;31:722–743.

Table 1-11

Recommendations for Clinical Competence in Percutaneous Transluminal Coronary Angiography: Minimum Recommended Number of Cases per Year	
Total number of cases	125
Cases as primary operator	75
Practicing, number of cases per year	50-75 to maintain competency

in an accredited fellowship program during which a minimum of 125 coronary angioplasty procedures must be performed, including 75 performed with the trainee as primary operator (Table 1-11).

Suggested Readings

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2

Arterial and Venous Access and Hemostasis for PCI

CONNIE N. HESS · SUNIL V. RAO · KIMBERLY A. SKELDING · MORTON J. KERN · MITCHELL W. KRUCOFF

Techniques for vascular access for interventional procedures are identical to those used for diagnostic catheterization. The initial approaches, assessment, and methods have been described in detail in *The Cardiac Catheterization Handbook*, 5th edition, and will be reviewed here with emphasis on interventional procedures. The site and type of access, most commonly either the femoral or radial artery, are determined by the anatomic and pathologic conditions and anticipated PCI techniques required.

As a first step, to avoid known pitfalls and potential complications, it is helpful to understand any previous difficulties encountered during diagnostic procedures. As is the case with diagnostic studies, assessment of all arterial pulses before and after the procedure is mandatory. For both diagnostic and interventional procedures, vascular access is the most common cause of procedural morbidity.

Percutaneous Femoral or Radial Artery Approach

Because femoral access is the most commonly used technique in the United States and because of the need for large-diameter interventional equipment, the femoral artery approach is often preferred to the radial artery approach. However, in recent years most labs using 6F guide catheters can easily employ the radial approach for both the diagnostic and the subsequent PCI. The radial approach has significantly fewer access-related complications and, in some studies, better late outcomes. The discussion of the radial technique will follow the femoral approach although operators familiar with current clinical data would advocate "radial first" when possible. Conditions in which radial (or, rarely, brachial) artery access should be favored are listed in Table 2-1.

Femoral Artery Puncture Technique

The proper position for femoral artery puncture should be in the common femoral artery, defined as that segment above the femoral artery bifurcation and below the internal epigastric artery (Fig. 2-1). This target zone can be identified by visualizing the head of the femur with a metal marker indicating the planned path of the needle by fluoroscopy. In a manner identical to diagnostic vascular access, the operator locates the artery and administers local anesthesia (see *The Cardiac Catheterization*

Table 2-1

Conditions in Which Radial Artery Access Should Be Favored

1. Claudication
2. Absent leg pulses
3. Femoral bruits
4. Prior femoral artery graft surgery
5. Extensive inguinal scarring from previous procedures
6. Surgery or radiation treatment near inguinal area
7. Excessively tortuous iliac system and lower abdominal aorta
8. Abdominal aortic aneurysm
9. Severe back pain or inability to lie flat
10. Downward origin of renal arteries (for renal artery stenting)
11. Patient request

Handbook, 5th ed., Chapter 2). Single front wall puncture (Fig. 2-2) is highly desirable for two reasons:

1. Reduces chances of bleeding in the setting of potent anticoagulation and antiplatelet agents.
2. Facilitates successful vascular closure device placement; if a second site puncture occurs, a vascular closure device cannot be used with confidence in obtaining hemostasis.

For these reasons, the supervising physician for PCI as well as diagnostic procedures should ensure proper arterial access in all patients, a fact especially important for those patients going on to intervention. Multiple punctures will be a source of bleeding and potential complications, including retroperitoneal hematoma, femoral pseudoaneurysms, or arteriovenous fistula (AVF) postprocedure. Femoral angiography before PCI is highly recommended to ensure proper access and justify deferment of proceeding to elective PCI should a high stick be identified with its potential for retroperitoneal bleeding. Femoral angiography after sheath insertion or before undertaking PCI will confirm placement in the common femoral artery.

When an interventional procedure is performed on a separate day after the diagnostic catheterization, femoral access on the contralateral side or radial access should be considered. Puncturing the same groin soon after diagnostic access may be associated with a higher incidence of bleeding or infection. Reaccess in punctures closed with some vascular closure devices can be performed. However, repuncture in an Angio-Sealed femoral artery is not recommended before 90 days; those closed with StarClose or Perclose may be reaccessed immediately, although there are two reports from the many thousands of patients noting the remote chance of reentering the central opening of the StarClose clip.

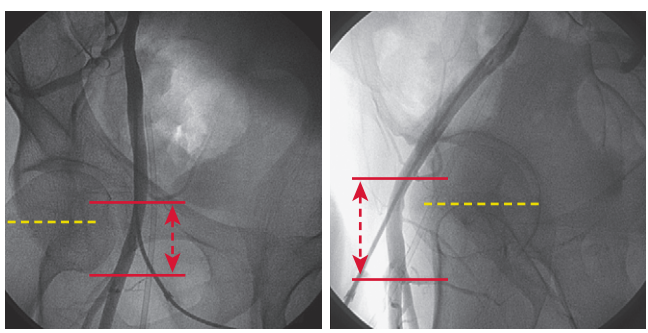


Figure 2-1 Femoral angiogram (*left*) AP view, (*right*) lateral view. The common femoral artery (CFA) has the inferior epigastric artery and bifurcation of the superficial and profunda femoral arteries as the top and bottom markers. Yellow dotted line is middle of femoral head. Lower red line is bifurcation of superficial and profunda femoral arteries; top red line is lower border of inferior epigastric artery. The arrow shows the target zone for proper puncture in the common femoral artery.

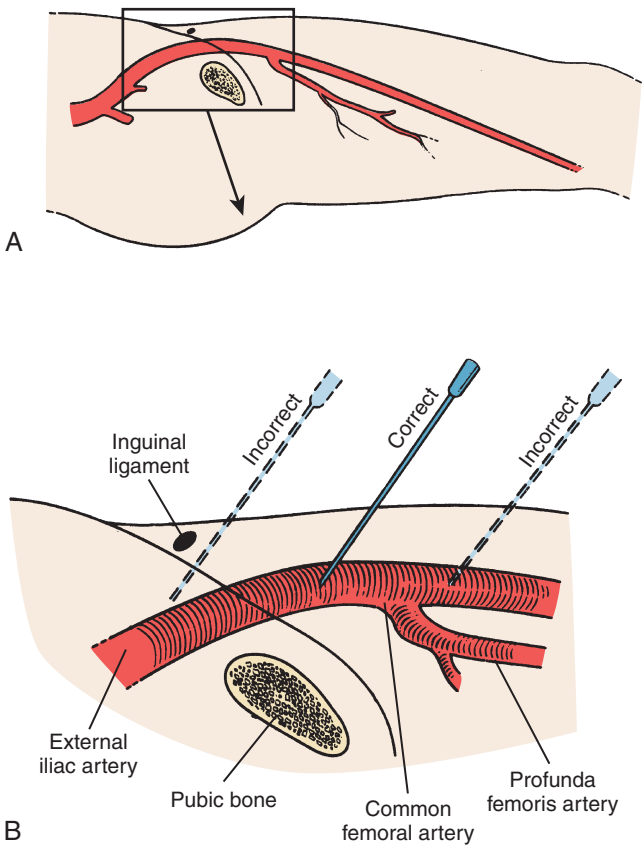


Figure 2-2 Technique of single-wall arterial puncture. **A.** Parasagittal cross-sectional diagram of inguinal region at level of femoral artery. **B.** Correct needle entry position is below inguinal ligament and above femoral artery bifurcation. Correct access is particularly critical for procedures. (From Kulick DL, Rahimtoola SH, eds. *Techniques and applications in interventional cardiology*. St. Louis, MO: Mosby, 1991: 3.)

Key Points for Femoral Arterial Access for Interventional Procedures

1. Consider radial access first because of its lower rate of femoral bleeding complications.
2. In obese patients, place a hemostat or marker over the planned puncture site and fluoroscopically visualize the femoral head.
3. Consider using a Doppler needle or other ultrasound guidance for deep or difficult femoral punctures.
4. If anticipating need for large bore equipment (e.g., rotablator or two stents for treating a bifurcation), use a ≥7F arterial sheath.

Percutaneous Femoral Vein Puncture

Femoral vein puncture is performed like the arterial puncture, as described in *The Cardiac Catheterization Handbook,* 5th edition, chapter 2. Indications for femoral venous sheath placement in patients undergoing PCI include the need for additional intravenous access for fluids and medications, a temporary pacemaker, or pulmonary artery pressure monitoring. Caution should be used to avoid inadvertent additional arterial punctures. For this reason, if femoral vein access is

needed, start with the vein access before arterial puncture. If the artery is inadvertently accessed, place the arterial sheath and then angle slightly more medially with the next puncture.

Radial Artery Access for PCI

The technique of radial artery access for diagnostic and interventional procedures has gained worldwide acceptance. Kiemeneij of the Netherlands pioneered the radial approach for coronary interventions, increasing the success rate, improving patient comfort, and providing a method for excellent hemostasis in the fully anticoagulated patient.

The transradial interventional (TRI) approach has several distinct advantages over femoral access. Bleeding complications from the radial artery approach are negligible compared to those of femoral access. The radial artery is easily accessible in most patients and is not located near significant veins or nerves. The superficial location makes for easy access and control of bleeding. In patients with a normal Allen's test, no significant clinical sequelae occur after radial artery occlusion because collateral flow to the hand occurs through the ulnar artery. Patient comfort is enhanced with the ability to sit up immediately after the procedure and when pre-medications wear off, they may walk around the room or be discharged.

While the fundamental principles of catheter manipulation remain the same as those used in femoral procedures, TRI is technically more variable. Basic changes in approach by both the operator and the catheterization lab staff are required to overcome the "radial first" learning curve. Some of the practical challenges encountered when learning to perform TRI and strategies to overcome them are highlighted in Table 2-2.

Clinical Evidence Favoring TRI

The radial approach offers several distinct advantages over femoral access without sacrificing procedural success and may be even more attractive given the reclassification of femoral closure devices as a class III recommendation. While there is a well-documented learning curve for transradial catheterization, data from both observational studies and randomized trials suggest that increased operator experience and transradial case volume are associated with significant reductions in procedural failure and, ultimately, no difference in success rates between radial and femoral approaches. Femoral artery access site complications, including retroperitoneal hematoma, AVF, pseudoaneurysm, arterial dissection, and neuropathy, are important contributors to patient morbidity and mortality, even when femoral closure devices are used. These complications are all distinctly rare in radial procedures.

With its superficial location, complications at the site of radial puncture are less common, noticed earlier, and easier to manage. Rates of major bleeding are significantly lower for transradial procedures, even in populations at high risk for arterial access complications, such as females and the elderly (Fig. 2-3). Data from patients of all ages suggest that this reduction in bleeding may translate into reduced rates of death and ischemic events. In addition, patient comfort and satisfaction are enhanced by transradial access, as patients can sit up immediately postprocedure and ambulate as soon as their sedation has worn off. Compared with femoral technique, transradial catheterization leads to improved quality of life postprocedure and is preferred by patients.

Patient Selection for TRI

TRI presents an important first-line option for many patients undergoing coronary intervention, but proper patient selection is central to achieving optimal outcomes. Early in the learning curve, gaining experience with diagnostic procedures in patients with less complex anatomy and conditions is recommended. As experience and confidence increase, patient selection can be liberalized.

Table 2-2

Challenges to Starting a Radial Program

- Patient setup
  - Prep wrist with patient's arm at his or her side (radial artery parallel to femoral artery)
  - Prep femoral artery simultaneously in case of crossover
  - Use either a rectangular platform or 2 "banjo" arm boards underneath patient's arm to create a working space distal to patient's hand
  - Place towels on working space to elevate working space to level of wrist
  - For left radial cases, elevate left arm using pillows to bring left radial above left groin or have patient bring left arm across body after obtaining left radial artery access
- Radial artery access
  - Small-caliber artery
    - Check contralateral radial artery
  - Spasm
    - Intra-arterial nitroglycerin, calcium channel blockers
    - Patient sedation
    - Use smaller French size catheters
  - Repeat access
    - Check patency of artery (ultrasonography or reverse Allen test*); obtain access more proximally
- Traversing the radiobrachial region
  - Radiobrachial angiogram for any resistance to advancing the wire or catheter
  - Radial loop: use 0.014-inch hydrophilic wires to traverse and straighten loop
  - Consider femoral access bailout if unable to traverse radial loop or if there is significant patient discomfort
- Traversing the chest arteries
  - Have patient take a deep breath to straighten subclavian/innominate arteries and subclavian/innominate-aortic junction to direct catheter to ascending aorta
  - For extreme z-curves, use hydrophilic 0.035-inch wires to direct catheters into ascending aorta
- Engaging the coronary arteries
  - Judkins curves: use longer JR curve (e.g., JRS), shorter JL curve (e.g., JL3.5)
  - Specialized curves (e.g., Kimny, Tiger, Jacky, Ikari, Amplatz)
  - Previous CABG: use left wrist with JR4/JL4 catheters, multipurpose catheter, or specialized curves

From Rao SV, Cohen MG, Kandzari DE, *et al.* The transradial approach to percutaneous coronary intervention: historical perspective, current concepts, and future directions. *J Am Coll Cardiol* 2010;55:2187–2195.

While there is some debate, confirmation of a normal Allen's test (see below) is strongly recommended. If the Allen's test is abnormal on one side, the contralateral side should be evaluated before changing to femoral access.

In general, TRI is *avoided* in patients in whom:

a. The radial artery is being considered for use in coronary artery bypass graft surgery or in whom hemodialysis via an AVF may be necessary, as well as in patients with an existing AVF.

b. There is known upper extremity vascular disease, such as severe atherosclerosis, extreme tortuosity, or vascular anomalies, or those with vasospastic disorders, including Raynaud's or Buerger's disease.

c. The procedures will likely to require 7F or larger guide catheters.

In addition, the presence of right- or left-internal mammary artery graft conduits may be less accessible from the contralateral wrist.

TRI is an especially good option for patients on systemic anticoagulation with elevated INR (international normalized ratio) and patients with suspicion of descending aortic dissection.

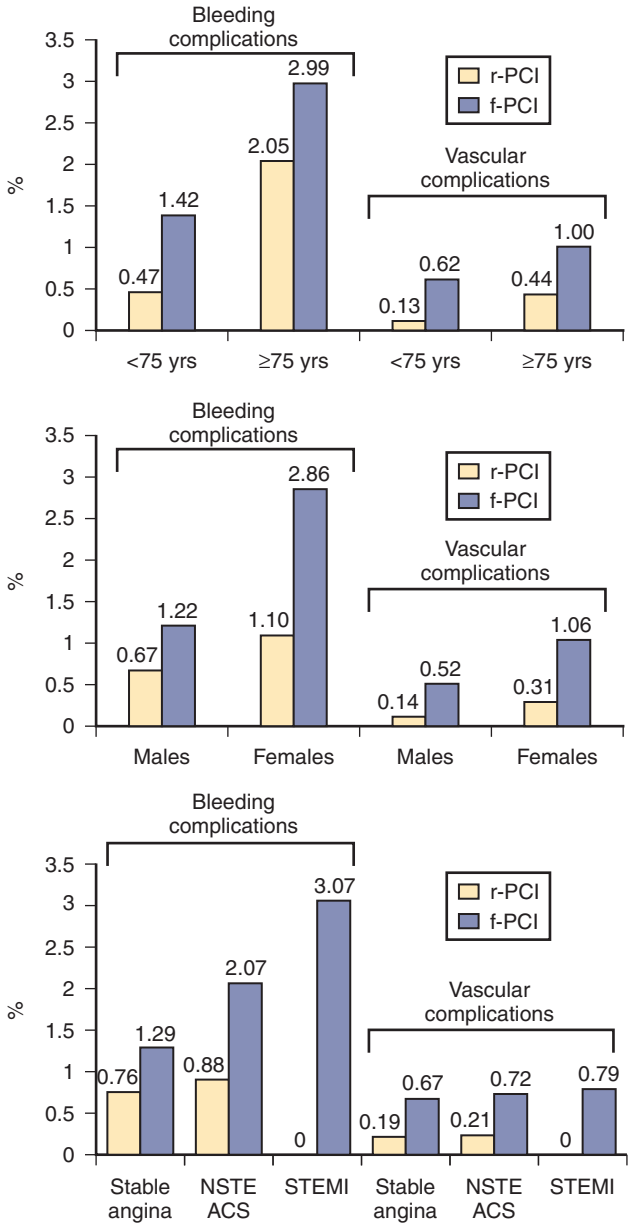


Figure 2-3 Bleeding and vascular complications in radial and femoral PCI. (Adapted from Rao SV, Ou FS, Wang TY, *et al.* Trends in the prevalence and outcomes of radial and femoral approaches to percutaneous coronary intervention: a report from the National Cardiovascular Data Registry. *JACC Cardiovasc Interv* 2008;1:379–386.)

Use of TRI in very time-sensitive settings, such as ST-elevation acute myocardial infarction, remains controversial. Studies suggest that transradial catheterization can be performed without significant delays in door-to-balloon time and without increasing procedure duration, radiation exposure, or contrast use in experienced labs with experienced operators. In all cases, these guidelines for patient selection should be balanced against the risks and benefits of radial versus femoral access, as even a patient with an abnormal Allen's test may benefit from TRI under certain circumstances.

Anatomy for Radial Access

Knowledge of the anatomy of the vessels of the upper extremity and aortic arch is essential information for becoming a TRI operator. The aortic arch gives off the great vessels: the innominate artery on the right and the common carotid and subclavian arteries on the left. The innominate artery becomes the right subclavian artery after the takeoff of the right common carotid. The lateral margin of the first rib demarcates the transition from subclavian artery to axillary artery. At the inferior border of the teres major muscle, the axillary artery continues as the brachial artery, which then bifurcates in most patients into the radial and ulnar arteries below the elbow. Some patients will have an anatomic variant in which the radial artery originates higher than the elbow. The radial artery then continues along the lateral aspect of the forearm into the wrist, where it passes over the scaphoid and trapezium bones and divides into the deep and superficial palmar arches. The flexor retinaculum overlies this area of the wrist. The deep and superficial branches of the radial artery communicate with corresponding divisions of the ulnar artery to complete the two palmar arches and provide dual, collateral blood flow to the hand in most patients (Fig. 2-4). Operators should familiarize themselves with the relevant anatomy to avoid cannulation of the radial artery too distally and to prepare for anatomic variants that may make traversing the path from radial artery to ascending aorta challenging.

Use of the Allen's Test

A strong recommendation for the radial procedure is the performance of the Allen's test. The Allen's test assesses the adequacy of the palmar arch and ulnar flow. It is performed as follows: The patient makes a fist pushing blood from the hand. The radial and ulnar arteries are compressed and simultaneously occluded. When the hand is opened, the palm appears blanched. Release of the ulnar artery should result in return of pink hand color within 8 to 10 seconds. (Fig. 2-5)

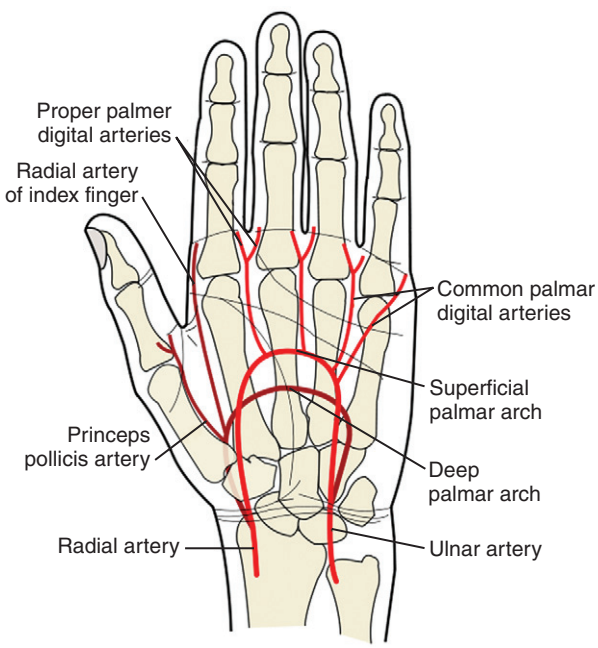


Figure 2-4 Radial artery and the anatomy of the hand.

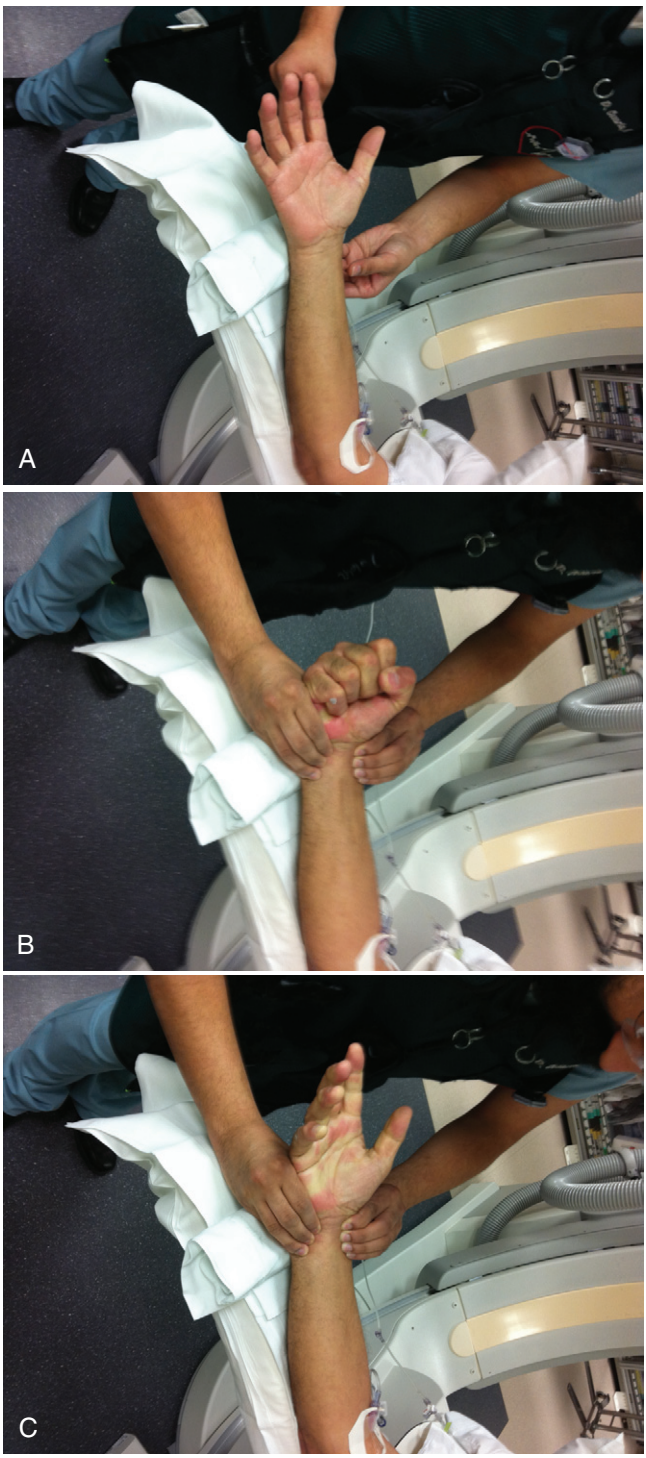


Figure 2-5 Manual Allen's test. **A,** Normally the palm is pink. **B,** A fist is made and the radial and ulnar arteries are compressed. **C,** The hand is open and blanched after compression of both ulnar and radial artery.

Continued

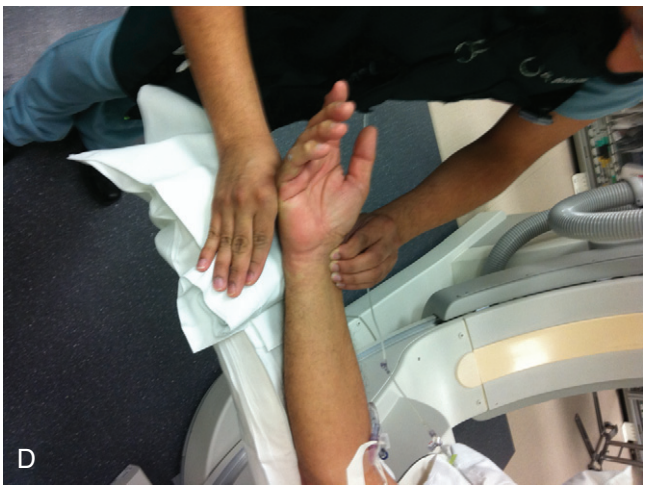


Figure 2-5, cont'd **D,** The palm is pink after release of ulnar artery with radial artery occluded.

Another and more objective measurement of satisfactory ulnar flow can be documented by pulse oximetry. Using the pulse oximeter, the pulse wave is displayed with both arteries open (Fig. 2-6a). The radial artery is then compressed and the pulse wave of ulnar flow observed (Figs. 2-6b, 2-6c). A reverse Allen's test can also be performed by occluding the ulnar artery. It is recommended for patients with a history of previously accessed radial arteries either for catheterization or arterial blood gases. The results of the oximetric Allen's test are divided into four grades of waveforms: type A, no change in pulse wave; type B, damping of waveform that returns to normal within 2 minutes; type C, loss of phasic pulse waveform that returns within 2 minutes; type D, loss of pulse waveform without recovery within 2 minutes. Although use of the Allen's test and grading of the results for patient selection safety concerns may not be well supported by data, in some areas, this may be considered standard of community practice. In such cases, radial artery cannulation is recommended with types A or B results, can be considered with type C results, and contraindicated with type D results.

Room and Patient Setup

Transradial coronary angiography can be performed from either the right or left arm. In general, the right arm is more convenient, as most catheterization labs are set up with the operator on the right side of the patient and the video screens on the left. Use of the right arm obviates the need to reach over the patient. Recent comparisons have suggested that left radial access with a more similar approach to the ascending aortic as that of femoral angiography may take less time and use less contrast than the right radial approach, especially early in the learning curve. During catheterization via the left radial artery, such as in patients with a left internal mammary artery graft, the left arm should be comfortably adducted over the patient's body toward the operator (standing on the right side) after access has been obtained. The pulse oximeter is placed on the index finger of the ipsilateral hand used for radial access. Some labs display the pulse oximetry waveforms at all times.

For either right or left radial approaches, correct positioning and preparation of the patient's arm are important for successful arterial access (Fig. 2-7). The arm board, typically a rectangular or banjo-shaped board, is securely placed under the patient's torso to provide support for the patient's arm and catheterization equipment. After the distal forearm has been shaved, the arm is placed on the arm board. In some labs the arm is placed at the patient's side, such that the radial

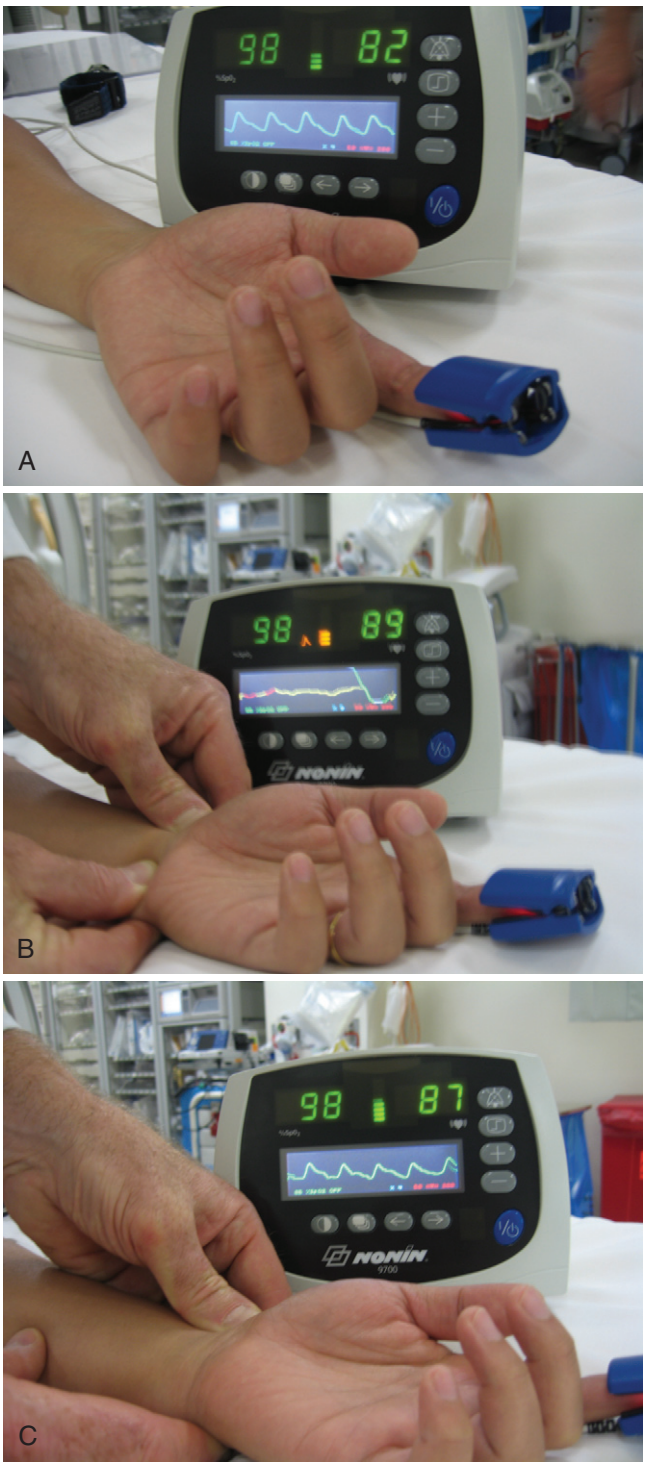


Figure 2-6 Oximetric Allen's test. **A,** Before radial or ulnar artery compression, pulse oximeter waveform is normal. **B,** Waveform is flat when both radial and ulnar arteries are compressed. **C,** Pulse waveform is normal when only ulnar is released. Radial artery is still compressed. This is a type A response. Type B is blunted waveform, and type C is flattened wave.

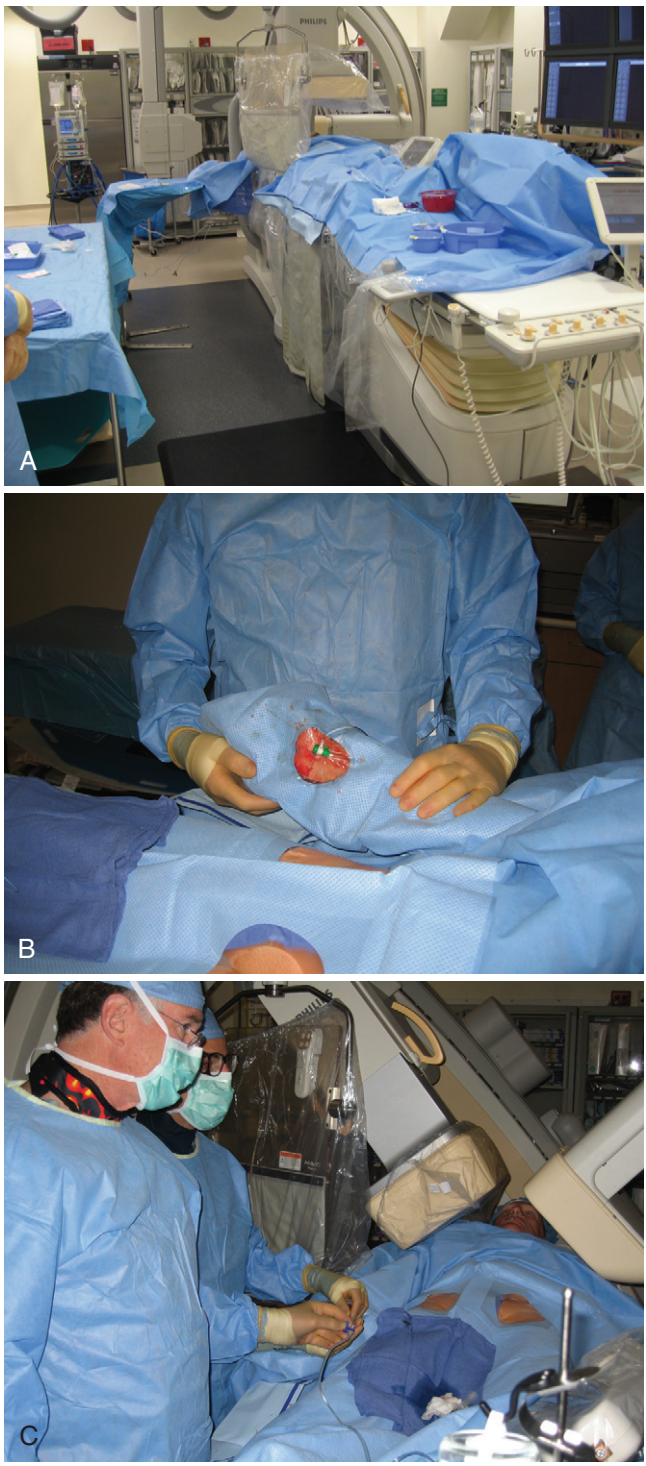


Figure 2-7 **A,** Right arm is positioned extended on arm board. **B,** After radial sheath insertion, the arm is moved to the patient's hip for introduction of catheters and **C,** performance of angiography and intervention.

and femoral arteries are in parallel. In other labs, the arm is moved to the patient's side after arterial access. This placement next to the leg decreases operator radiation exposure and removes the need for specialized drapes. For right radial cases, towels are stacked underneath and around the patient's arm to provide a level work space that is at the same elevation as the anterior surface of the patient's body. The wrist is supinated and hyperextended slightly, using a rolled towel or other soft object placed under the wrist. Over-hyperextension of the wrist should be avoided, as the arterial pulsation can be blunted by this maneuver. The arm can be stabilized with tape or an elastic bandage. An optional short (elbow to hand), cushioned arm board typically used for arterial pressure lines can also help to secure the wrist in an optimal position (Fig. 2-8). The short arm board is especially useful for left radial cases and allows for adduction of the whole arm toward the operator while maintaining correct positioning of the wrist.

After proper positioning of the patient's arm, a sterile field is created. A sterile top drape with a circular adhesive cutout in the middle is placed over the wrist, exposing the most distal portion of the forearm where the point of maximal radial arterial pulsation is felt. Several sterile towels are then draped around the sides of the exposed area. An innovative way to keep the patient's hand both sterile and free of blood during the procedure is to place a sterile glove on the patient's hand prior to the top drape (Fig. 2-9). The femoral artery should be prepped

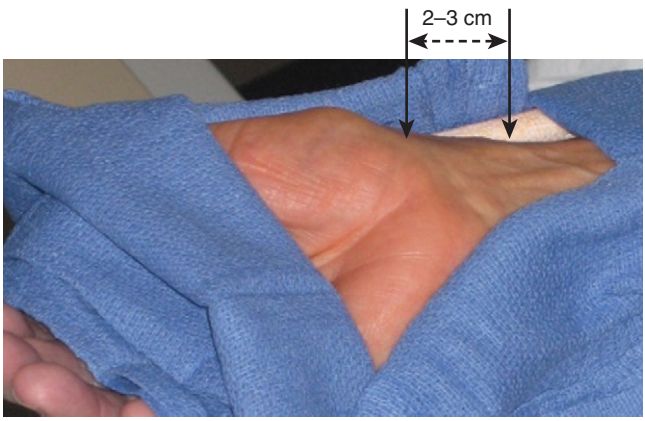


Figure 2-8 Draping of the hand with sterile towels.

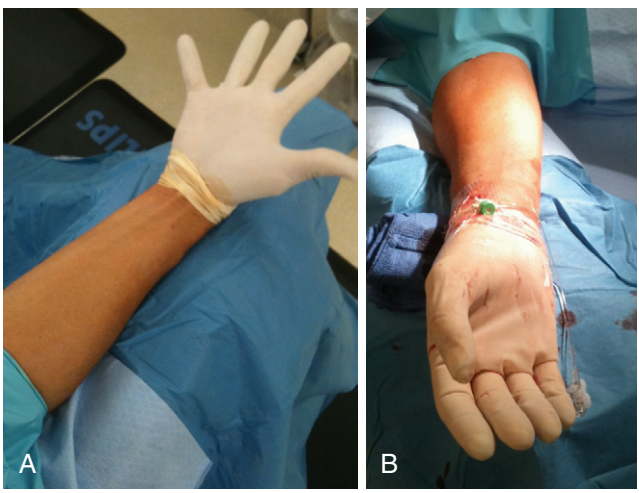


Figure 2-9 **A, B,** An alternative method to drape the hand is to cover the hand with a sterile glove.

and draped simultaneously in the event of conversion to a transfemoral approach (although converting from one radial to the other is frequently a better option) or the urgent need for a balloon pump.

Radial Artery Access and Sheath Introduction

The most common cause of failed transradial catheterization is unsuccessful radial arterial access, and the first radial attempt has the highest chance of success: an injured artery may spasm, making subsequent attempts more difficult. Operators should thus proceed slowly and carefully, especially when first learning to obtain radial artery access. Key to reducing local vasospasm is general sedation and mild analgesia coupled with adequate but limited local anesthesia.

Once draped, the radial pulse is palpated. The ideal puncture site is 1 to 2 cm proximal to the radial styloid, the bony prominence of the distal radius. Sites near the radial styloid risk puncture of the radial artery after its bifurcation and may make threading the guidewire difficult through a stretched and flattened radial artery. Extremely proximal punctures are more difficult to compress and can result in hematoma formation. A small amount (no more than 1 mL) of local anesthetic is injected subcutaneously, raising a small wheal similar to a tuberculosis skin test. Larger amounts of anesthetic can obscure the pulse. The course of the radial artery is fixed with the index and middle fingers of the nondominant hand. Using the other hand, the micropuncture catheter-over-needle system is inserted with the bevel facing up at a 30- to 45-degree angle to the skin along the direction of the radial artery until a flashback of blood is visualized. The system is advanced until the back wall of the vessel is punctured and blood flow stops. This is known as a "through and through" technique (Fig. 2-10). Occasionally, no flashback of blood is observed, although the operator is confident of an intra-arterial puncture. The catheter-needle system should continue to be advanced to complete the back wall puncture in this situation. The needle is then removed, and the catheter is withdrawn until its tip is intraluminal, as confirmed by freely flowing blood. A 0.018- or 0.025-inch straight-tip or slightly angulated guidewire is gently inserted using a twirling motion. There should be no or little resistance to wire introduction: if resistance is encountered, fluoroscopy should be used to immediately visualize the position of the wire. Once the wire is securely and freely in the vessel, the cannula is removed over the wire. Figure 2-11 shows the steps for radial sheath insertion.

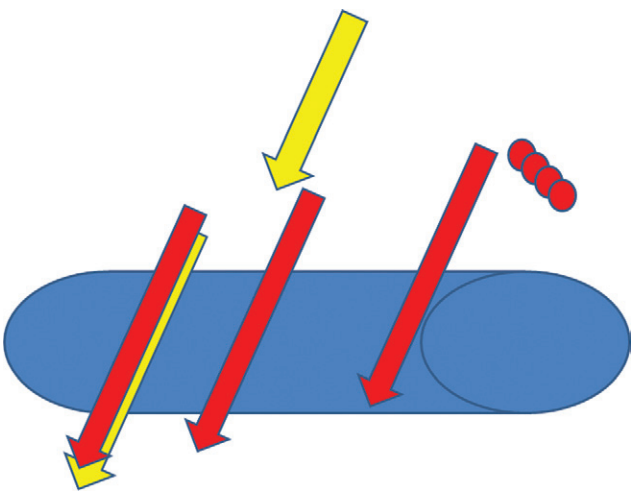


Figure 2-10 "Through and through" technique for radial puncture. (Reprinted from Nguyen TN, Colombo A, Hu D, *et al.,* eds. *Practical handbook of advance interventional cardiology*, 3rd ed. Copyright (2008) with permission from Blackwell.)

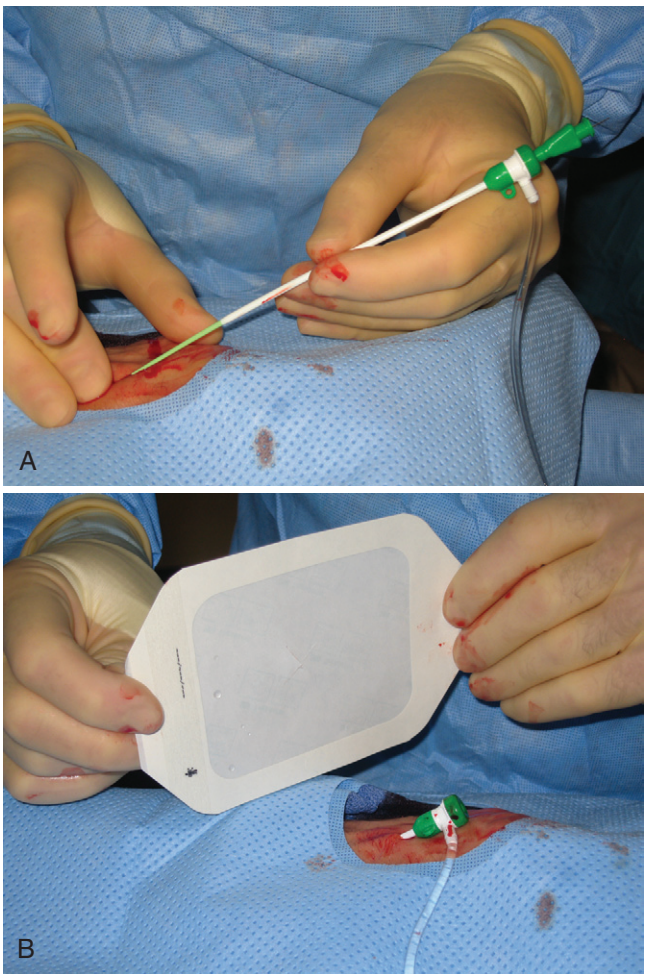


Figure 2-11 Radial artery access and sheath introduction. Once draped, the radial pulse is palpated. The point of puncture should be 1 to 2 cm cranial to the bony prominence of the distal radius. Administer small amount of lidocaine into the skin. Use the micro-puncture needle at 30- to 45-degree angulation; slowly advance until blood pulsates out of needle. It will not be a strong pulsation due to small bore of needle. Fix needle position and carefully introduce 0.018 guidewire with twirling motion. There should be little or no resistance to wire introduction. Remove needle. Make small incision over wire in preparation to introduce sheath (this step may be optional with some ultra-tapered dilators). **A,** Advance sheath over wire into artery. If sheath moves easily, advance to hub. If resistance is felt with sheath halfway in artery, remove wire and administer vasodilator cocktail. Reinsert wire and continue to advance sheath. **B and C,** Secure sheath with clear plastic dressing or suture. **D,** After sheath is positioned and flushed, the arm can now be moved to patient's side for catheter introduction.

Continued

Some operators prefer single anterior wall puncture of the radial artery using a bare metal needle. After the initial flashback of blood, the needle is advanced a millimeter further to ensure that the whole tip, not just the tip of the bevel, is intraluminal. If blood continues to flow freely, the needle is fixed, and a 0.025-inch straight-tip wire is advanced into the artery. The needle is then removed. Note that only metal guidewires should be used with bare metal needles, as plastic-coated wires used in this scenario can be shredded if they are pulled back against the bevel.

Most radial artery sheaths have a tapered tissue dilator and vary in French size and length, ranging from 10 to 36 cm long. In our experience, the combined use of a graduated dilator system and hydrophilic-coated

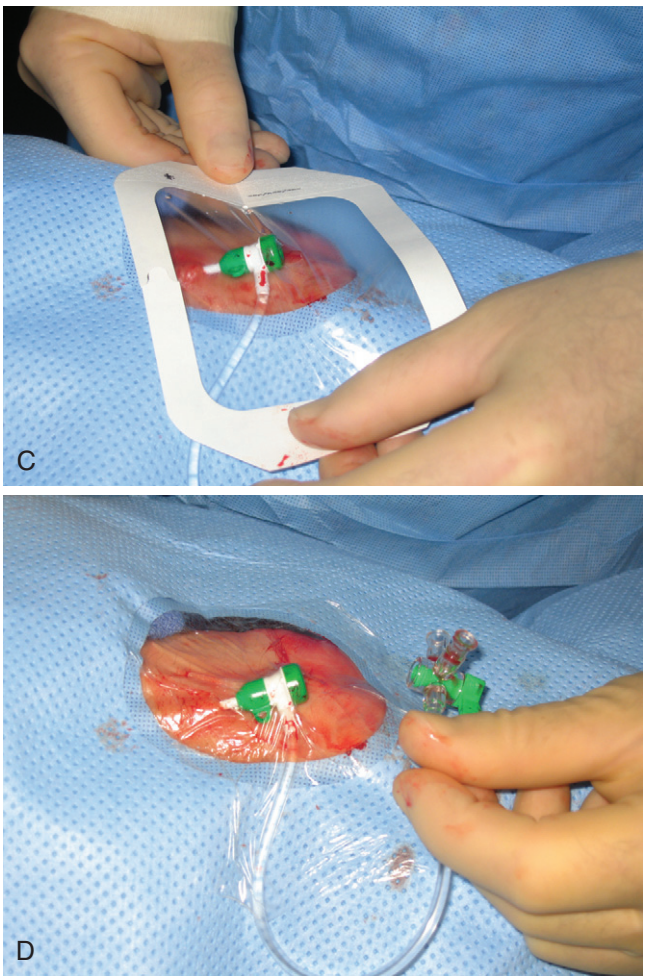


Figure 2-11, cont'd

sheath typically obviates the need for a skin nick prior to sheath insertion. Some operators still prefer to make a small incision over the wire in preparation for sheath introduction. Hydrophilic-coated sheaths can reduce radial artery spasm and pain upon sheath withdrawal, as well as postprocedural inflammatory reactions. Some operators advocate using long sheaths for patient comfort and better catheter manipulation. In patients with smaller stature, however, long sheaths may reside in the brachial artery, and the impact of using longer sheaths on long-term patency of the radial artery is unknown. After loading the sheath onto the wire, the sheath is held close to the distal tip to avoid bending of the equipment. Steady but firm pressure is applied until the dilator has advanced into the artery. The same steady pressure is used to advance the sheath past the dilator–sheath transition point into the artery. If there is resistance, use wet gauze to make the hydrophilic sheath slicker; gentle rotation during advancement also can facilitate sheath insertion. Alternatively, the wire can be removed with the sheath halfway in and then reinserted after administration of a vasodilator cocktail through the dilator. Once the sheath is fully advanced to the hub, the dilator and guidewire are removed together, and the sheath is flushed. A large Tegaderm placed over the head of the sheath can secure the system without the need for sutures. A nick in the Tegaderm at the opening of the sheath diaphragm allows ready access for catheters and guidewires.

Concomitant Medications

Medications are crucial adjuncts to successful TRI, as the radial artery is very vasoactive, and flow around the sheath at the site of radial access is sluggish, increasing the risk for thrombus formation. Anxiety and high sympathetic tone are significant contributors to vasospasm, making the use of local anesthetic, sedation, and analgesia important factors in keeping patients comfortable and relaxed. Once access is achieved, intra-arterial injection of a spasmolytic agent, such as nitroglycerin, verapamil, diltiazem, adenosine, or papaverine, is essential for minimizing vasospasm and discomfort. Calcium channel blockers may be longer lasting than nitrates, although they are also associated with an intense burning sensation and should be diluted to mitigate discomfort. Spasmolytics can be repeated as necessary throughout the procedure during catheter exchanges, if hemodynamics allow. For anticoagulation, weight-adjusted unfractionated heparin (UFH) 40 to 70 U/kg up to 5000 U is administered to prevent thromboembolic complications and radial artery occlusion. This can be given immediately after insertion of the radial artery sheath, although some operators prefer to wait until successful passage of a guidewire into the ascending aorta has been achieved in case of need to convert to the femoral approach. Administration of UFH *intravenously* is preferred, as it causes less discomfort than intra-arterial injection. A sample regimen of drugs and doses used in our lab is provided in Table 2-3.

Angiographic Catheter Selection

Careful catheter selection for the radial approach is important. Table 2-4 lists the most commonly used catheters. The standard preformed diagnostic Judkins or Amplatz catheter shapes may be used but require more manipulation for selective engagement of the coronary ostia. For selective engagement of the left coronary ostium, a Judkins left 3.5 catheter is typically used. Several catheters that can be used to approach both the left and the right coronary arteries have been developed (Fig. 2-12). A decrease in catheter exchanges has been shown to decrease the incidence of spasm. Use of the left radial artery approach provides easier manipulation of the standard preformed Judkins shapes with minimal effort. The left arm should be brought over the abdomen so that the operator can work from his or her usual position on the right side of the patient.

Table 2-3

Medical Regimen for Radial Catheterization

Before Procedure
Topical anesthetic cream over the radial artery (optional)
Sedation: 0.5-1.0 mg Versed and 50 mcg fentanyl
Typically given together, but one or the other may be used in the elderly or in patients with respiratory compromise.
Local anesthetic 1% lidocaine
Use no more than 0.5-1 mL of lidocaine.
After Sheath Insertion (Before Catheter Insertion)
Intra-arterial spasmolytic
Nitroglycerin 100-200 mcg for most patients
Verapamil 2.5 mg diluted into 10 mL of blood or saline
Intravenous unfractionated heparin 40 U/kg bolus up to a maximum of 5000 U
After Procedure and Before Sheath Removal
Verapamil 1-2.5 mg (optional) IA

Table 2-4

Most Commonly Used Catheters for Radial Coronary Angiography

Right Coronary Artery
1. Judkins right catheter
2. Amplatz right catheter
3. Amplatz left catheter
4. Jacky
5. Tiger, special shapes
Left Coronary Artery
1. Jacky
2. Tiger, special shapes
3. Judkins left catheter (typically 3.5 cm)
4. Multipurpose catheter
5. Amplatz left catheter
Vein Grafts
1. Multipurpose catheter
2. Amplatz left catheter
3. Judkins right catheter

Coronary Cannulation From the Radial Approach

The angiographic catheter is premounted on a 260-cm exchange-length 0.035-inch guidewire and inserted several centimeters into the sheath. The guidewire should be gently advanced through the arm. In the beginning, it is helpful to watch advancement of the wire under fluoroscopy to become familiar with normal anatomy. Later, it is often not necessary to use fluoroscopy until the wire has reached the axillary artery. At this point, fluoroscopic guidance is important to avoid cannulation of side branches, such as the mammary or vertebral arteries. If resistance is encountered, or the patient complains of discomfort, fluoroscopic visualization and even gentle contrast injection by hand can be used to investigate the source of resistance and for potential complications.

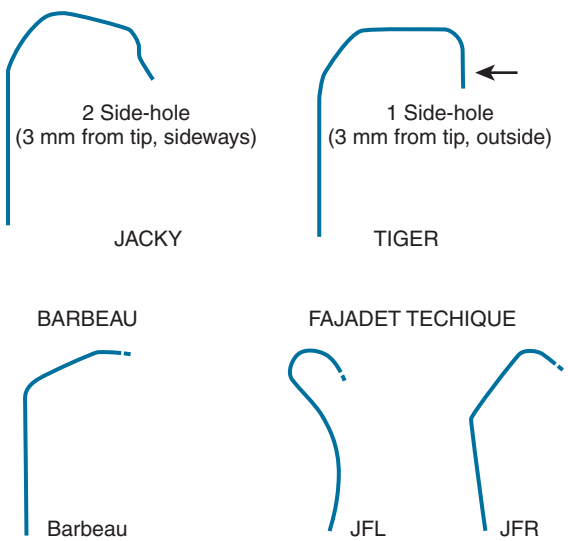


Figure 2-12 Catheter configurations designed for radial artery access coronary angiography.

Once the wire has reached the entry of the subclavian artery into the aorta, the patient is instructed to take a deep inspiration (the "magic breath"), which can often help to straighten the angle from the innominate into the aorta and direct the wire into the ascending rather than descending aorta. Alternatively, the catheter can be advanced into the aortic arch and, with counterclockwise rotation, can be used to guide the wire into the ascending aorta. A left anterior oblique (LAO) camera position can help delineate the ascending from descending aorta when positioning the guidewire. Once access has been obtained to the ascending aorta, the 260-cm exchange wire should be used to maintain that position during all catheter exchanges.

Transradial PCI

The basic principles of coronary intervention from the wrist are very similar to those used from the leg, and the learning curve for transradial PCI mainly involves gaining experience with guide catheter insertion and positioning. Compared with diagnostic catheters with tapered, soft tips, guide catheters should be advanced more gently until well above the elbow. Tortuous vessels straightened by a guidewire may create tissue invaginations on which the stiffer front edge of guide catheters can catch and even perforate.

Once the guide catheter is positioned into the ostium of the target vessel, the PCI procedure is identical whether from femoral or radial approach. As with the diagnostic technique, deep breath holds during cine runs should be avoided with transradial catheterization, as deep breaths may lead to catheter dislodgement from the coronary. Another important difference is the limitation on guide catheter size used for TRI. There are reports of use of 7F and 8F guide catheters from the radial approach in selected patients. However, these larger sizes may not be used in everyone, while the radial conduit in both males and females will routinely accommodate 5F and 6F catheters. Large-lumen catheters suitable for TRI accommodate rotablator burrs and simultaneous two-stent and two-balloon techniques, supporting performance of complex PCI procedures from the wrist without worry about bleeding from the more intensive anticoagulant and antiplatelet regimens used in those settings.

Guide Catheters

In general, there are two types of radial guide catheters: (1) dedicated left and right coronary catheters and (2) universal catheters, intended to cannulate both the left and right coronaries with a single instrument. Unlike diagnostic procedures, which generally involve cannulation of both left and right coronary arteries, many PCI procedures involve only one or the other, making dedicated left and right catheters very useful and familiar to work with. For multivessel procedures involving right and left coronaries, universal guide catheters, such as the Kimny, Barbeau, and MAC 3030, may obviate the need for exchanges but may require more manipulation to intubate the coronaries. Furthermore, although such universal guide shapes can intubate both coronaries, they may not provide sufficient guide support for procedures in both coronaries. Thus, most experienced labs favor the use of traditional, dedicated catheters for PCI. Examples of guiding catheters are shown in Figure 2-13.

Guides that work well from the leg—EBU, XB, Judkins, and Amplatz shapes—all work equally well from the wrist, although the process of intubation of the coronary is somewhat different between the two techniques. A useful tip for guide catheter intubation from the wrist is to leave the 0.035-inch wire in the guide, feeding the back end out through the Tuohy-Borst connector and carefully flushing out air. The wire can

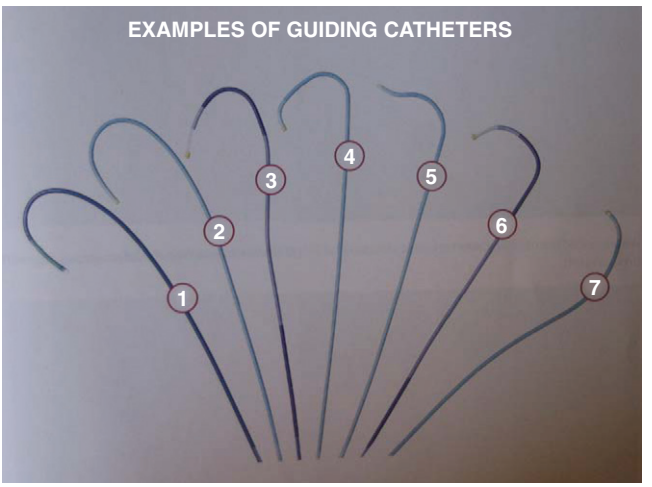


Figure 2-13 Examples of guiding catheters. (*1*) EBU, (*2*) XB, (*3*) Voda, (*4*) Judkins left, (*5*) Amplatz left, (*6*) Patel right, (*7*) Judkins right. (From Patel, T *et al. Patel's atlas of transradial intervention: the basics*. Seattle, WA: Sea Script Company, 2007.)

then safely add torque control, and contrast can be injected to ensure good positioning in the coronary before the wire is withdrawn completely. Also important to note is that guide manipulation through the wrist may initially be counterintuitive: significant tortuosity in the subclavian or innominate artery can interfere with normal transmission of torque, causing unexpected results from standard catheter manipulations. Pulling back on the hub of the guide with counterclockwise torque may have the reverse effect than from the leg and can cause the tip to advance in the aortic root. In order to have the guide move backward, the catheter should be advanced, pushing the fulcrum downward into the aortic root and withdrawing the catheter tip from the coronary ostium. With practice, operators can develop the ability to predict and even utilize such paradoxical responses to guide catheter manipulation in patients with significant tortuosity or anatomic variants.

Although each catheterization lab has its own preferences for guide catheter choice, good options for left coronary cannulation include the EBU, XB, Ikari, and Judkins left catheters. These catheters should be delivered over the guidewire into the left coronary cusp below the ostium of the left main. The catheter is then advanced with counterclockwise torque to facilitate cannulation of the ostium. If catheter tip adjustment is necessary once in the left main, pullback (sometimes with clockwise rotation) will allow for more coaxial engagement. Subselecting the left anterior descending artery can be achieved by slight advancement of the catheter, while pulling the guide back will subselect the left circumflex artery. If using a Judkins left (JL) guide, certain adjustments in catheter size should be made because of the different orientation of the catheter in the aorta. When approaching via the right radial artery, engagement of the left coronary typically requires a 0.5-cm smaller curve catheter than that used for transfemoral catheterization. Thus, TRI from the right radial artery is typically accomplished using a JL3.5. In contrast, the standard JL4 can be used from the left radial artery. For very high anterior left main origins, an Amplatz guide catheter may be useful.

Preferred options for right coronary artery cannulation will again vary based on cath lab preference. Amplatz right and left, multipurpose, and Ikari and Judkins right (JR) catheters can all be used. TRI using a JR guide from the right radial artery requires a 1-cm larger curve than that used from the leg, typically a JR5 catheter, while TRI via the left radial artery can be achieved with the same size curve as from the leg, often

the standard JR4. The AL 0.75 guide shape often provides excellent support and control for more challenging PCI of the right coronary artery requiring secure backup from the right radial approach. As with transfemoral interventions, a second wire can also be used to provide extra support, especially for ostial lesions.

Coronary Artery Bypass Graft Cannulation

For patients who have undergone coronary artery bypass surgery, knowledge of graft anatomy is important for planning the radial approach. In general, patients who have had internal mammary artery (IMA) grafts placed are most easily approached via the ipsilateral radial artery. Several types of guide catheters, including the JR and internal mammary, can be used to cannulate the IMA. The IMA can be engaged on the initial advancement of the catheter toward the ascending aorta to avoid having to direct the guidewire into the ascending aorta twice. The catheter should be positioned proximal to the takeoff of the IMA and then slowly pulled back with clockwise torque until the IMA is cannulated.

Catheterization of the contralateral IMA obviates the need for bilateral radial arterial access but can be technically challenging. Cannulation of the left IMA via right radial access has been shown to be successful using specially designed catheters or long lubricious guidewires that can establish a position well distal into the left arm over which the catheter can track to the level of the IMA. For example, engagement of the left IMA from the right arm can sometimes be accomplished by first advancing a JL curve catheter into the left subclavian artery and passing an exchange-length glide-wire far down into the arm. The JL is then exchanged over the wire for an internal mammary catheter. If needed, manual compression of the left brachial artery or a blood pressure cuff can be used to anchor the wire in the contralateral arm during advancement of the internal mammary catheter. In general, cannulation of IMA grafts via the ipsilateral radial artery remains much more consistent and is recommended if possible, particularly for PCI.

Saphenous vein graft (SVG) interventions may also be more easily achieved from the left arm than the right. Judkins right, Amplatz, and multipurpose guide catheters can all be used for vein grafts, especially those arising from the anterior surface of the aorta. Universal catheters will often successfully cannulate SVGs on either side of the aorta but may not consistently provide adequate backup for PCI.

Troubleshooting Access

Operators should become familiar with complexities, challenges, and management of complications in the setting of diagnostic procedures and catheters to help with potential difficulties that may be encountered during TRI. Some of the more common ones are discussed below.

Radial artery spasm is a common problem. Risk factors include female gender, younger age, small radial artery diameter, diabetes, anxiety, unsuccessful access at first attempt, and prolonged catheter manipulation. Judicious use of sedation, analgesia, and spasmolytic agents is important not only for prevention but also treatment of spasm. Arterial spasm may result in a diminished or even absent pulsation during attempts at arterial access. If this occurs, operators can wait for the spasm to subside, attempt radial arterial access again at a more proximal site, or give a sublingual nitroglycerin. If spasm is intense and irreversible, it may become necessary to switch to a completely different site altogether—ideally to the contralateral radial artery. In the event of severe spasm during sheath removal at the end of the case, withdrawal of the sheath gently but steadily will often minimize patient discomfort. In addition

to pharmacologic therapies, warm compresses over the forearm can be used to relax the spastic artery. In extreme rare cases, an axillary block to relax the radial artery or even the involvement of a vascular surgeon may be necessary to remove the sheath. Excessive force should never be applied, as this may result in avulsion or rupture of the radial artery.

Sensitivity to any resistance during advancement of the guidewire after sheath insertion is an important part of radial technique. There should be a low threshold for use of fluoroscopy. Gentle hand injection of contrast through a catheter or through the sheath should be performed to identify the cause of resistance. Angiography may reveal tortuosity of the artery, the presence of side branches, or an abnormal takeoff of the radial artery (typically proximal to the elbow off the brachial artery).

Radial Artery Stenosis

Radial artery stenosis or occlusion can also cause difficulty with wire advancement. Depending on the finding, a Wholey wire or hydrophilic-coated wire may aid in traversing tortuosity or navigating arterial branches.

Radial Artery Loop

An arterial loop does not necessarily preclude a transradial approach, as passage of a 0.014-inch hydrophilic coronary wire can sometimes straighten out tortuous loops, allowing for smooth advancement of catheters. Subintimal positioning of the wire may be demonstrated by the presence of a dissection plane on radial artery angiography. If this occurs, the procedure can usually proceed, if the wire can be advanced into an intraluminal position. Insertion of a long radial artery sheath or a catheter across the dissection can help tack up the intimal flap and heal the dissection by the time the procedure ends. Repeat radial arterial angiography at the end of the case should be performed to assess for any residual dissection. For severe dissection or perforation that has been tamponaded by the catheter or a long sheath, the guide catheter can be withdrawn over a wire just proximal to the insult, and injection confirming closure of the wound should be performed prior to guidewire removal. This will protect the true lumen until the result is documented.

Sheath Removal, Radial Artery Hemostasis, and Postprocedure Care

Hemostasis can be achieved by manual compression or through use of a mechanical device, ranging from a simple plastic hemodialysis band compressing a gauze bullet over the radial artery puncture to specifically designed compression bands, such as RadiStop (St. Jude Medical) or TR Band (Terumo). The TR Band is popular for its ease of use and the ability to directly visualize the puncture site through the clear plastic. Regardless of device chosen, there are a number of common and important steps to be taken to ensure hemostasis.

Given the superficial position and easy compressibility of the radial artery, checking an activated clotting time is not necessary prior to sheath removal. The band should be positioned loosely around the wrist with the compression portion of the device positioned to cover the skin nick and arteriotomy site. Another dose of antispasmolytic agent should be administered just before the sheath is pulled to minimize radial artery spasm and patient discomfort. The sheath should be removed slowly and smoothly while slowly tightening the band (either by pulling or by inflating the pressure bladder). A common mistake is tightening the band too aggressively before the sheath is completely removed, leading to patient discomfort. When using a TR Band, the sheath should be pulled out several centimeters, and the area should be cleaned and wiped dry. The green mark is centered over the site of arterial puncture, and the band is secured

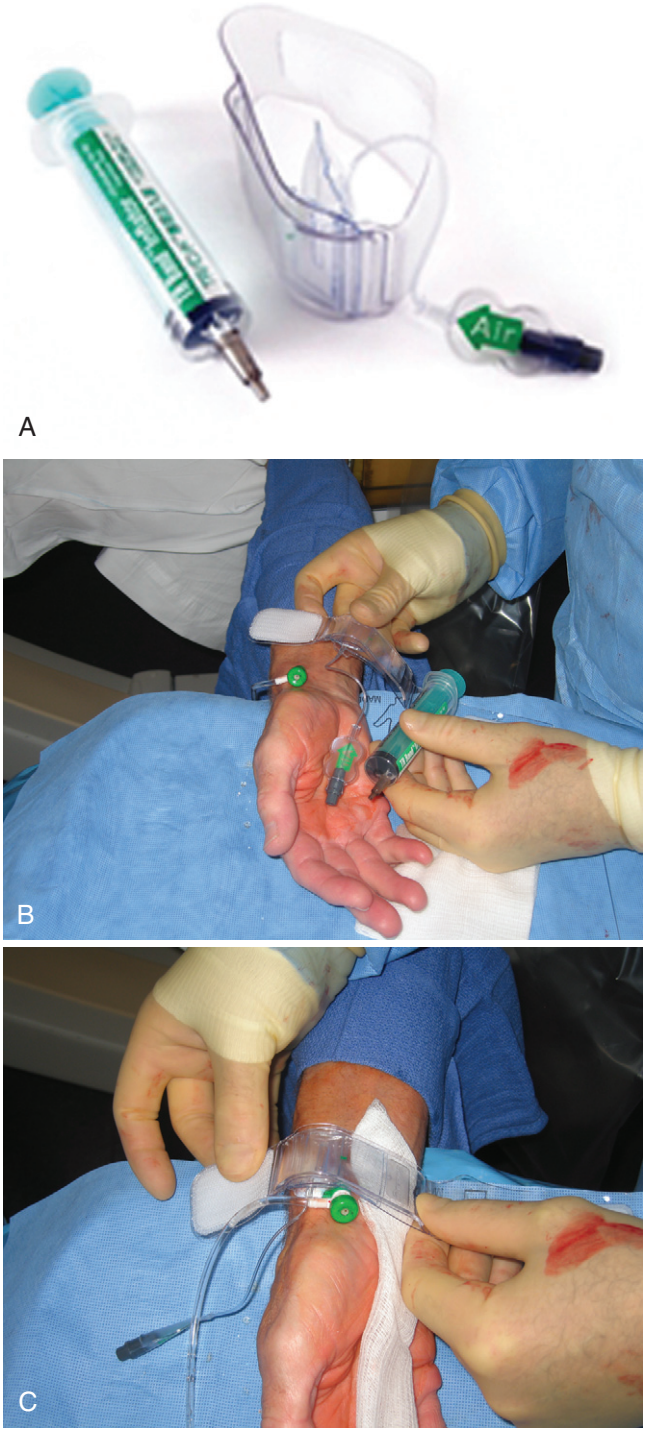


Figure 2-14 **A,** Terumo band with inflatable compression pad. **B,** Band applied around wrist with green dot over puncture. **C,** A thin gauze wick is placed beneath band to absorb blood when pressure is released to assess proper compression pressure in pad.

Continued

tightly around the wrist (Fig. 2-14). Fifteen milliliters of air should be injected into the TR Band port as the rest of the sheath is removed. The TR Band is slowly deflated until bleeding occurs, at which point 1 to 2 mL of air should be reinserted into the band. A residual plethysmographic waveform should be present after occlusion of the

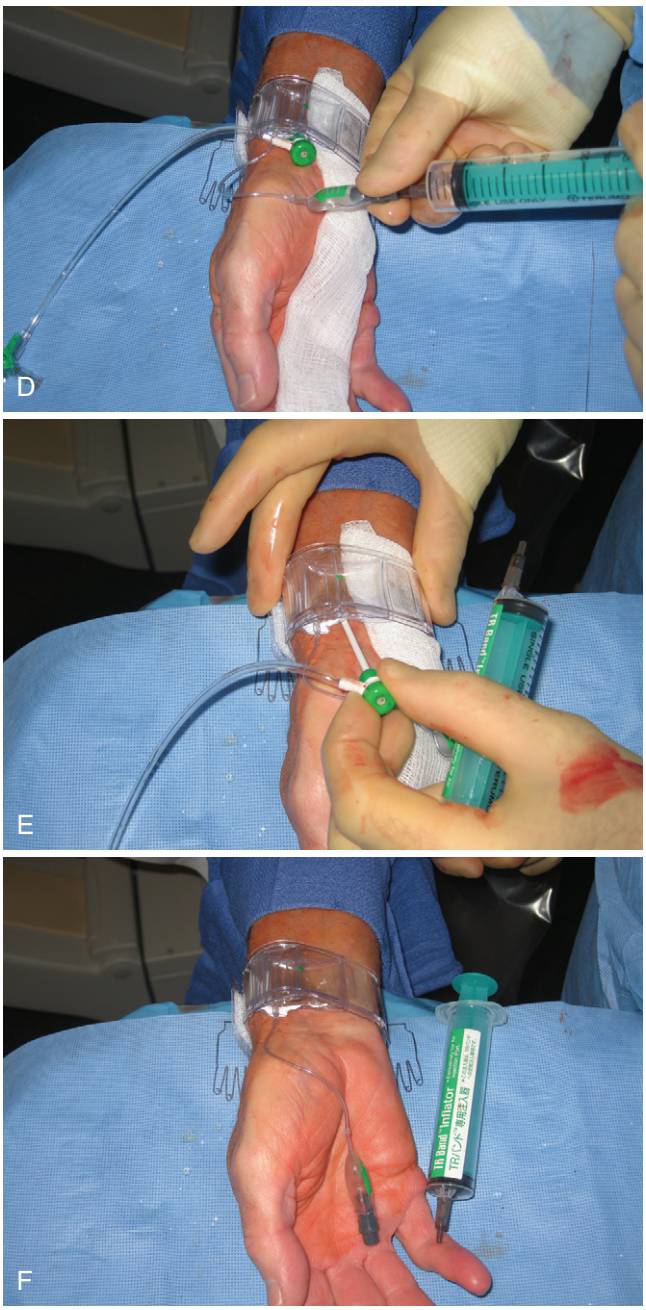


Figure 2-14, cont'd **D,** Compression pad inflated. **E,** Sheath removed. **F,** Final result.

ulnar artery (i.e., a normal reverse modified Allen's test), confirming patency of the radial artery. This technique, known as "patent hemostasis," reduces the incidence of radial artery occlusion. If there is no flow due to the compression band, removing 1 mL air at a time until a blood flash is visualized and observing may establish a patent hemostasis level of compression. Our lab uses the following TR Band deflation protocol: the TR Band is left undisturbed for 30 minutes (for diagnostic procedures) or 90 minutes (for interventional procedures) after initial inflation and achievement of hemostasis. Three milliliters

of air are then removed every 15 minutes until complete deflation of the band. If bleeding occurs, 3 mL of air are reinserted, and the timer is restarted. Once the band is deflated and removed, a sterile dressing is applied.

Patients who have undergone TRI can be active postprocedure as soon as their sedation has worn off and are typically ready for discharge 2 hours after removal of the TR Band. Important restrictions include not using the affected wrist for 24 hours. Patients are instructed to elevate the arm and hold pressure in the event of small hematoma formation and to report large hematomas or significant forearm or hand pain.

Complications

Radial Artery Spasm

Some spasm during sheath withdrawal is common. The sheath should be removed quickly but gently to produce the shortest duration of discomfort (if any). Despite all precautions, if radial artery spasm occurs or persists, consider administering more significant analgesics and sedation. If spasm is severe and the sheath is immovable, the following actions can be undertaken:

1. Calcium channel blockers (e.g. nicardipine, nifedipine, verapamil, diltiazem)
2. More analgesia and sedation
3. Warm compresses over the forearm to relax the spastic artery
4. Nitroglycerin 200 mcg intra arterial; repeated if necessary

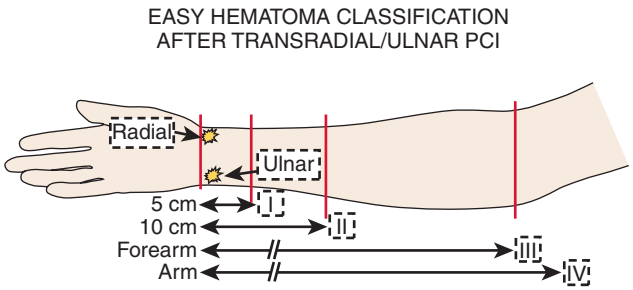
If this fails, wait for an hour and try again. During this time, maintain proper sedation and deep analgesia (morphine). If nothing helps, an axillary block might be required to relax the radial artery. Never apply excessive force, as this might result in rupture or avulsion of the radial artery. Ultimately, the vascular surgeon can be consulted to remove the sheath, but this is rare.

Arm Hematoma

In the early stages of a transradial program, an unrecognized hematoma can develop even under the watchful eyes of a provider. These hematomas can be more subtle than those seen from the transfemoral approach, and no overt bleeding is recognized especially since the arm is draped, and swelling is not recognized until the end of the procedure. Patients complaining of pain or paresthesia (numbness) warrant a close evaluation. Check under the drapes. Developing hematomas can be averted with a careful arm-wrapping technique. After obtaining radial puncture hemostasis, wrap the arm loosely with gauze and secondarily wrap from the elbow to the wrist with elastic tape or an ace bandage providing compression to the forearm. While this is in place, recheck your hemostasis device and reposition if needed. After a few short minutes, remove the tape and recheck the forearm; if it is not softer, re-wrap with slightly higher tension and recheck hemostasis device.

The most serious complication of forearm bleeding and hematoma is compartment syndrome with resultant hand ischemia. This is an extremely rare but dangerous problem that requires surgical fasciotomy when it occurs. A less dangerous but significantly debilitating complication that has been reported after transradial catheterization is chronic regional pain syndrome, or reflex sympathetic dystrophy. This complication, thought to be related to prolonged access site compression, is extremely rare and conservatively managed.

Figure 2-15 provides a guide to radial artery hematoma complications and the management of these problems.



Grade	I	II	III	IV	V
Incidence	≤5%	<3%	<2%	≤0.1%	<0.01%
Definition	Local hematoma, superficial	Local hematoma with moderate muscular infiltration	Forearm hematoma and muscular inflitration below the elbow	Hematoma and muscular inflitration extending above the elbow	Entire arm (compartment syndrome)
Treatment	Analgesia Additional bracelet Local ice	Analgesia Additional bracelet Local ice	Analgesia Additional bracelet Local ice Inflated BP cuff	Analgesia Additional bracelet Local ice Inflated BP cuff	Consider surgery
Notes	Inform physician	Inform physician	Inform physician	Inform physician	STAT call to physician

Figure 2-15 Diagram of forearm hematoma classification and its management. Modified from Bertrand *et al. Circulation* 2006;114(24):2646–2653. Reprinted with permission from Kern MJ. *Transradial 101 handbook*. Malvern, PA: HMP Communications, 2011.

Radial Artery Occlusion

Approximately 3% to 5% of patients undergoing transradial coronary angiography develop radial artery occlusion. This is an asymptomatic complication, and 50% of such occlusions undergo spontaneous recanalization. Risk factors for radial artery occlusion include duration of catheterization time, longer length of sheath, high sheath-to-artery diameter ratio, insufficient anticoagulation, and prolonged compression time. Postprocedure radial arterial thrombosis rates are reported from 1% to 10%. These are usually asymptomatic but can cause arm soreness and discomfort. A vascular ultrasound is used to evaluate patency and adequacy of ulnar flow. If ulnar flow is adequate, supportive treatment with acetaminophen and warm compresses are all that is needed. Brachial arterial thrombosis is a very rare complication and should be treated by thrombectomy and followed by an evaluation for hypercoagulable state.

Rare Complications

Pseudoaneurysm is a rare complication that can be diagnosed by ultrasound and treated with compression or thrombin injection. Radial artery dissections and perforations are also rare events that will both seal internally with guide catheter placement. The use of hydrophilic sheaths has been infrequently associated with the formation of sterile abscesses, or granulomas. These typically develop 2 to 3 weeks postprocedure and rarely require drainage.

Key Points for Radial Artery Access

1. Always perform Allen's test. Proceed if type A or B response. Consider if type C response.
2. Use adequate patient sedation and access site anesthesia.
3. Use clues gained during diagnostic study for left or right arm access and coronary cannulation.

4. Work with the wrist close to the patient's body. Bring the left wrist onto the left hip for easier manipulations.
5. Use vasodilators and nitroglycerin during sheath removal if vasospasm causes pain.

Transforming a Catheterization Laboratory Program to TRI

Transforming a catheterization lab into a successful transradial program requires insight and commitment from all the members of the lab. Data consistently suggest that in the early stages of TRI experience, procedures are longer with greater radiation exposure for operators and greater contrast exposure for patients. These initial differences between femoral and radial approaches disappear with experience. Anticipating the inevitable "learning curve" associated with radial procedures is important in managing operator and staff expectations. Recognizing the importance of high procedural volume and committed focus on patient safety and benefit is also key to overcoming this early inefficiency.

In addition to managing perspective and expectations, proper lab setup and staff training play a crucial role in the conversion from transfemoral to transradial procedures. Transradial catheterization equipment must be readily available, and the staff should be trained to perform the modified Allen's test using pulse oximetry prior to patient preparation. The staff must also be trained in the setup of the patient's wrist using an arm board. Staff comfort and the "atmosphere" of the cath lab may importantly affect the patient on the table, and patient comfort can directly impact the success of a transradial approach, as anxiety-related high sympathetic tone contribute to radial artery spasm. A TRI program should take measures to improve the overall environment for staff and patients alike, such as by playing soothing music and through liberal use of conscious sedation.

Successful conversion to TRI offers a number of benefits for the program and hospital. Caring for patients on strict bed rest after a femoral case is time consuming, whereas patients are ambulatory almost immediately after a TRI procedure. The transradial versus transfemoral approach decreases nursing workload during recovery and decreases patient length of stay. Overall, adopting transradial access for catheterization leads to reduced use of resources during patient recovery, earlier patient discharge, and significant cost savings for the hospital.

Training Options

An important obstacle to the adoption of the transradial approach by many established "transfemoralists" and new fellows is the lack of exposure to, and formal training in, transradial catheterization at many institutions. Learning to perform cardiac catheterizations via femoral access remains an important skill, but early exposure to the transradial approach is key to building both a facility and comfort level with the technique. To this end, training programs should consider introducing both transradial and transfemoral approaches together from the start. Operators interested in learning transradial techniques should make use of educational transradial websites (www.transradialuniversity.com, www.transradialworld.org) as well as transradial workshops, live courses, and simulators.

TRI is an increasingly popular alternative to transfemoral procedures and provides a remarkable advance in patient comfort and safety without sacrificing procedural success or efficiency in appropriately selected patients. In experienced hands, TRI is considered the primary technique with transfemoral as the alternative. However, the shift to TRI as a primary invasive option requires significant training and commitment to overcome the learning curve. While this discussion is not meant to be all-inclusive, it will hopefully serve as a useful starting point for those interested in learning about transradial intervention.

Percutaneous Brachial Artery Access

In general, percutaneous brachial artery puncture should be abandoned in favor of radial access. For interventional procedures, brachial access is undesirable, since control of bleeding in the postprocedure period is often difficult. Brachial artery cutdown is no longer a standard technique. The brachial approach provides access to the descending aortic vasculature and may be advantageous in some lower extremity or renal procedures when lower extremity access is unavailable.

Additional Arterial and Venous Access for High-Risk Interventions

For patients at high risk of complications who may require urgent placement of a pacemaker and intra-aortic balloon pump (IABP) or another hemodynamic support device, an additional arterial or venous access is helpful. In some patients, monitoring pulmonary artery and/or wedge pressure may help medical management during a complex procedure. For IABP or temporary pacemaker use as a standby maneuver, a small 5F sheath introducer can be placed in the opposite femoral artery or vein at the beginning of the procedure, permitting immediate vascular access if urgent hemodynamic or pacing support is required. Two venous cannulae can be placed in one femoral vein if multiple venous catheters are anticipated. Remember, before IABP insertion, abdominal and iliac angiography should be performed to identify any significant peripheral vascular disease.

Overcoming Difficult Vascular Access Problems

Excessive Vessel Tortuosity

The most frequently encountered difficulty in advancing guide catheters is tortuosity of the iliac or subclavian vessels, a condition often found in elderly patients. A steerable 0.038-inch flexible guidewire (e.g., Wholey) is excellent for negotiating tortuous vessels. Its flexible, atraumatic, gently curved tip is steerable, increasing safety. In cases of extreme tortuosity, a right Judkins diagnostic catheter may be used to help direct the guidewire tip and control the advancement of the guidewire. Angiograms will delineate the arterial course and any other obstructive lesions. Once the guidewire is beyond the tortuous or narrowed segments, a long catheter exchange guidewire will be needed thereafter. A longer (>30 cm) vascular sheath can be positioned, but kinks from tortuous segments will increase friction with guide catheter movement. The trade-off of multiple friction points for some straightening of the vessel against the guide catheter kinking is often worth the effort. Catheter exchanges over a long 300-cm extra-stiff exchange wire will facilitate advancement of catheters across tortuous or atherosclerotic segments.

Commonly selected equipment for tortuous vessel problems includes:

1. Wholey 0.035-inch steerable guidewires
2. Long 300-cm regular exchange guidewires
3. Long 300-mg extra-stiff exchange guidewires
4. Long arterial sheaths in 23 or 90 cm

Peripheral Vascular Disease

Peripheral vascular disease (PVD) complicates access as well as guide catheter manipulation. Weak femoral pulses often indicate atherosclerotic obstruction at the level of the femoral, common iliac, or aortoiliac bifurcation. Inability to advance the guidewire to the central aortic position requires angiography to determine further maneuvers

needed to negotiate the femoral approach. In such patients, abdominal aortography and peripheral angiography are necessary to evaluate the extent of obstructive disease with focal iliac stenosis. Should a coronary intervention be required, some operators advocate iliac stent placement before proceeding with PCI. PVD may require the use of the radial approach. In patients with PVD of the lower extremities, coexistent subclavian atherosclerosis may also complicate arm access.

Inguinal Scarring or Access Through Site With Previous Vascular Closure Device

Inguinal scarring may be present in patients having multiple prior interventional procedures, aortofemoral bypass surgery, femoral bypass cannula access, IABP repair, or radiation therapy. In some of these patients, there may also be a synthetic arterial conduit graft. If possible, an alternative access site should be selected. Otherwise, access of a severely fibrotic or scarred groin or through a femoral bypass graft requires successive dilations with 5, 6, 7, and 8 French dilators before inserting a vascular sheath one size smaller. Most vascular closure device manufacturers indicate that reaccess through a site with a recently placed closure device can be performed without a problem if the device has no internal artery fixation component. Caution should be used when reaccessing all sites but especially those closed with Angio-Seal, although no reports of Angio-Seal anchor dislodgement during reaccess have been reported. Access of sites closed with such devices after 2 to 4 weeks is thought to be safe. However, the contralateral femoral artery should be considered in most cases for patient comfort. Entrapment of a StarClose clip during placement in a scarring groin has been reported.

Hemostasis After Femoral PCI

Complications related to vascular access management are the most significant cause of morbidity and prolonged PCI hospitalization. Timely and safe removal of the arterial sheath with minimal patient discomfort should be the goal of a successful PCI. Improved outcomes have been associated with using smaller sheaths, discontinuation of post-PCI heparin infusions, early removal of the sheath, and the use of vascular closure devices. Although results are improving, resources (both staff and equipment) necessary for appropriate sheath care and hemostasis should not be minimized.

Immediate Sheath Removal

The arterial and venous sheaths are not routinely left in place after PCI. The presence of a vascular sheath in a heavily anticoagulated patient predisposes to peri-sheath hemorrhage and local or retroperitoneal hematoma. Most laboratories remove sheaths within a few hours after the procedure or immediately remove the sheath in the laboratory and obtain hemostasis with a vascular closure device. Whenever possible, avoid overnight heparin infusion with next-day sheath removal.

PCI Sheath Removal

Sheath removal after PCI may occur in the lab, holding area, or patient bedside. Manual sheath removal proceeds as described for diagnostic procedures. Several points should be kept in mind:

1. Adjust bed height or use a foot stool so as to be able to exert maximal pressure for puncture site compression with minimal fatigue.
2. Ensure good intravenous ac cess.
3. Give local anesthetic 10 to 20 mL of 1% lidocaine (to the skin around the sheath and intravenous analgesics before sheath removal).

4. Have atropine and Demerol ready and within reach.
5. Before removing the sheath, check that the heparin is stopped, the activated clotting time (ACT) is less than 150 seconds, vital signs are stable, no chest pain is present, and there are no plans for recatheterization.
6. If arterial and venous sheaths were used, remove the arterial sheath first, preserving good venous access in case the peripheral IV stops working. Avoid prolonged pressure on the femoral vein. Prolonged venous occlusion, especially with pressure devices, may cause venous thrombosis. Check the leg and foot for cyanosis.
7. The duration of pressure holding, usually 20 to 45 minutes, depends on the sheath size, ACT, and ease of control of the bleeding.
8. When longer pressure application is needed after removal of a large sheath, IABP catheter, or cardiopulmonary support cannula, the FemoStop (St. Jude Medical) or similar compression device is the preferred method of arterial compression (Fig. 2-16). Compression devices provide a stable pressure, relative patient comfort, and easy adjustment of the degree of pressure applied. Compression devices are not intended for unsupervised use. The duration of pressure application should be kept to a minimum to decrease complications such as skin necrosis, nerve compression, or venous thrombosis.

Femoral Compression Systems

Some laboratories employ mechanical C-type clamps to assist in puncture site hemostasis. The clamp is effective but must be applied carefully

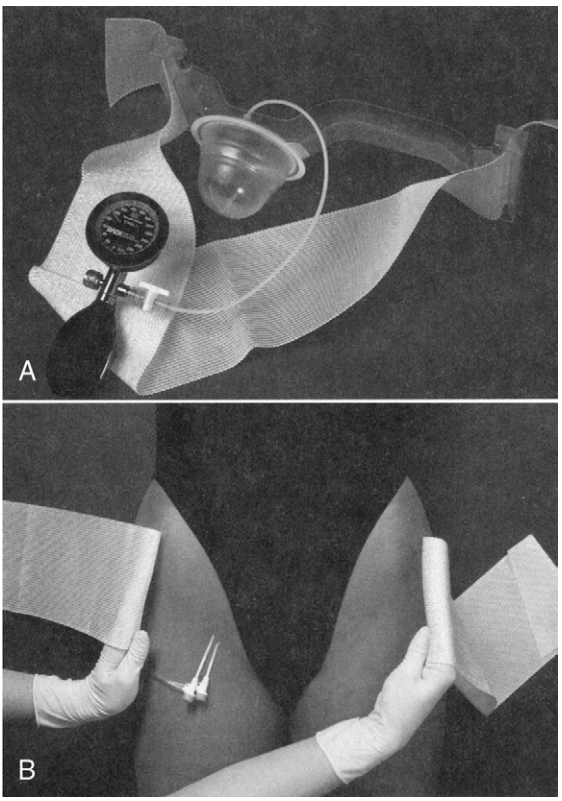


Figure 2-16 Use of the FemoStop **A**. Before proceeding, examine puncture site carefully; note and mark edges of any hematoma; record current blood pressure. **B,** Position belt. The belt should be aligned with the puncture site equally across both hips.

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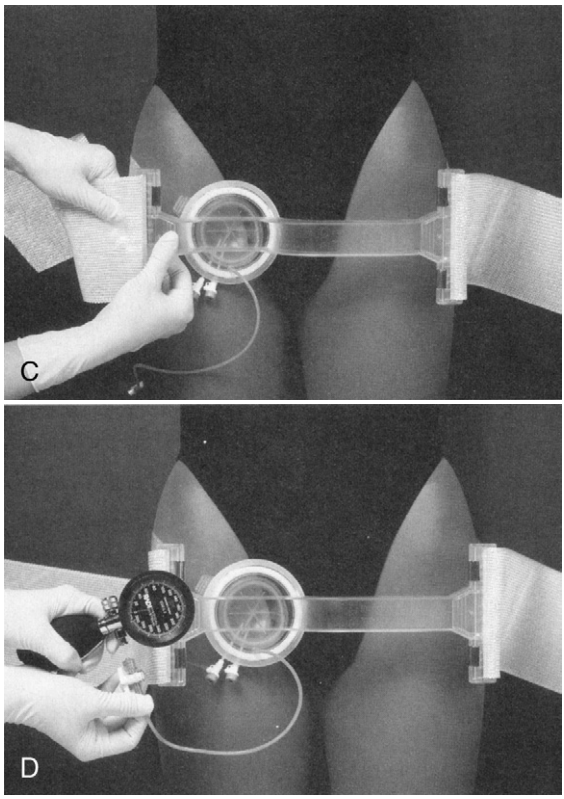

Figure 2-16, cont'd Center the dome and adjust belt. **C,** The dome should be centered over the arterial puncture site above and slightly toward the midline of the skin incision. The sheath valve should be below the rim of the pressure dome. Attach belt to ensure a snug fit. The center arch bar should be perpendicular to the body. **D,** Connect dome pressure pump.

Continued

by a trained individual and must be monitored frequently for misalignment, bleeding, or excessive pressure with limb ischemia (Fig. 2-17).

The FemoStop system (St. Jude Medical; Fig. 2-16) is an air-filled, clear plastic compression bubble that molds to the skin contours. It is held in place by straps passing around the hips. The amount of pressure applied is controlled with a sphygmomanometer gauge. The clear plastic dome permits visualization of the puncture site. The FemoStop is mostly used for patients in whom prolonged compression is anticipated or if bleeding persists despite prolonged manual or C-clamp compression. The duration of FemoStop compression and time to removal of the device varies depending on the patient and staff protocols. In some hospitals, the time from application to removal may be less than 30 minutes. In other patients in whom hemostasis is required, the device may be left at a lower pressure for longer.

Ambulation After Sheath Removal

Depending on sheath size and success of a vascular closure device, bed rest varies from 2 to 8 hours. Generally, ambulation can occur 2 to 4 hours after sheath removal using a vascular closure device. Ambulation should be gradual based on the timing of conscious sedation. Palpation for pulsatile mass and auscultation for bruits should be performed before the patient is discharged. Risk factors for pseudoaneurysm include continued anticoagulation after sheath removal, large sheaths (>10F), hematoma, and low puncture site. These considerations still must be applied to patients who have received a vascular closure device.

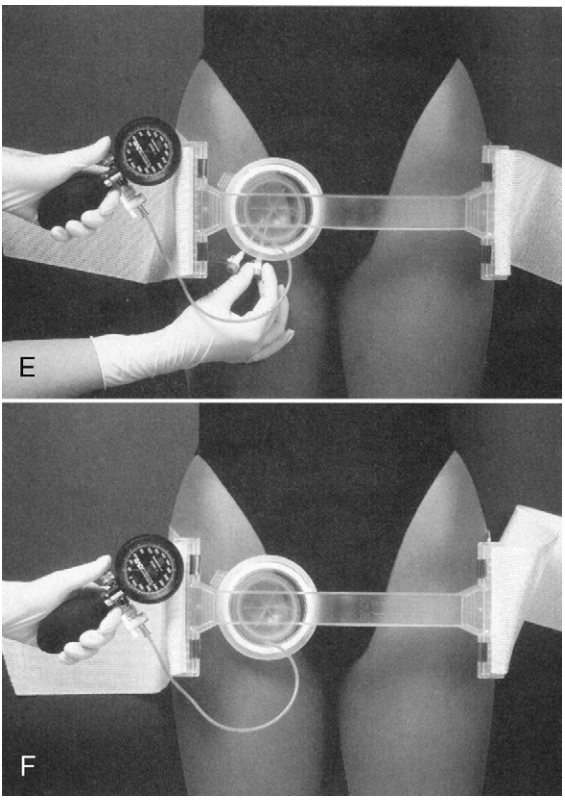

Figure 2-16, cont'd **E,** for the arterial sheath, pressurize dome to 60-80 mm Hg and remove sheath and increase pressure in dome to 10-20 mm above systolic arterial pressure. Maintain full compression for 3 minutes. **F,** Reduce pressure in dome by 10-20 mm Hg every few minutes until 0 mm Hg. Check arterial pulse. Observe for bleeding. After hemostasis has been obtained, remove FemoStop and dress wound. (From Kern, MJ. *The cardiac catheterization handbook,* 4th ed. Philadelphia: Mosby, 2003: 67–69.)

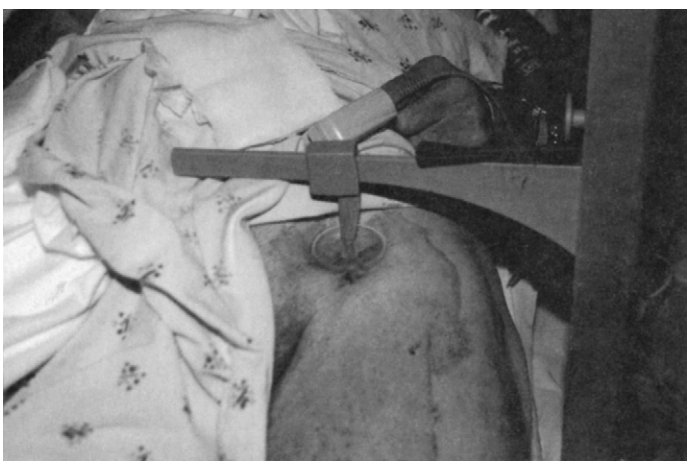

Figure 2-17 Picture of patient with the Compressor mechanical device in position over the femoral artery puncture site. (From Kern, MJ. *The cardiac catheterization handbook*, 4th ed. Philadelphia: Mosby, 2003: 66.)

Vascular Closure Devices and In-Lab Hemostasis

Immediate hemostasis can be achieved in the catheterization suite using one of several vascular closure devices. Before selecting the device, femoral angiography from an oblique projection will indicate the suitability of the device and perhaps which device should be selected. Note that the ipsilateral oblique view (e.g., the right anterior oblique [RAO] for right femoral artery) best displays the bifurcation of the profunda and superficial femoral branches.

Vascular closure devices were developed both to obtain quick safe hemostasis and to improve patient comfort by decreasing the time patients lie flat after the procedure. The decision to use a closure device must include the consideration of device-related complications that would not occur with standard manual compression. Nonetheless, vascular closure device safety has been demonstrated in diagnostic catheterization and interventions. Most catheterization laboratories report high success rates for various closure devices used directly after PCI in fully anticoagulated patients receiving antithrombins, heparin, or glycoprotein receptor blockers. However, a learning curve exists for these devices. New-generation closure devices have steeper learning curves, faster time to deployment, and are more efficient. Four commonly used devices are shown in Table 2-5.

For repeat procedures, re-stick in the same vessel is inadvisable for 90 days but can be performed if necessary. In this case the operator should attempt to access the artery 1 to 2 cm above or below the site of the previous device placement.

Key Points in Postprocedure Sheath Care and Hemostasis

1. "Do it right the first time." The best results stem from a meticulous arterial puncture, correct sheath placement, and careful removal and hemostasis.
2. For transport to the holding area, after the sheath is secured in place, insert an appropriately sized obturator in the sheath to prevent sheath kinking and bleeding before sheath removal.
3. Use a clear transparent dressing over the puncture site for easy visualization of bleeding. Do not use a wad of gauze under the dressing, as the combination of blood and gauze is an excellent culture media for bacteria.
4. Inspect and palpate the puncture site and distal pulses at each postprocedure check.
5. A downward trend in blood pressure and upward trend in heart rate are early warnings of a possible retroperitoneal hematoma forming. Back pain, abdominal pain, and confusion are also signs associated with blood loss. Consider taking an early computed tomography (CT) scan. Hypotension after PCI should be assumed to be due to bleeding until the operator has identified an alternate cause (e.g., vagal reaction, ischemia, tamponade, overmedicated).

Complications of Arterial Access

Hemorrhage

The most common complication from femoral cardiac catheterization is hemorrhage and local hematoma formation, increasing in frequency with the increasing size of the sheath, the amount of anticoagulation, and the degree of obesity of the patient.

Table 2-5

Vascular Closure Devices

Device	On the Market	Mechanism	Advantages	Disadvantages	Sheath Sizes	Ipsilateral Access < 90 Days
Angio-Seal (St Jude Medical, St. Paul, MN) 	1997 to present	Collagen and suture mediated	Secure closure, long track record	Intra-arterial component, possible thromboembolic complications, infection related to wick	6F and 8F	1 cm higher
Perclose (Abbott Vascular, Redwood City, CA) 	1997 to present	Suture mediated	Secure closure	Intra-arterial component, steep learning curve, device failure may require surgical repair	5F-8F	No restrictions
StarClose (Abbott Vascular, Redwood City, CA) 	2005 to present	Nitinol clip	No intra-arterial component	Adequate skin tract needed to prevent device failure	5F, 6F	Not fully established
Mynx (Access Closure, Mountain View, CA) 	2007 to present	PEG hydrogel plug	No intra-arterial component, potential use in PVD	Possible intra-arterial injection of sealant	5F-7F	No restrictions

PEG, polyethylene glycol; PVD, peripheral vascular disease.

Other common complications (in order of decreasing frequency) include retroperitoneal hematoma, pseudoaneurysm, AVF formation, arterial thrombosis secondary to intimal dissection, stroke, sepsis with or without abscess formation, and cholesterol or air embolization. The frequency of these complications is increased in high-risk procedures; critically ill elderly patients with extensive atheromatous disease; patients receiving anticoagulation, antiplatelet, and fibrinolytic therapies; and patients receiving concomitant interventional procedures. Compared to the femoral approach, the brachial (but not radial) approach carries a slightly higher risk of vascular complications.

Infections and Other Rare Events

Infections are more frequent in patients undergoing repeat ipsilateral (same site) femoral punctures or prolonged femoral sheath maintenance (within 1-5 days). Cholesterol embolism, manifesting with abdominal pain or headache (from mesenteric or central nervous system ischemia), skin mottling ("blue toes"), renal insufficiency, or lung hemorrhage, may be a clinical finding in up to 30% of high-risk patients.

Retroperitoneal Hematomas and Pseudoaneurysms

A retroperitoneal hematoma should be suspected in patients with hypotension, tachycardia, pallor, a rapidly falling hematocrit postcatheterization, lower abdominal or back pain, or neurologic changes in the leg with the puncture. This complication is associated with *high femoral arterial puncture* and full anticoagulation. Pseudoaneurysm is a complication associated with *low femoral arterial puncture* (usually below the head of the femur). In the past, all femoral pseudoaneurysms were routinely repaired by the vascular surgeon to avoid further neurovascular complication or rupture. With ultrasound imaging techniques, these false channels can be easily identified, and nonsurgical closure can be selected. Manual compression of the expansile growing mass, guided by Doppler ultrasound with or without thrombin or collagen injection, is an acceptable therapy for femoral pseudoaneurysm. Figure 2-18 shows a femoral artery dissection induced by access difficulties. Figure 2-19 shows a femoral AVF. Note simultaneous contrast filling of both artery and vein. Remember these complications are not applicable to radial artery PCI, but a severely overly anticoagulated patient can have spontaneous bleeding from previously uninvolved areas (e.g., retroperitoneal, renal, etc).

PCI Guide Catheters and Coronary Access

Compared to diagnostic catheters, the unique handling characteristics of coronary guide catheters may not be appreciated by the novice operator. Key points regarding PCI guiding catheters are listed below.

1. Catheter advancement and torque should always be gentle and gradual.
2. If the catheter is not engaged with standard manipulations, a different size or shape should be tried early instead of forcing the catheter into the vessel.
3. Deep cannulation of the vessel should be avoided.
4. Guide catheter size should be appropriate for the diameter of the proximal vessel. For ostial disease, consider guide catheters with side holes to permit perfusion when the guide is wedged in the ostium.

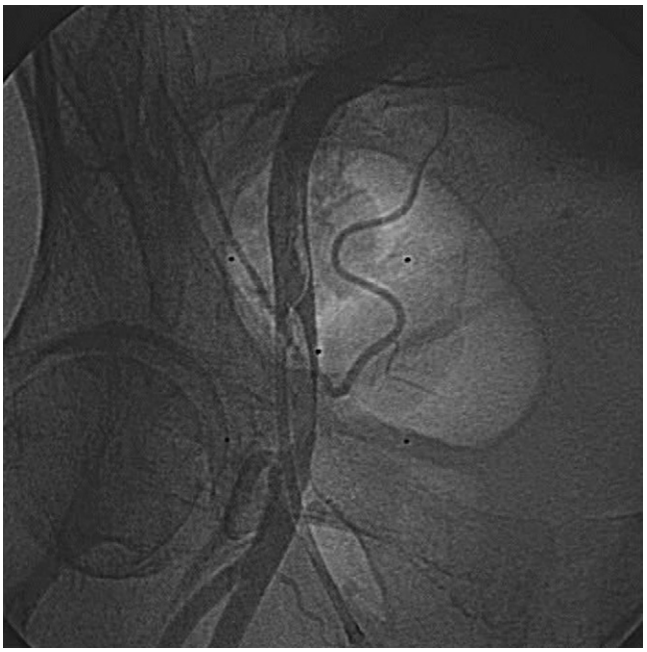

Figure 2-18 Angiogram of femoral artery dissection.

5. Catheter size and shape are selected to be minimally traumatic while providing optimal backup support.
6. Most procedures can be accomplished with Judkins-type (femoral) guide catheters although the sweeping curve of the Q shape is widely used as well.
7. The coronary arteries in which good backup guiding support is most difficult to achieve are, in order of difficulty, the right,

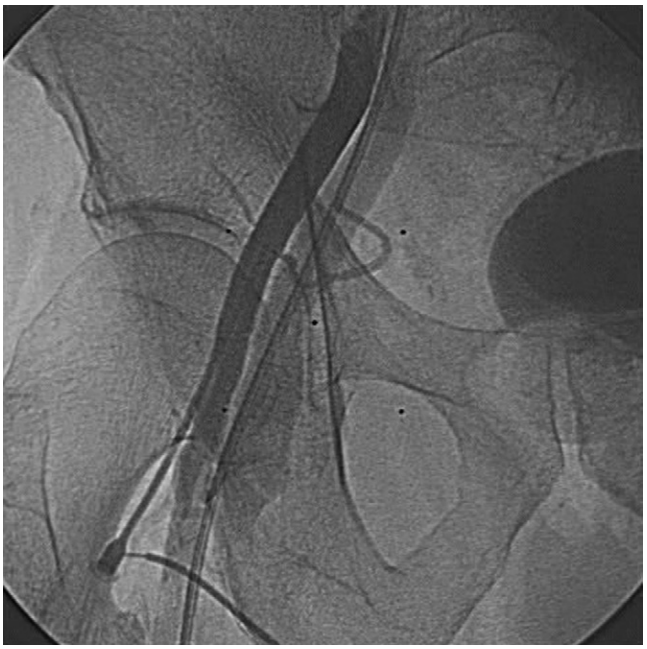

Figure 2-19 Angiogram of femoral artery arteriovenous fistula (AVF).

circumflex, and left anterior descending coronary arteries. Aortic root dimension and rotation of the root relative to the axis of the arch may also interfere with guide catheter positioning and backup support. SVGs and the use of the IMA have unique problems but are less frequent occurrences.

Coronary Guiding Catheter Types

Guide catheters (Fig. 2-20) are available in a wide variety of shapes duplicating diagnostic catheter shapes and several novel curves. Tip shapes are listed in Table 2-6. Guide catheters with various modifications, including short tips, smoother curves, half-sizes, or anterior or posterior tip directions, are available.

Judkins Guide Catheters

The Judkins left coronary catheter has a double curve. The length of the segment between the primary and the secondary curve determines the size of the catheter (i.e., 3.5, 4.0, 5.0, or 6.0 cm). The proper size of the left Judkins catheter depends on the length and width of the ascending aorta. In a small person with a small aorta, a 3.5-cm catheter is appropriate, while in a large person or in one with an enlarged or dilated ascending aorta (e.g., as a result of aortic stenosis, regurgitation, or Marfan syndrome), a 5.0- or 6.0-cm catheter may be required. The length of the Judkins curve is helpful to selectively direct the PCI wire.

A left 4-cm Judkins catheter fits in most adult patients with the catheter tip aligned with the long axis of the left main coronary trunk. A smaller (3.5-cm) catheter in the same patient will tip upward, favoring subselective left anterior descending artery (LAD) engagement. A larger (5.0-cm) catheter in the same patient will tip downward and favors subselective circumflex cannulation. A slight counterclockwise rotation of the catheter may be necessary to improve alignment of the catheter tip with the left main trunk. When the coronary orifice is not cannulated appropriately, the catheter should be replaced with a better fitting one rather than manipulated into the coronary artery.

For the radial approach, use a JL3.5 instead of 4.0. Seating the catheter with a deep breath may be helpful.

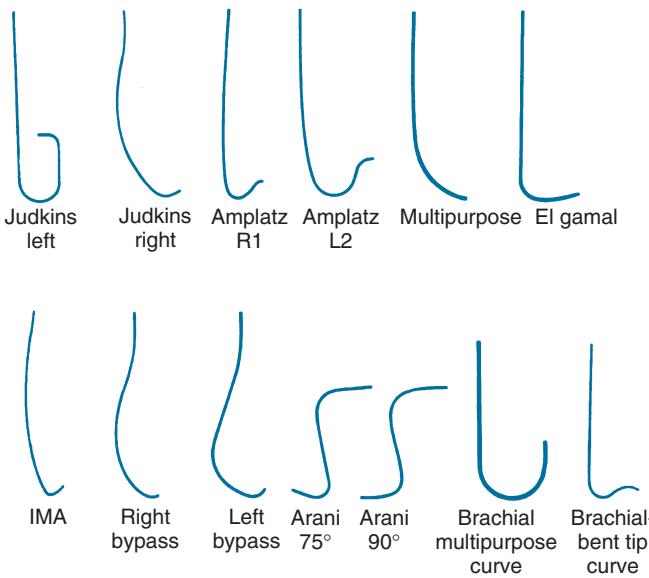

Figure 2-20 Common guiding catheter shapes.

Table 2-6

Types of Guide Catheters		
Guide	**Advantages**	**Disadvantages**
For LAD lesions		
JL4	Routine placement	Backs out
AL2	Easy to place, good backup	May dissect ostium
For RCA		
JR4	Easy use	Poor backup
Hockey stick	Deep seating	Deep seating
Multipurpose	Deep seating	Deep seating
Arani	Excellent backup	Difficult to engage, deep seating
For Tortuous RCA		
Left Amplatz	Excellent backup	Difficult to engage, deep seating
For Circumflex Lesions		
JL4	Routine placement	Backs out
AL2	Easy to place, good backup	May dissect ostium
Voda	Easy to seat, deep engagement, excellent backup	
Multipurpose	Good backup	Difficult to seat
Bypass Grafts	**Alternative Catheters**	
RCA, grafts	Hockey stick	
RCA	Arani	
Circumflex	Voda	

Amplatz Guide Catheters

The left Amplatz-type catheter is a preshaped half-circle with the tip extending perpendicular to the curve. Amplatz catheter sizes (left 1, 2, and 3; and right 1 and 2) indicate the diameter of the tip curve. In most normal-sized adults, AL2 and AR1 (modified) Amplatz catheters give satisfactory results.

Special attention should be given to using Amplatz catheters. In the LAO projection, the tip is advanced into the left aortic cusp. Further advancement of the catheter causes the tip to move upward into the left main trunk. It is necessary to push and torque the Amplatz catheters slightly to disengage the catheter tip by backing it upward and out of the left main ostium. If the catheter is pulled instead of first being advanced, the tip moves downward and into the left main or circumflex artery. Unwanted deep cannulation of the circumflex might tear this branch or the left main trunk.

Amplatz catheters have a higher incidence of coronary dissection than Judkins-type catheters. However, Amplatz catheters often provide superior backup support.

The AR1 (modified) catheter has a smaller but similar hook-shaped curve. The catheter is advanced into the right coronary cusp, as with a Judkins right catheter. The catheter is rotated clockwise 45 to 90 degrees. The same maneuver is repeated at different levels until the right coronary artery is entered. After coronary injections, the catheter may be pulled, advanced, or rotated out of the coronary artery. Amplatz catheters are very helpful and frequently used from the radial approach. Extra backup can be obtained using an AL2 for an upward takeoff right coronary artery.

Saphenous Vein and Internal Mammary Artery Graft Catheters

There are right and left graft and internal mammary catheters with shapes similar to their diagnostic counterparts. As in diagnostic angiography, they also may be useful in cannulation of native vessels with unusual origins or proximal courses.

The right coronary vein graft catheter is similar to a right Judkins catheter with a more downward-pointing primary curve, allowing cannulation of a vertically oriented coronary artery vein graft.

The left vein graft catheter is similar to the right Judkins catheter with a smaller and more upward-pointing secondary curve, allowing easy cannulation of SVGs supplying the left anterior descending and left circumflex territories. Such grafts are usually placed higher and more anterior than right of the IMA at the juncture of the subclavian and common carotid arteries.

Guide Catheters for the Radial Approach

Guide catheters from the radial artery approach include the same as those used for the femoral approach, as well as specially curved catheters designed by various interventionalists to provide increased backup support from the arm (Figs. 2-20, 2-21). These catheters were discussed earlier, in the Guide Catheters section.

Special Features of Guide Catheters

Small-Bore (<6F) Guide Catheters

Coronary angioplasty can be performed using large-lumen guide catheters (≤ 6F). Use of diagnostic and guide catheters of ≤ 5F has also been reported. Small-bore catheters are associated with less femoral bleeding and allow early patient ambulation. They can be easily used from the radial approach. When extraordinary backup is needed, deep cannulation of the vessel can be accomplished easily and possibly with less trauma than with larger (>7F) guiding catheters.

Guide Catheters With Side Holes

In general, most guide catheters should not require side holes so that one can detect the pressure damping that suggests ostial disease. Side hole catheters are very useful for PCI in small right coronary or graft

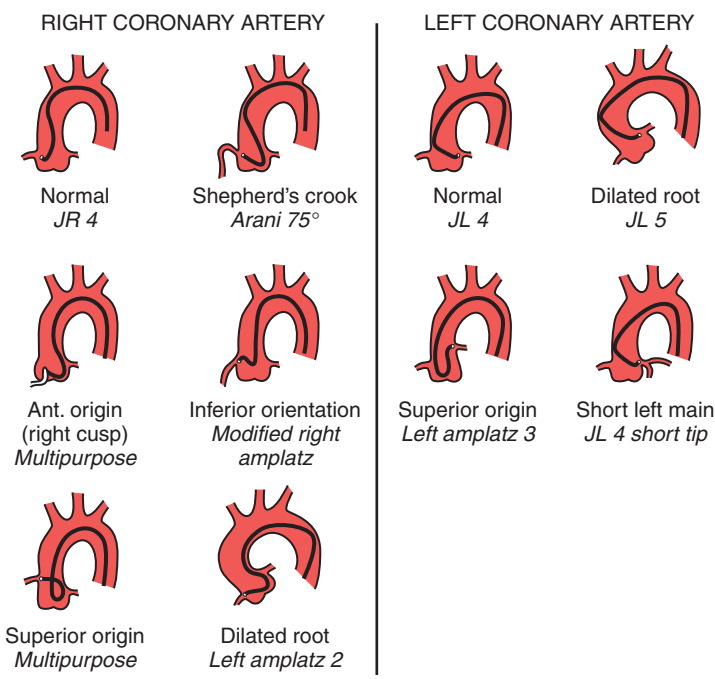

Figure 2-21 Guide catheter selection based on anatomic variations in aortic root width and coronary artery orientation. (Adapted from Safian R, Grines C, Freed M. *The new manual of interventional cardiology.* Birmingham, MI: Physicians' Press, 1999.)

vessels when pressure damping cannot be overcome by catheter repositioning. When using side hole guides, measurement of the translesional pressure (see fractional flow reserve [FFR], Chapter 13 Lesion Assessment) must be carefully reviewed. Undetected proximal pressure gradients due to the side holes may occur, invalidating distal gradient evaluations.

Cannulating Difficult Coronary or Graft Ostia

Left Coronary Artery Problems

Short Left Main, Separate Ostial Left Anterior Descending, and Circumflex Arteries

For the LAD, use a left Judkins catheter that is one size smaller than that usually selected (i.e., 3.5 cm instead of 4.0 cm; Figs. 2-22, 2-23). Selective cannulation of the LAD in patients with a short left main artery may be needed. For the circumflex ostium (Fig. 2-23), withdraw the standard 4-cm left Judkins catheter and rotate it counterclockwise. Alternatively, using a left Judkins catheter that is one size larger is helpful. An Amplatz-type catheter is especially useful for cannulating the circumflex ostium separately, but it must be used with care to avoid dissection.

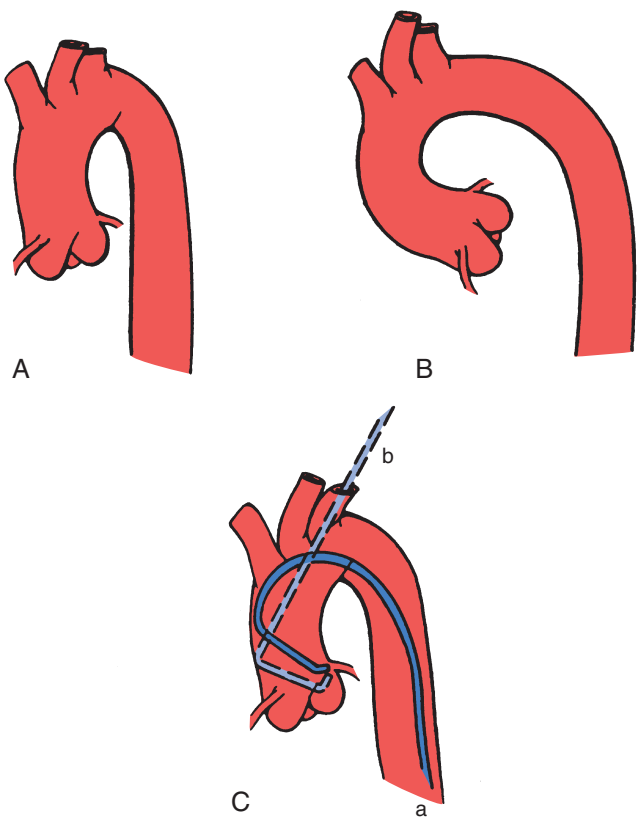

Figure 2-22 Anatomic variation of aortic arch, root, and valve plane. **A,** Normotensive. **B,** Hypertensive. **C,** Changes in secondary curves of Judkins left catheter when inserted via the femoral approach (*a*) or from the left radial or brachial approach (*b*). The right brachial approach can also be used. (From Topol EJ. *Textbook of interventional cardiology*, 2nd ed. Philadelphia: Saunders, 1994: 553.)

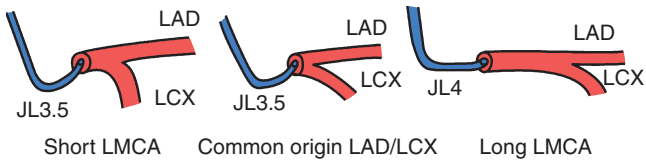

Figure 2-23 Left anterior descending artery guide catheter positioning with different secondary curve sizes. (From Jang GD. *Angioplasty*. New York: McGraw-Hill, 1987: 303.)

High Left Coronary Artery Takeoff

An unusually high origin of the left main coronary artery from the aorta usually can be cannulated using an Amplatz-type catheter.

Wide Aortic Root

In patients with a relatively horizontal or wide aortic root with upward takeoff of the left main coronary artery, use a large-curve left Judkins (5 or 6 cm), an Amplatz-type left coronary catheter, or a Voda-shaped catheter.

Posterior Origin of Left Main

Slight counterclockwise rotation and advancement of the left Judkins catheter may bring the tip to the left main. Sometimes it may be necessary to use a posterior out-of-plane tip. Another option is a left Amplatz catheter.

Right Coronary Artery Problems

The origin of the right coronary artery shows more variation than the left coronary artery. Extra backup support is difficult to obtain with standard JR4-type catheters. Directing the catheter tip to the right in the usual fashion using the lateral view permits easy cannulation of the slightly anterior origin of the right coronary artery in the right cusp.

High and Upward Takeoff of a Right Coronary Artery

A relatively high origin of the right coronary artery may require a left or right (modified) Amplatz-type catheter (Fig. 2-24).

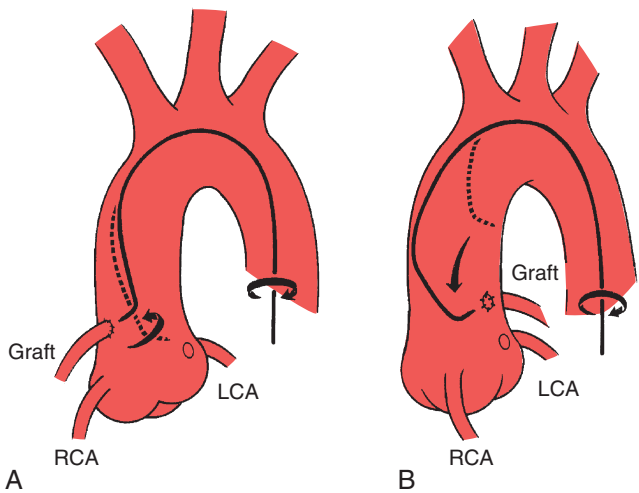

Figure 2-24 **A and B,** Method of use for Judkins right catheter in cannulating saphenous venous bypass graft conduits. (From Tilkian AG, Daily EK. *Cardiovascular procedures: diagnostic techniques and therapeutic procedures*. St. Louis, MO: Mosby, 1986.)

Wide Aortic Root

In a patient with a horizontal and wide aortic root, cannulation of the right coronary orifice may require an Amplatz or hockey-stick catheter.

"Shepherd's Crook" Right Coronary Artery

In this situation, a right Judkins catheter provides poor support. A left Amplatz (0.75 to 1), hockey-stick, or Arani catheter may provide better support, especially for relatively distal lesions. However, deep cannulation of the vessel is frequent with these catheters, and proximal vessel trauma can occur, especially in a small aortic root.

Anomalous Coronary Artery Origin

The most frequent anomaly is a circumflex origin from a proximal right coronary artery, or a separate orifice just posterior to the right coronary artery orifice. When there is a common trunk, a right Judkins catheter may be sufficient. A separate left circumflex orifice can be entered by rotating the right Judkins more posteriorly. Because of the downward course of the proximal circumflex, better engagement and support may be obtained by a right bypass, Amplatz, or multipurpose guide catheter.

Extreme anterior or left coronary cusp origin of the right coronary artery can be engaged by using a left Amplatz catheter. A more leftward origin of an anomalous right coronary artery (which also tends to be higher) can be entered using a left bypass guide.

Saphenous Vein Bypass Grafts (Figs. 2-25, 2-26)

To decrease the manipulation time and select the best catheter shape, the diagnostic angiogram should be reviewed carefully for the location of the aortic anastomosis and proximal course of the vessel. Anatomic landmarks should be noted. Because of the potential risk of embolization, avoid unnecessary manipulation of catheters inside the ostium, especially in old grafts that may contain atherosclerotic material.

Right Coronary Bypass Vein Graft Catheterization

The right coronary vein graft usually can be entered using a 4-cm right Judkins-type catheter (Fig. 2-26). The right coronary catheter is placed in the ascending aorta at a level slightly higher than the expected level of the right coronary vein graft orifice, and the catheter is rotated clockwise from 45 to 90 degrees. This will cause the catheter tip to move along the border of the ascending aortic silhouette in the LAO position.

When the right graft is anastomosed to the far right side of the aorta, a counterclockwise, rather than clockwise, rotation of the catheter may be necessary. In some cases the right Judkins or right bypass catheter may fall short of the ostium, in which case an Amplatz or multipurpose catheter may work. In this situation, the catheter tip is pointed toward the left-hand side of the screen in the anteroposterior (AP) or RAO position. Advancement or withdrawal while rotating the catheter tip might be necessary for graft engagement. In the case of right vein graft vertical takeoff, the right coronary Judkins catheter tip may be directed upward rather than downward into the lumen, making adequate opacification of the vein graft difficult. In this case, a right coronary bypass vein graft catheter should be used. Because of the downward primary curve, the right vein graft catheter tip usually aligns more parallel to the axis of the graft. Be careful, as the catheter has a tendency to move deeply down into the vein graft. A right modified Amplatz catheter can also be used for horizontal or vertical takeoff vein grafts.

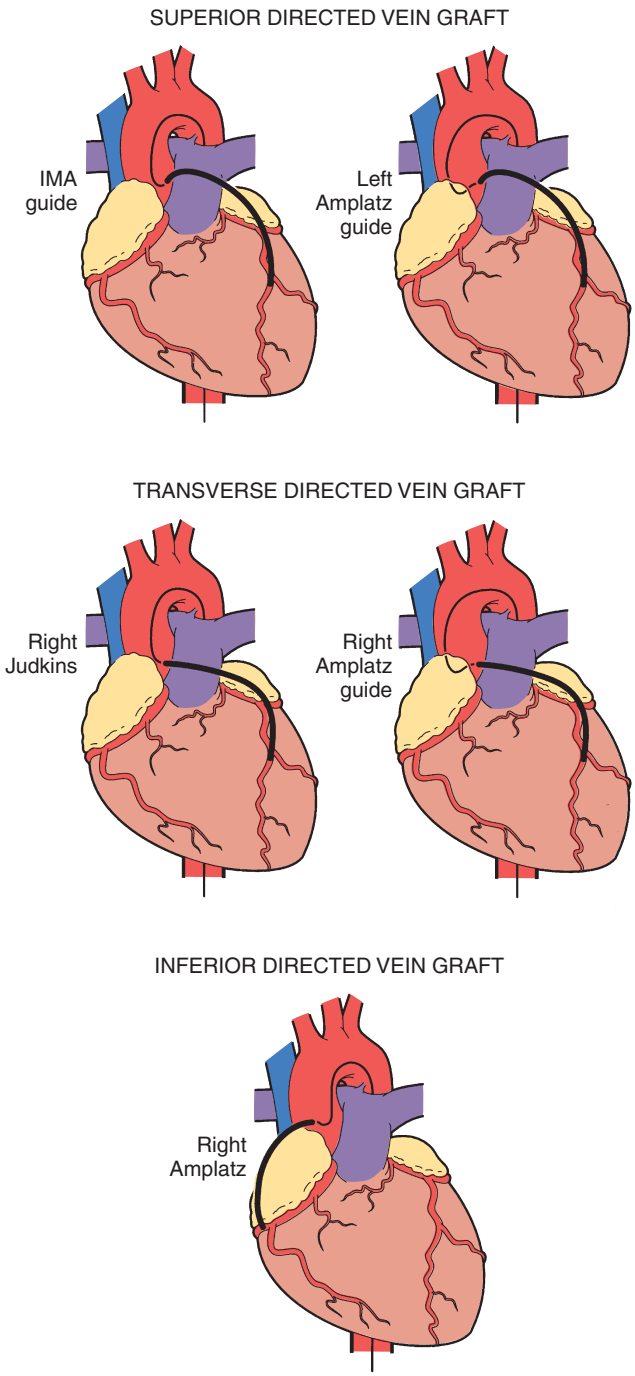

Figure 2-25 Saphenous vein graft (SVG) ostium orientations. Different guide catheters should be selected based on the angle of graft takeoff, superior, transverse, or inferior orientation. (From Pinkerton CA, Slack JD, Orr CM, *et al.* Percutaneous transluminal coronary angioplasty in patients with prior myocardial revascularization surgery. *Am J Cardiol* 1988;61:15G–22G.)

Left Anterior Descending Vein Graft Catheterization

The right Judkins catheter is placed at a level slightly higher than the expected level of the orifice of the anterior descending vein graft, and 30- to 45-degree clockwise rotation is applied. The catheter tip will appear foreshortened in the LAO view and will be pointing toward the

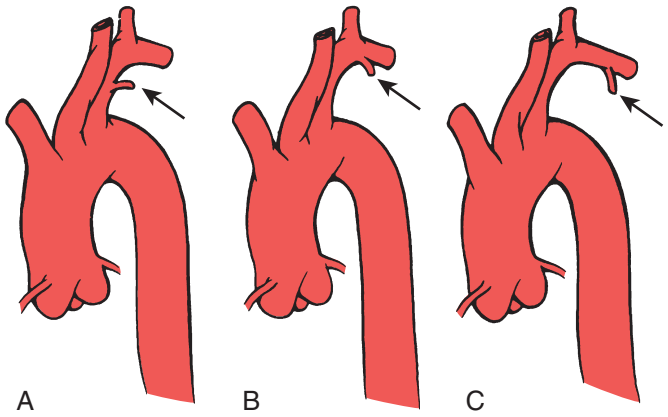

Figure 2-26 Anatomic variation of the origin of the internal mammary artery (IMA) from the subclavian artery: **A,** proximal; **B,** mid; **C,** distal. Although the femoral approach is easier for anatomy **A,** the ipsilateral brachial approach is more difficult than might appear initially. (From Topol EJ. *Textbook of interventional cardiology*, 2nd ed. Philadelphia: Saunders, 1994: 560.)

right-hand side of the ascending aorta silhouette in the RAO view. In some patients, it may be necessary to use a left coronary vein graft catheter or left Amplatz catheter. A slight clockwise rotation of the catheter at the level of the expected aortic anastomosis site will often engage the ostium.

The left anterior descending graft may course horizontally or downward after the origin. In some cases, however, it makes an upward curve before it turns toward the apex. In these cases, the need for stronger backup support may require the use of a left Amplatz catheter or deep cannulation using a hockey stick–shaped catheter.

Circumflex Vein Graft Catheterization

Repeating the same maneuvers described for left anterior descending vein graft cannulation using right Judkins or left vein graft catheters will usually produce a successful result.

Internal Mammary Artery Graft Cannulation

The left IMA originates anteriorly from the caudal wall of the subclavian artery and is distal to the vertebral artery origin. There are many variations in the shape of the aortic arch and origin and direction of the subclavian artery (Fig. 2-27). The left subclavian artery can be entered using an IMA catheter. The catheter is advanced into the aortic arch up to the level of the origin of the left subclavian artery. The guidewire is left in the catheter. Subsequently, the catheter is withdrawn slowly and rotated counterclockwise. The catheter tip is deflected cranially, usually engaging the left subclavian artery at the top of the aortic knob in the anteroposterior projection. The guidewire is advanced into the subclavian artery. The catheter is advanced. The guidewire is withdrawn. More than one attempt is often necessary to engage into the subclavian artery. Once the subclavian artery is engaged, the catheter is advanced slightly over a guidewire beyond the internal mammary orifice. A J-tipped or a Wholey wire is helpful to guide the catheter into the subclavian artery. Once the catheter has been advanced beyond the takeoff of the IMA, the catheter is withdrawn slowly and small contrast injections are given to visualize the IMA orifice. The catheter tip should be directed caudally and anteriorly. At the level of the orifice of the internal mammary, a slight counterclockwise rotation and advancement may be necessary to cannulate the artery.

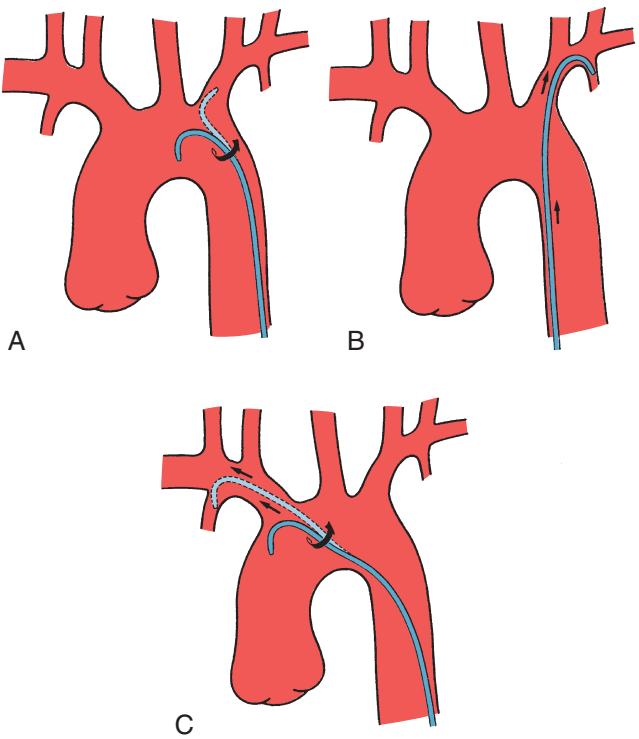

Figure 2-27 A–C, Technique of catheterization of the internal mammary artery (IMA). Clockwise rotation is employed for both left and right IMA engagement. (From Tilkian AG, Daily EK. *Cardiovascular procedures: diagnostic techniques and therapeutic procedures.* St. Louis, MO: Mosby, 1986.)

Vigorous manipulation of the catheter and deep intubation of the IMA should be avoided because of the hazard of dissection. Initially, as with most cannulations, only catheters without side holes should be used. Pressure damping indicates potentially dangerous deep cannulation. During injection of contrast medium, the patient should be reminded to expect discomfort in the shoulder and anterior chest wall.

Right Internal Mammary Artery

Right IMA cannulation is more difficult than left IMA cannulation. The right brachiocephalic truncus is entered using a right Judkins catheter by rotating the tip with a counterclockwise rotation at the level of the brachiocephalic truncus (see Fig. 2-22). The catheter is advanced into the subclavian artery over a guidewire. The rest of the cannulation procedure is similar to that described for left IMA graft cannulation.

In patients for whom cannulation of the subclavian artery is not possible because of excessive tortuosity or obstructive lesions, an IMA catheter can be introduced through an arm (ipsilateral) artery and advanced beyond the mammary artery orifice over a guidewire. The catheter is withdrawn slowly by making frequent, small contrast injections, then seated in the usual fashion for PCI. Table 2-6 shows types of guide catheters and their advantages and disadvantages.

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3

Angiography for Percutaneous Coronary Interventions 

MORTON J. KERN

Angiography for percutaneous coronary interventions (PCIs) requires establishing the precise lesion length, morphology and degree of calcification (or thrombus), as well as the relationship to side branches and their associated ostial involvement with coronary artery disease (CAD). Before PCI, the angiographer should acquire the following additional angiographic detail:

1. Establish the relationship of coronary ostium to aorta for guide catheter selection.
2. Verify target vessel, pathway, and angle of entry.
3. Confirm lesion length and morphology using additional angulated views eliminating vessel overlap.
4. Separate associated side branches and degree of ostial atherosclerosis.
5. Visualize distribution of collateral supply.
6. Determine the true (maximally vasodilated) diameter of the coronary artery at the target site.

Optimal definition of ostial and proximal coronary segment is critical to guide PCI catheter selection. Assessment of calcium from angiography is less reliable than intravascular ultrasound (IVUS) imaging but still serves a useful purpose in assessing need for rotational atherectomy and risks associated with the procedure.

Classical terminology for angiographic projections with regard to left and right anterior oblique, cranial and caudal angulation, and lateral projections remains as defined in previous discussions of diagnostic coronary angiography (see *The Cardiac Catheterization Handbook*, 5th edition, Chapter 4).

Visualization of vessel bifurcations, origin of side branches, the portion of the vessel proximal to a significant lesion, and previously "unimportant" lesion characteristics (length, eccentricity, calcium, and the like) will assist in device selection and identifying potential procedural risk. For total chronic vessel occlusions, the distal vessel should be visualized as clearly as possible by injecting the coronary arteries that supply collaterals and taking cineangiograms with panning long enough to visualize late collateral vessel filling and the length of the occluded segment.

Optimal radiographic imaging is also critical to determining a successful intervention, enhancing accurate interpretation of procedure results. Modification of panning technique to reduce motion artifact during imaging, optimal use of beam restrictors (collimation) to reduce scatter, and improved contrast media delivery can enhance clinical results. A working knowledge of the principles of radiographic imaging permits the interventionalist to improve imaging outcomes.

Radiation exposure is higher in PCI than diagnostic procedures. Continued awareness of the inverse square law of radiation propagation will reduce the exposure to patient, operators, and the catheter lab team. Obtaining quality images should not necessitate increasing the ordinary procedural radiation exposure to either the patient or catheterization personnel.

Common Angiographic Views for Angioplasty

The routine coronary angiographic views described below should include those that best visualize the origin and course of the major vessels and their branches in at least two different (preferably orthogonal) projections. Naturally, there is a wide variation in coronary anatomy, and appropriately modified views will need to be individualized. The nomenclature for angiographic views is described in Chapter 4 of *The Cardiac Catheterization Handbook*, 5th edition, but will be reviewed briefly here, emphasizing the interventionalist's thinking.

Position for Anteroposterior Imaging

The image intensifier is directly over the patient, with the beam perpendicular to the patient lying flat on the x-ray table (Figs. 3-1, 3-2). The anteroposterior (AP) view or shallow right anterior oblique (RAO) displays the left main coronary artery in its entire perpendicular length. In this view, the branches of the left anterior descending (LAD) and left circumflex coronary arteries branches overlap. Slight RAO or left anterior oblique (LAO) angulation may be necessary to clear the density of the vertebrae and the catheter shaft in the thoracic descending aorta. In patients with acute coronary syndromes, this view will exclude left main stenosis, which can preclude or complicate PCI. The AP cranial view is excellent for visualizing the LAD with septals moving to the left (on screen) and diagonals to the right, helping wire placement.

Position for Right Anterior Oblique Imaging

The image intensifier is to the right side of the patient. The RAO caudal view shows the left main coronary artery bifurcation with the origin and course of the circumflex/obtuse marginals, intermediate branch, and proximal left anterior descending segment well seen. The RAO caudal view is one of the best two views for visualization of the circumflex artery. The LAD beyond the proximal segment is often obscured by overlapped diagonals.

The RAO or AP cranial view is used to open the diagonals along the mid and distal LAD. Diagonal branch bifurcations are well visualized. The diagonal branches are projected upward. The proximal LAD and circumflex usually are overlapped. Marginals may overlap, and the circumflex is foreshortened.

For the right coronary artery (RCA), the RAO view shows the mid RCA and the length of the posterior descending artery and posterolateral branches. Septals supplying an occluded LAD via collaterals may be clearly identified. The posterolateral branches overlap and may need the addition of the cranial view.

Position for Left Anterior Oblique Imaging

In the LAO position, the image intensifier is to the left side of the patient. The LAO/cranial view also shows the left main coronary artery (slightly foreshortened), LAD, and diagonal branches. Septal and diagonal branches are separated clearly. The circumflex and marginals are foreshortened and overlapped. Deep inspiration will move the density of

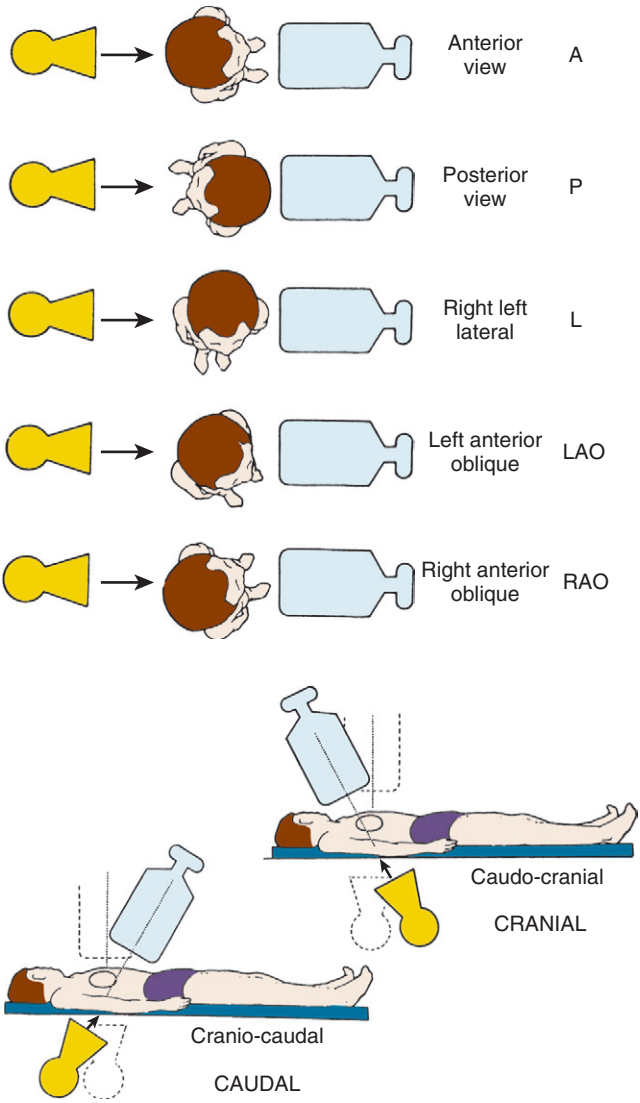


Figure 3-1 Nomenclature for angiographic views. (Modified from Paulin S. Terminology for radiographic projections in cardiac angiography. *Cathet Cardiovasc Diagn* 1981;7:341.)

the diaphragm out of the field. The LAO angle should be set so that the course of the LAD is parallel to the spine and stays in the "lucent wedge" bordered by the spine and the curve of the diaphragm. Cranial angulation tilts the left main coronary artery down and permits view of the LAD/circumflex bifurcation (Fig. 3-3). Too steep an LAO/cranial angulation or shallow inspiration produces considerable overlapping with the diaphragm and liver, degrading the image.

For the RCA, the LAO/cranial view shows the origin of the artery, its entire length, and the posterior descending artery bifurcation (crux). Cranial angulation tilts the posterior descending artery down to show vessel contour and reduces foreshortening. Deep inspiration clears the diaphragm. The posterior descending artery and posterolateral branches are foreshortened.

The LAO/caudal view ("spider" view; Fig. 3-3) shows a foreshortened left main coronary artery and the bifurcation of the circumflex and LAD. Proximal and mid portions of the circumflex and the origins of obtuse marginal branches are usually seen excellently. Poor image

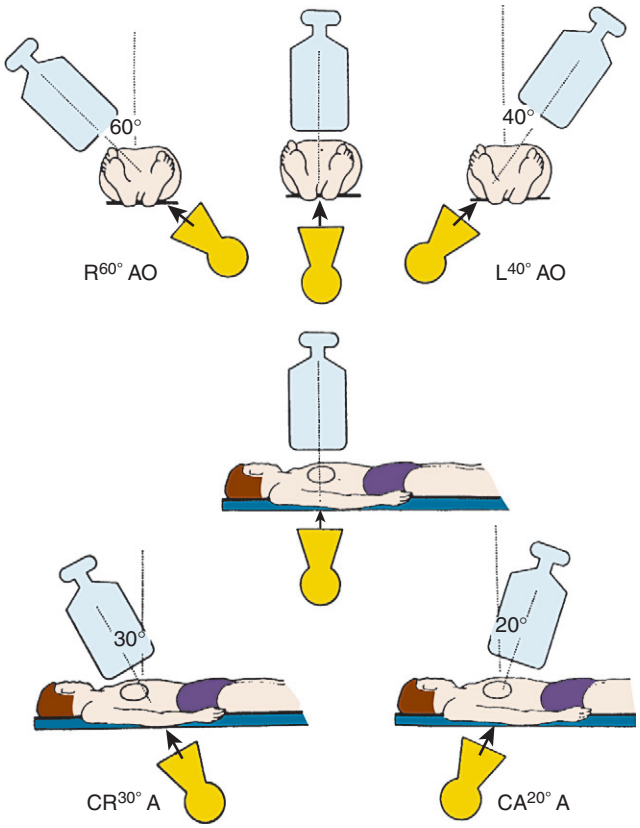


Figure 3-2 Nomenclature for angiographic views. CR, cranial; CA, caudal; A, anterior; R, right; AO, anterior oblique. (Modified from Paulin S. Terminology for radiographic projections in cardiac angiography. *Cathet Cardiovasc Diagn* 1981;7:341.)

quality may be due to overlapping of diaphragm and spine. The LAD is considerably foreshortened in this view.

A left lateral view shows the mid and distal LAD best. The LAD and circumflex are well separated. Diagonals usually overlap. The course of the (ramus) intermediate branch is well visualized. This view is best to see coronary artery bypass graft (CABG) conduit anastomosis to the LAD. For the RCA, the lateral view also shows the origin (especially in those with more anteriorly oriented orifices) and the mid RCA well. The posterior descending artery and posterolateral branches are foreshortened.

Angulations for Saphenous Bypass Grafts

Coronary artery saphenous vein grafts are visualized in at least two views (LAO and RAO). It is important to show the aortic anastomosis, the body of the graft, and the distal anastomosis. The distal runoff and continued flow or collateral channels are also critical. The graft vessel anastomosis is best seen in the view that depicts the native vessel best. A general strategy for graft angiography is to perform the standard views while assessing the vessel key views for specific coronary artery segments (Table 3-1) to determine the need for contingency views or an alteration/addition of special views. Therefore, the graft views can be summarized as follows:

1. RCA graft: LAO cranial/RAO and lateral
2. LAD graft (or internal mammary artery): lateral, RAO cranial, LAO cranial, and AP (the lateral view is especially useful to visualize the anastomosis to the LAD)
3. Circumflex (and obtuse marginals) grafts: LAO and RAO caudal.

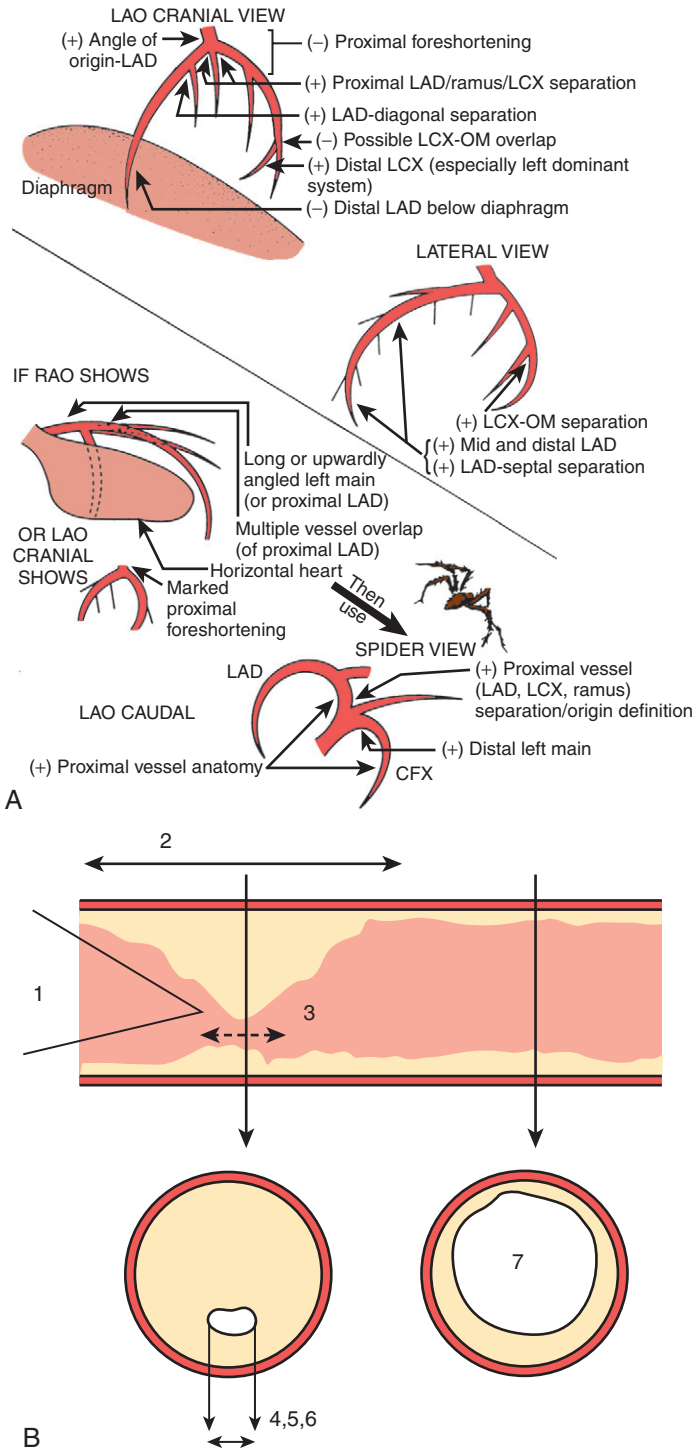


Figure 3-3 **A,** Diagrammatic view of left coronary artery demonstrating special positioning to best observe branch segments. (From Boucher RA, Myler RK, Clark DA, *et al*. Coronary angiography and angioplasty. *Cathet Cardiovasc Diagn* 1988;14:269–285.) **B,** Diagram of factors producing resistance to flow across a coronary stenosis. (*1*) Entrance angle, (*2*) Length of disease, (*3*) Length of stenosis, (*4*) Minimal lumen diameter, (*5*) Minimal lumen area, (*6*) Eccentricity of lumen, (*7*) Area of reference vessel segment.

Table 3-1

Recommended "Key" Angiographic Views for Specific Coronary Artery Segments

Coronary Segment	Origin/Bifurcation	Course/Body
Left main	AP	AP
	LAO cranial	LAO cranial
	LAO caudal*	
Proximal LAD	LAO cranial	LAO cranial
	RAO caudal	RAO caudal
Mid LAD	LAD cranial	
	RAO cranial	
	Lateral	
Distal LAD	AP	
	RAO cranial	
	Lateral	
Diagonal	LAO cranial	RAO cranial, caudal, or straight
	RAO cranial	
Proximal circumflex	RAO caudal	LAO caudal
	LAO caudal	
Intermediate	RAO caudal	RAO caudal
	LAO caudal	Lateral
Obtuse marginal	RAO caudal	RAO caudal
	LAO caudal	
	RAO cranial (distal marginals)	
Proximal RCA	LAO	
	Lateral	
Mid RCA	LAO	LAO
	Lateral	Lateral
	RAO	RAO
Distal RCA	LAO cranial	LAO cranial
	Lateral	Lateral
PDA	LAO cranial	RAO
Posterolateral	LAO cranial	RAO cranial
	RAO cranial	RAO cranial

*Horizontal hearts.
AP, anteroposterior; *LAD,* left anterior descending; *LAO,* left anterior oblique; *PDA,* posterior descending artery (from RCA); *RAO,* right anterior oblique; *RCA,* right coronary artery. From Kern MJ, ed. *The cardiac catheterization handbook,* 2nd ed. St Louis, MO: Mosby, 1995: 286.

Techniques for Coronary Arteriography

Imaging During Respiration

During diagnostic angiography, deep inspiration moves the diaphragm away from the heart to see the vessels without density overlap. However, when working with PCI equipment, deep inspiration may change the proximal course of the artery and the spatial relation of the lesion to anatomic landmarks. Knowing where the lesion is relative to these landmarks is important. Guiding angiograms should be taken in such a way that frequent inspiratory effort leading to patient fatigue during manipulation is not necessary. Select a view requiring minimal inspiratory breath holding while providing an optimum presentation of the lesion.

Power Injection Versus Hand Injection for Coronary Arteriography

Power injection of the coronary arteries has been used in thousands of cases in many laboratories and is equal in safety to hand injection. A power injector at a fixed setting may require several injections to find

the optimal contrast delivery flow rate. Power injectors now incorporate hand controls, permitting precise operator touch-sensitive variable volume injection (Acist, Bracco Diagnostics) as well as a computer touch screen for precise contrast delivery settings. Typical settings for power injections are the following:

- Right coronary artery: 6 mL at 2–3 mL/sec; maximum pressure 450 psi
- Left coronary artery: 10 mL at 4–6 mL/sec; maximum pressure 450 psi

Panning Techniques

Many laboratories use x-ray image mode sizes of <7 inch diameter, which precludes having the entire coronary artery course visualized without panning over the heart to include late filling of the distal arterial or collateralized segments. In addition, in most views some degree of panning will be necessary to identify regions that are not seen from the initial setup positioning. Some branches may unexpectedly appear later from collateral filling or other unusual anatomic sources.

Angiographic TIMI Classification of Blood Flow

Thrombolysis in myocardial infarction (TIMI) flow grading has been used to assess, in a qualitative fashion, the degree of restored perfusion achieved after thrombolysis or angioplasty in patients with acute myocardial infarction. Table 3-2 provides descriptions used to assign TIMI flow grades.

Table 3-2

Thrombolysis in Myocardial Infarction (TIMI) Flow: Grade and Blush Scores

TIMI Flow Grade	Description
Grade 3 (complete reperfusion)	Anterograde flow into the terminal coronary artery segment through a stenosis is as prompt as anterograde flow into a comparable segment proximal to the stenosis. Contrast material clears as rapidly from the distal segment as from an uninvolved, more proximal segment.
Grade 2 (partial reperfusion)	Contrast material flows through the stenosis to opacify the terminal artery segment. However, contrast enters the terminal segment perceptibly more slowly than more proximal segments. Alternatively, contrast material clears from a segment distal to a stenosis noticeably more slowly than from a comparable segment not preceded by a significant stenosis.
Grade 1 (penetration with minimal perfusion)	A small amount of contrast flows through the stenosis but fails to fully opacify the artery beyond.
Grade 0 (no perfusion)	There is no contrast flow through the stenosis.

Myocardial Blush Grade

0 No myocardial blush or contrast density. Myocardial blush persisted ("staining").
1 Minimal myocardial blush or contrast density.
2 Moderate myocardial blush or contrast density but less than that obtained during angiography of a contralateral or ipsilateral noninfarct-related coronary artery.
3 Normal myocardial blush or contrast density, comparable with that obtained during angiography of a contralateral or ipsilateral noninfarct-related coronary artery.

Modified from Sheehan F, Braunwald E, Canner P, *et al.* The effect of intravenous thrombolytic therapy on left ventricular function: a report on tissue-type plasminogen activator and streptokinase from the Thrombolysis in Myocardial Infarction (TIMI) Phase I Trial. *Circulation* 1987;72:817–829.

Classification of Distal Angiographic Contrast Runoff

The distal runoff is classified into four stages (also known as TIMI grade):

- Normal distal runoff (TIMI 3)
- Good distal runoff (TIMI 2)
- Poor distal runoff (TIMI 1)
- Absence of distal runoff (TIMI 0)

TIMI Frame Count

Contrast runoff is now performed quantitatively by using cine frame counts from the first frame of the filled catheter tip to the frame where contrast is seen filling a predetermined distal arterial end point. Myocardial blood flow has been assessed angiographically using the TIMI score for qualitative grading of coronary flow. TIMI flow grades 0 to 3 have become a standard description of coronary blood flow in clinical trials. TIMI grade 3 flows have been associated with improved clinical outcomes.

The method uses cineangiography with 6 F catheters and filming at 30 frames per second. The number of cine frames from the introduction of dye in the coronary artery to a predetermined distal landmark is counted. The TIMI frame count for each major vessel is thus standardized according to specific distal land marks. The first frame used for TIMI frame counting is that in which the dye fully opacifies the origin of the artery and in which the dye extends across the width of the artery touching both borders with antegrade motion of the dye. The last frame counted is when dye enters the first distal landmark branch. Full opacification of the distal branch segment is not required. Distal landmarks used commonly in analysis are listed here:

1. For the LAD, the distal bifurcation of the LAD artery
2. For the circumflex system, the distal bifurcation of the branch segments with the longest total distance
3. For the RCA, the first branch of the posterolateral artery

Typically a normal contrast frame count reflecting normal flow is 24 ±10 frames. The TIMI frame count (TFC) can further be corrected for the length of the LAD. The TFC in the LAD requires normalization or correction for comparison to the two other major arteries. This is called corrected TIMI frame count (CTFC). The average LAD is 14.7 cm long, the right 9.8 cm, and the circumflex 9.3 cm, according to Gibson et al. CTFC accounts for the distance the dye has to travel in the LAD relative to the other arteries. CTFC divides the absolute frame count in the LAD by 1.7 to standardize the distance of dye travel in all three arteries. Normal TFC for the LAD is 36 ± 3, and CTFC 21 ± 2; for the circumflex artery TFC = 22 ± 4; for the RCA TFC = 20 ± 3. TIMI flow grades do not correspond to measured Doppler flow velocity or CTFC. High TFC may be associated with microvascular dysfunction despite an open artery. A CTFC of less than 20 frames was associated with low risk for adverse events in patients following myocardial infarction. A contrast injection rate increase of more than 1 mL/sec by hand injection can decrease the TFC by two frames. The TFC method provides valuable information relative to clinical response after coronary intervention.

TIMI Myocardial Blush Grades (MBG)

Washout of contrast from the microvasculature in the acute infarction patient is coupled to prognosis. Better blush scores indicate better myocardial salvage. The MBG scoring is shown in Table 3-2.

Angiographic Classification of Collateral Flow

Collateral flow can be seen and classified angiographically. The late opacification of a totally or subtotally (99%) occluded vessel through antegrade or retrograde channels will assist in correct guidewire

placement, lesion localization, and a successful procedure. The collateral circulation is graded angiographically as follows:

- Grade 0: No collateral branches are seen.
- Grade 1: Very weak (ghostlike) opacification is seen.
- Grade 2: Opacified segment is less dense than the source vessel and filling slowly.
- Grade 3: Opacified segment is as dense as the source vessel and filling rapidly.

Collateral visualization will help establish the size of the recipient vessel for the purposes of selecting an appropriately sized balloon. Determining whether the collateral circulation is ipsilateral (e.g., proximal RCA to distal RCA collateral supply) or contralateral (e.g., circumflex to distal RCA collateral supply) and exactly which region will be affected should collateral supply be disrupted is important in order to be able to gauge procedural risk. The evaluation of collaterals must be included when making decisions on which vessels should be protected or lost during coronary angioplasty.

Assessment of Coronary Stenoses

The degree of an angiographic narrowing (stenosis) is reported as the estimated percentage lumen reduction of the most severely narrowed segment compared to the adjacent angiographically normal vessel segment, seen in the worst x-ray projection. Because the operator uses visual estimations, an exact evaluation is impossible. There is a ± 20% variation between readings of two or more experienced angiographers. Stenosis severity alone should not always be assumed to be associated with abnormal physiology (flow) and ischemia. Moreover, CAD is a diffuse process, and thus minimal luminal irregularities on angiography may represent significant albeit non-obstructive CAD at the time of angiography. The stenotic segment lumen is compared with a nearby lumen that does not appear to be obstructed but that may have diffuse atherosclerotic disease. This explains why postmortem examinations and IVUS imaging describe much more plaque than is seen on angiography. The percent diameter is estimated from the angiographically normal adjacent segment. Because coronary arteries normally taper as they travel to the apex, proximal segments are always larger than distal segments, often explaining the large disparity between several observers' estimates of stenosis severity. *Area stenosis* is always greater than *diameter stenosis* and assumes the lumen is circular, whereas the lumen is usually eccentric. In general, four categories of lesion severity can be assigned:

1. Minimal or mild CAD, narrowings < 50%
2. Moderate, stenosis between 50% and 75%
3. Severe, stenosis between 75% and 95%
4. Total occlusion

Technical note: Stenosis anatomy should not be confused with abnormal physiology (flow) and ischemia, especially for lesions 40% to 70% narrowed. For nonquantitative reports, the length of a stenosis is simply mentioned (e.g., LAD proximal segment stenosis diameter 25%, long or short). Other features of the coronary lesion may not be appreciated by angiography and require IVUS imaging. Anatomic factors producing resistance to coronary flow include factors producing resistance to flow across a coronary stenosis, such as entrance angle, length of disease, length of stenosis, minimal lumen diameter, minimal lumen area, eccentricity of lumen, area of reference vessel segment, and viscosity (Fig. 3-3B).

Quantitative Coronary Angiography

The degree of coronary stenosis is quantitated from the cineangiogram and, in clinical practice, is usually a visual estimation of the percentage of diameter narrowing using the presumed proximal normal arterial

segment and the ratio of the normal diameter to the stenosis diameter. This technique is widely applicable in clinical practice but is inadequate for the quantitative methodology done in most research studies. The intraobserver variability may range between 40% and 80%, and there is frequently as wide as a 20% range on interobserver differences. Quantitative methodology uses digital calipers or automated or manual edge detection systems. Densitometric analysis with digital angiography also provides quantitative lesion measurements.

Coronary Lesion Descriptions for Angioplasty

There are at least three major classifications of lesion severity (Table 3-3). These classifications were derived from large studies in which the characteristics of the lesions were associated with different clinical outcomes of the techniques and times of the study. These are helpful to assess risk for adverse cardiac events in the performance of PCI.

General characteristics of the artery proximal to the lesion dilated are as follows:

1. Tortuosity
   - None/mild = straight proximal segment or only one bend of ≥60 degrees
   - Moderate = two bends of ≥ 60 degrees proximal to the lesion
   - Severe = three or more bends of ≥ 60 degrees proximal to the lesion
2. Arterial calcification
   - Light = proximal artery wall calcification (not necessarily the lesion) seen as thin line(s)
   - Heavy = easily seen calcification

Angiographic characteristics of the dilated target lesion are as follows:

3. Arrangement of the lesion(s)
   - Tandem = two lesions located within one balloon length (i.e., both lesions can be covered during a single balloon inflation)
   - Sequential = two lesions located at a distance longer than the balloon
4. Length
   - Discrete = ≥5 mm in length
   - Tubular = 5–10 mm in length
   - Diffuse = >10 mm in length
5. Eccentricity
   - Concentric = lumen axis is located along the long axis of the artery or on either side of it, but by no more than 25% of the normal arterial diameter
6. Ostial
   - Lesion is located at the aorto-ostial or bifurcation points
7. Side branch
   - Bypassable side branch ≥1.5 mm
8. Contour
   - Smooth, irregular, or ulcerated
9. Thrombus
   - Definite = intraluminal, round filling defect, visible in two views, largely separated from the vessel wall and/or documentation of embolization of this material
   - Possible = other filling defects not associated with calcification, lesion haziness, irregularity with ill-defined borders, intraluminal staining at the total occlusion site

Table 3-3

ACC/AHA Lesion-Specific Characteristics

Type A Low Risk	Type B Medium Risk	Type C High Risk
Discrete (<10 mm length)	Tubular (10–20 mm length)	Diffuse (>2 cm length)
Concentric	Eccentric	
Readily accessible	Moderate tortuosity of proximal segment	Excessive tortuosity of proximal segment
Nonangulated segment, <45 degrees	Moderately angulated segment, 45–90 degrees	Extremely angulated segments >90 degrees
Smooth contour	Irregular contour	
Little or no calcification	Moderate to heavy calcification	
Less than totally occlusive	Total occlusion <3 months old	Total occlusions >3 months old ± bridging collaterals
Not ostial in location	Ostial in location	
No major branch involvement	Bifurcation lesions requiring double guidewires	Inability to protect major side branches
Absence of thrombus	Some thrombus present	Degenerated vein grafts with friable lesions
Procedure success rate 92%	Procedure success rate 76%	Procedure success rate 61%
Complication rate 2%	Complication rate 10%	Complication rate 21%

SCAI Lesion-Specific Characteristics

Type I	Type II	Type III	Type IV
Patent and does not meet criteria for ACC/AHA type C lesion	Patent and meets any criteria for type C lesion	Occluded and does not meet any criteria for type C lesion	Occluded and meets any criteria for type C lesion
Procedure success rate 98%	Procedure success rate 94%	Procedure success rate 91%	Procedure success rate 80%
Complication rate 2.4%	Complication rate 5.1%	Complication rate 9.8%	Complication rate 10.1%

Ellis Lesion-Specific Classification

Class I Low Risk	Class II Moderate Risk	Class III High Risk	Class IV Highest Risk
No risk factors	1–2 moderate correlates and the absence of strong correlates	≥3 moderate correlates and the absence of strong correlates	Either of the strongest correlates
Complication rate 2.1%	Complication rate 3.4%	Complication rate 8.2%	Complication rate 12.7%

Moderately strong correlates:
Length ≥ 10 mm
Lumen irregularity
Large filling defect
Calcium + angle ≥ 45 degrees
Eccentric
Severe calcification
SVG age ≥ 10 years

Strongest correlates:
Nonchronic total occlusion
Degenerated SVG

Note: If more than two medium risk factors are present, lesion is classified as type B2 and is considered complex.

National Cardiovascular Disease Registry® Cath PCI Registry® v4.3.1 *Coder's Data Dictionary*, 2008.

Note: Major complications were the composite of in-hospital death, acute myocardial infarction, emergency angioplasty, or emergency coronary artery bypass surgery. Lesion success was defined as a >20% decrease in stenosis with a residual stenosis of <50%.

Krone RJ, Shaw RE, Klein LW, *et al.* Evaluation of the American College of Cardiology/American Heart Association and the Society for Coronary Angiography and Interventions lesion classification system in the current stent era of coronary interventions (from the ACC-National Cardiovascular Data Registry). *Am J Cardiol* 2003;92:389–394.

Note: Complication defined as death, myocardial infarction, or emergent coronary artery bypass grafting.

Ellis SG, Guetta S, Miller D, *et al.* Relation between lesion characteristics and risk with percutaneous intervention in the stent and glycoprotein IIb/IIIa era: an analysis of results from 10,907 lesions and proposal for new classification scheme. *Circulation* 1999;100:1971–1976.

10. Stenosis calcification

    Calcification at the actual lesion site

11. Angulation

    None/mild = lesion located on a straight segment or a bend of <45 degrees.

    Moderate = 45–90 degrees bend.

    Severe = bend of >90 degrees. Bend should be evaluated in end-diastolic frame.

Use of the SYNTAX Score to Describe PCI Risk Versus CABG

In 2009, the SYNTAX trial compared multivessel PCI (including patients with left main narrowings) to CABG. The angiograms of the patients were analyzed and given SYNTAX scores. The SYNTAX score is an angiographic grading tool to determine the complexity of CAD. The results of this randomized study demonstrated that patients who had high SYNTAX scores (>34) did better with CABG compared to PCI than those with lower SYNTAX scores, in whom PCI had similar major adverse cardiac events with lower stroke rates.

The SYNTAX score was derived from preexisting lesion classifications, which included the American Heart Association (AHA) classification of coronary artery tree segments modified for the arts study, the Leaman score, the American College of Cardiology/American Heart Association (ACC/AHA) lesion classification system, the total occlusion classification system, the Duke and International Classification for Patient Safety (ICPS) classification system for bifurcation lesions, and a consensus opinion from among the world's experts.

The SYNTAX score is the sum of the points assigned to each individual lesion identified in the coronary tree with >50% diameter narrowing in vessels >1.5 mm diameter. The coronary tree is divided into 16 segments according to the AHA classification (Fig. 3-4). Each segment is given a score of 1 or 2 based on the presence of disease; this score is then weighted based on a chart, with values ranging from 3.5 for the proximal LAD to 5.0 for left main, and 0.5 for smaller branches. The branches <1.5 mm in diameter, despite having severe lesions, are not included in the SYNTAX score. The percent diameter stenosis is not a consideration in the SYNTAX score—only the presence of a stenosis from 50% to 99% diameter, < 50% diameter narrowing, or the total occlusion. A multiplication factor of 2 is used for non-occlusive lesions and 5 is used for occlusive lesions, reflecting the difficulty of PCI.

Further characterization of the lesions adds points. For example, a total occlusion duration >3 months, a blunt stump, a bridging collateral image, the first segment visible beyond the total occlusion, and a side branch >1.5 diameter all receive 1 point. For trifurcations, one diseased segment gets 3 points, two diseased segments get 4 points, three diseased segments get 5 points, and four disease segments get 6 points. For bifurcation lesions, 1 point is given for types a, b, and c; 2 points are given for types d, e, f, and g; and 1 point is given for an angulation >70 degrees. Additionally, an aorto-ostial lesion is worth 1 point, severe tortuosity of vessel is worth 2 points, lesion length >20 mm is worth 1 point, heavy calcification is worth 2 points, thrombus is worth 1 point, and diffuse disease or small vessel is at 1 point per segment involvement. For multiple lesions, less than three reference vessel diameters apart, these are scored as a single lesion. However, at distance greater than three vessel diameters, these are considered separate lesions. The types of bifurcations are shown in Figure 3-5. Segments in which bifurcations are evaluated are those involving the proximal LAD and left main, the mid LAD, the proximal circumflex, mid circumflex, and crux of the RCA. With regard to trifurcation lesions, these also are additive in number

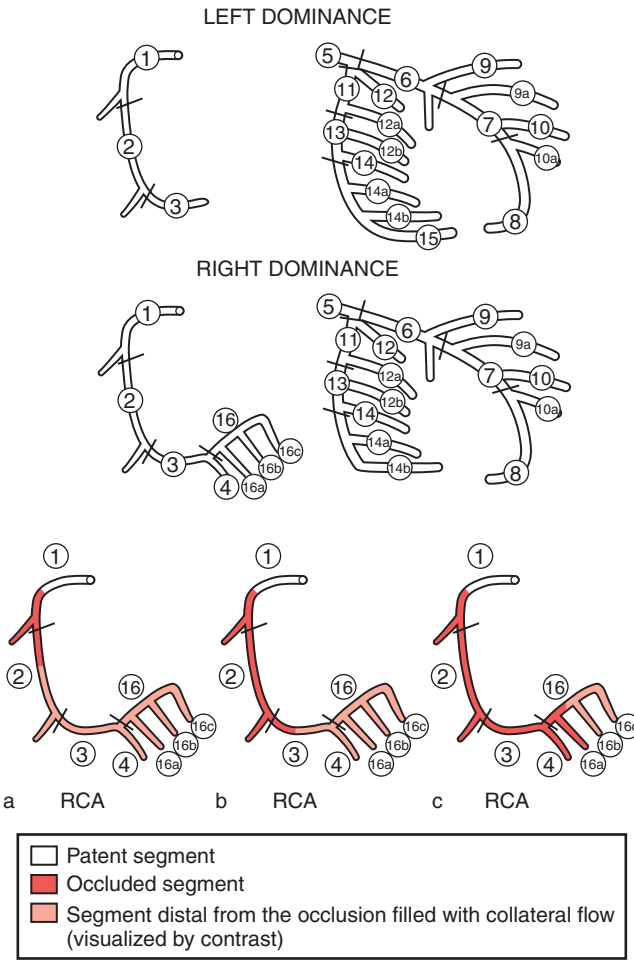


Figure 3-4 SYNTAX diagram. Definition of the coronary tree segments.

1. RCA proximal: From the ostium to one half the distance to the acute margin of the heart.
2. RCA mid: From the end of first segment to acute margin of heart.
3. RCA distal: From the acute margin of the heart to the origin of the posterior descending artery.
4. Posterior descending artery: Running in the posterior interventricular groove.

16. Posterolateral branch from RCA: Posterolateral branch originating from the distal coronary artery distal to the crux.

16a. Posterolateral branch from RCA: First posterolateral branch from segment 16.

16b. Posterolateral branch from RCA: Second posterolateral branch from segment 16.

16c. Posterolateral branch from RCA: Third posterolateral branch from segment 16.

5. Left main: From the ostium of the LCA through bifurcation into left anterior descending and left circumflex branches.
6. LAD proximal: Proximal to and including first major septal branch.
7. LAD mid: LAD immediately distal to origin of first septal branch and extending to the point where LAD forms an angle (RAO view). If this angle is not identifiable, this segment ends at one half the distance from the first septal to the apex of the heart.
8. LAD apical: Terminal portion of LAD, beginning at the end of previous segment and extending to or beyond the apex.
9. First diagonal: The first diagonal originating from segment 6 or 7.

9a. First diagonal a: Additional first diagonal originating from segment 6 or 7, before segment 8.

Continued

Figure 3-4, cont'd

10. Second diagonal: Originating from segment 8 or the transition between segments 7 and 8.
10a. Second diagonal a: Additional second diagonal originating from segment 8.
11. Proximal circumflex artery: Main stem of circumflex from its origin of left main and including origin of first obtuse marginal branch.
12. Intermediate/anterolateral artery: Branch from trifurcating left main other than proximal LAD or LCX. It belongs to the circumflex territory.
12a. Obtuse marginal a: First side branch of circumflex running in general to the area of obtuse margin of the heart.
12b. Obtuse marginal b: Second additional branch of circumflex running in the same direction as 12.
13. Distal circumflex artery: The stem of the circumflex distal to the origin of the most distal obtuse marginal branch, and running along the posterior left atrioventricular groove. Caliber may be small or artery absent.
14. Left posterolateral: Running to the posterolateral surface of the left ventricle. May be absent or a division of obtuse marginal branch.
14a. Left posterolateral a: Distal from 14 and running in the same direction.
14b. Left posterolateral b: Distal from 14 and 14 a and running in the same direction.
15. Posterior descending: Most distal part of dominant left circumflex when present. It gives origin to septal branches. When this artery is present, segment 4 is usually absent. (Adapted from Sianos G, Morel MA, Kappetein AP, *et al.* The SYNTAX score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention* 2005;1:219–227.) *LAD,* left anterior descending; *LCX,* left circumflex; *RAO,* right anterior oblique; *RCA,* right coronary artery.

of segments involved. The SYNTAX score algorithm then sums each of these features for a total SYNTAX score. Table 3-4 summarizes the SYNTAX grade categories. A computer algorithm is then queried and a summed value is produced.

The SYNTAX score was validated using a series of patients undergoing three-vessel PCI, such as the ARTS II trial. The variables were then associated with outcome events in the PCI studies. Low SYNTAX scores are <18, intermediate SYNTAX scores range from 18 to 27, and high SYNTAX scores are >27. High scores are associated with increasing cardiac mortality, major adverse cardiac events, and a specific, predefined combination of end points. The SYNTAX angiographic grading system was used alone to identify potential risk for revascularization. When comparing all clinical and angiographic factors, it turns out that the SYNTAX score—in addition to age, gender, smoking, diabetes, and acute coronary syndromes—is one of the highest predictors of cardiac mortality and major adverse cardiac events in patients undergoing

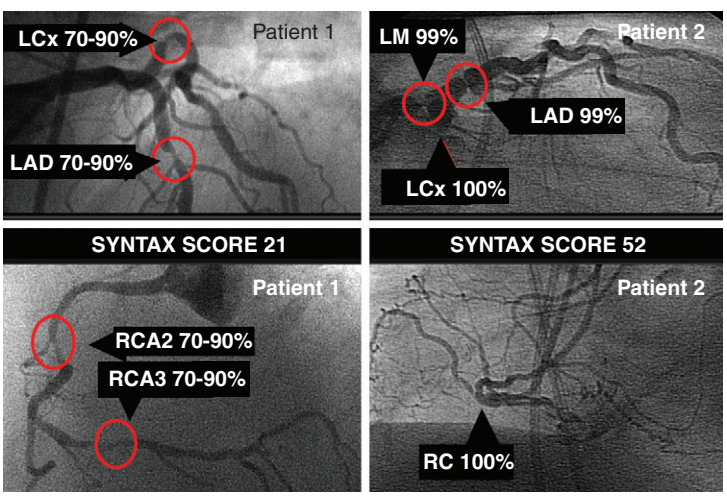


Figure 3-5 Example of SYNTAX score and specific angiographic anatomy.

Table 3-4

The SYNTAX Score Algorithm

1. Dominance
2. Number of lesions
3. Segments involved per lesion, with lesion characteristics
4. Total occlusions with subtotal occlusions:
   a. Number of segments
   b. Age of total occlusions
   c. Blunt stumps
   d. Bridging collaterals
   e. First segment beyond occlusion visible by antegrade or retrograde filling
   f. Side branch involvement
5. Trifurcation, number of segments diseased
6. Bifurcation type and angulation
7. Aorto-ostial lesion
8. Severe tortuosity
9. Lesion length
10. Heavy calcification
11. Thrombus
12. Diffuse disease, with number of segments

multivessel and, specifically, unprotected left main PCI. A SYNTAX score of >34 also identifies a subgroup with a particularly high risk of cardiac death independent of age, gender, acute coronary syndrome, ejection fraction, euro SCORE, and degree of revascularization.

The SYNTAX score is a useful differentiator for the outcome of patients undergoing three-vessel PCI. In Figure 3-5, examples of the types of SYNTAX score are provided on figures from the original paper. The patients with the highest scores have the highest risk and the lowest scores, the lowest risk. The SYNTAX scores can be divided into three tertiles. The high scores indicate complex conditions and represent greatest risks to patients undergoing PCI. High scores have the worst prognosis for revascularization with PCI compared to CABG surgery. Equivalent or superior outcomes for percutaneous intervention were noted in comparison to CABG surgery for patients in the lowest two tertiles (Fig. 3-6). The best discriminating feature of the SYNTAX score was between the lowest and highest tertiles of grading.

Problems and Solutions in the Interpretation of Coronary Angiograms

The basic issues regarding angiography are described in detail in Chapter 4 of *The Cardiac Catheterization Handbook,* 5th edition. This section briefly directs our attention to these same issues specifically directed at the PCI procedure.

Coronary target lesions may be obscured by *vessel overlap*. This may be the most common problem preventing accurate assessment of lesion length, especially for the proximal segments with large vessel and branches coursing across one another. Because a clear view of the target vessel and its stenosis is needed, multiple angles are required to reveal the proximal and distal extent of the lesions under consideration.

Poor contrast opacification of the vessel may lead to a false impression of an angiographically significant lesion or lucency that could be considered a clot. Inadequate mixing of contrast and blood presents as a luminal irregularity. A satisfactory bolus injection of contrast must be delivered. Large intravascular equipment may not permit this to occur, and the operator must consider whether a larger guide catheter is needed to see the lesion better. Enhanced contrast delivery can be achieved by obtaining better coaxial engagement of the guiding catheter or using a larger catheter, injecting during Valsalva maneuver phase III, or using a power injector.

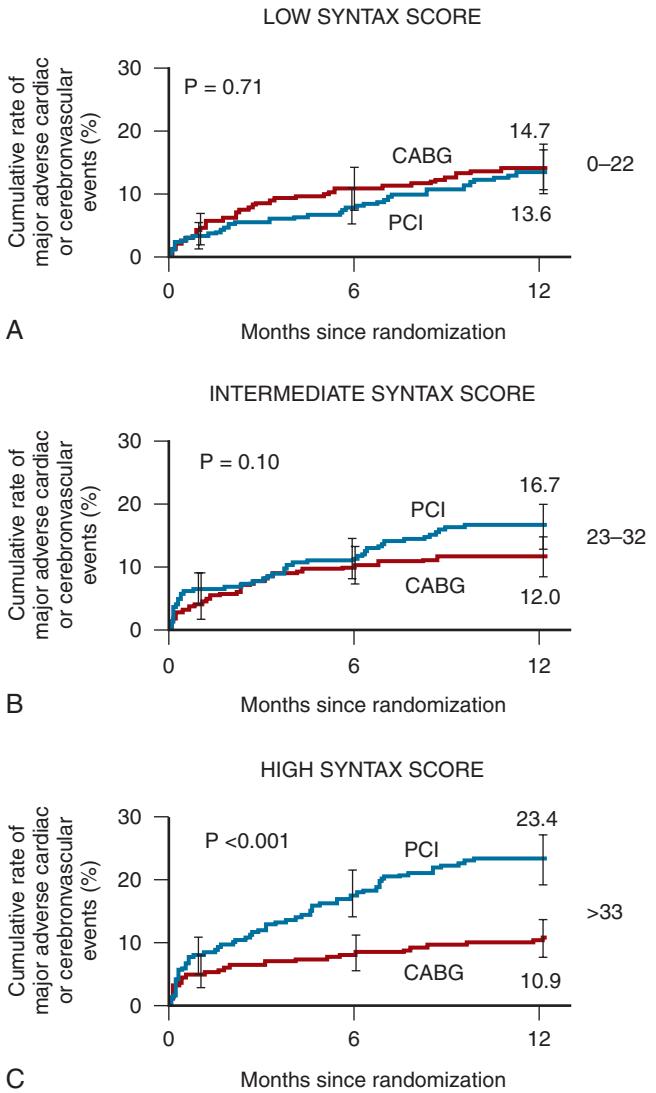


Figure 3-6 Outcomes of PCI vs. CABG by SYNTAX scores. From Serruys PW, Morice MC, Kappetein AP, *et al.* Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease (The SYNTAX Trial). *N Engl J Med* 2009;360:961–972. *CABG,* coronary artery bypass graft; *PCI,* percutaneous coronary intervention.

Catheter-induced spasm may appear as a fixed stenotic lesion, mistaken for a true organic lesion. This has been observed in both right and left (and left main) coronary arteries. These spastic segments may be single and proximal or may be multiple and located some distance from the ostium. Nitroglycerin should be administered in every case prior to initiating intervention, especially if there is any possibility of catheter-induced spasm. Repositioning of the catheter and administration of nitroglycerin (100–200 mcg through the catheter) may clarify if the presumed lesion is structural and not spastic. Often a change to a smaller diameter (6F or 5F) catheter, or catheters that do not seat deeply, may help.

Angiography for PCI of the left main coronary artery is straightforward for aorto-ostial and mid-body left main lesions but requires demonstration of the LAD/CFX ostia in cases of distal left main stenosis. Optimal views to identify the left main coronary artery remain the same as for those during diagnostic studies, with a shallow RAO with cranial or caudal angulation often providing an excellent view. In addition,

complementary LAO caudal view (spider view) will display the left main artery in an orthogonal projection. An additional problem is the appreciation of the hemodynamically significance of the left main stenosis especially when the angiographic narrowing is of questionable severity. For this situation, fractional flow reserve (FFR) measurement can provide the hemodynamic severity with a value of >0.80 having a low 5-year major adverse cardiac event rate. Some operators prefer IVUS before performing revascularization (see Chapter 13).

Another common problem for PCI is the negotiation of a tortuous left circumflex coronary artery. The origin of the CFX and its angle of departure from the left main should be shown in several projections to demonstrate whether it is steeply angled cranially or caudally. Guide catheter selection for the circumflex artery often requires longer guides (i.e., 4.0 JL4 guides, left Amplatz, or Voda) with special tips.

A discussion of the angiography of anomalous coronary arteries is provided in Chapter 4 of *The Cardiac Catheterization Handbook*, 5th edition. PCI for these arteries is performed in a routine fashion once stable guide catheter position is achieved.

Angiographic and Video Imaging Systems

In modern interventional practice, video display systems and fluoroscopy provide excellent digital angiographic imaging for PCI procedures. High-quality imaging problems still exist for obese patients and procedures that require extreme angulation to see certain locations of the coronary tree. Digital imaging archival storage has replaced cine-angiographic film and permits immediate review of images from any location that has computer access to the image storage system. A full discussion of the angiographic and imaging system are provided in *The Cardiac Catheterization Handbook*.

Radiographic Contrast Media for PCI

The contrast material is selected from several commercially available solutions with varying features of osmolarity, viscosity, and sodium content found to be appropriate for the specific procedure to be conducted. The most common contrast media for PCI is nonionic or low-osmolar contrast agents because of safety, patient tolerance, and cost. Selection of a nonionic or low osmolar contrast agent for the particular interventional procedure is, to a large extent, a matter of personal preference.

Radiation Exposure During PCI

Coronary angioplasty will deliver greater x-ray exposure than diagnostic studies because of the more complicated and time-consuming nature of the procedure. Previous studies have demonstrated that operator exposure is 93% greater for angioplasty than for routine diagnostic coronary angiography. This increase is due to longer fluoroscopy times in angioplasty without corresponding longer cineradiography times. Because of the angled projections used in coronary angioplasty, increased x-ray exposure may be present. The scattered x-ray dose has been reported to be four times higher with angioplasty than with diagnostic cardiac catheterization (Fig. 3-7).

Fluoroscopy Times

A study by Pattee et al. (1993) of radiation risk to patients from coronary angioplasty indicated that radiation doses varied considerably during the procedure because of large differences in exposure times.

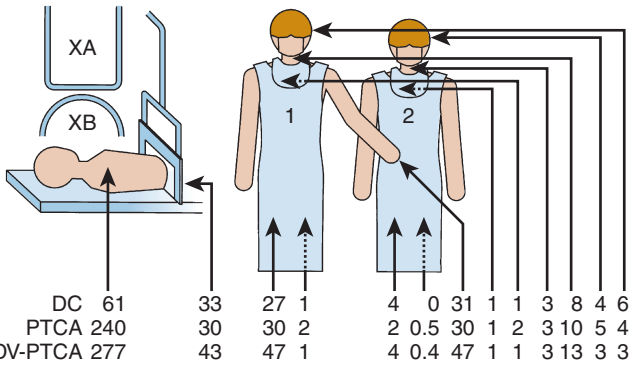


Figure 3-7 Radiation exposure rates for two operators during coronary angioplasty. *DC,* Diagnostic catheterization; *V-PTCA,* double-vessel percutaneous transluminal coronary angioplasty; *XA,* x-ray amplifier in plane A; *XB,* x-ray amplifier in plane B. (Modified from Finci L, Meier B, Steffenino G, *et al.* Radiation exposure during diagnostic catheterization and single- and double-vessel percutaneous transluminal coronary angioplasty. *Am J Cardiol* 1987;60:1401–1403.)

Table 3-5

Organ Doses and Risks of Cancer Mortality for an Average Coronary Angioplasty Procedure

Organ	Organ Dose (cGy)*	Cancer Risk Mortality ($\times 10^{-6}$)
Red bone marrow	2.29	92
Bone (surfaces)	2.29	9.2
Lung	9.35	636
Thyroid	0.99	5.9
Breast (women)	4.89	157
Total risk		
Men		743
Women		899

*1 Gy = 1 J/kg = 1 rad.
From Pattee PL, Johns PC, Chambers RJ. Radiation risk to patients from percutaneous transluminal coronary angioplasty. *J Am Coll Cardiol* 1993;22:1044–1051.

Skin exposures estimated for PCI are, on average, higher than for other x-ray procedures and the cancer mortality risk does not exceed the mortality risk of bypass surgery (Table 3-5). Good professional practice requires maximal benefit-to-risk ratio for angioplasty procedures employing high-dose fluoroscopy or cineradiography. Device specific procedure times may be longer than routine stent placement (Table 3-6).

Table 3-6

Estimated Radiation Entrance Exposure of Patients Using Phantom Model Data

Procedure	Fluoroscopy (R)	Cine (R)
Isolated balloon angioplasty	43	25
Isolated directional coronary atherectomy	32	23
Directional coronary atherectomy + balloon angioplasty	66	29
Isolated laser coronary angioplasty	45	18
Laser coronary angioplasty + balloon angioplasty	57	27
Elective stenting	52	27
Emergency stenting	96	41

From Federman J, Bell MR, Wondrow MA, *et al.* Does the use of new intracoronary interventional devices prolong radiation exposure in the cardiac catheterization laboratory? *J Am Coll Cardiol* 1994;23:347–357.
R, RAD.

Table 3-7

Radiation Dose and Angulation	
View	**Dose (Relative Increase)**
Image Intensifier Position	
RAO 30–60 degrees	1
LAO 30–60 degrees	2.6–6.1
Increasing Angulation	
LAO 30 degrees	1
LAO 60 degrees	3
LAO 90 degrees	9

LAO, left anterior oblique; *RAO,* right anterior oblique.

Angulated views increase radiation exposure. Left anterior oblique views produce 2.6 to 6.1 times the dose of radiation for the operator of equivalently angled RAO views (Table 3-7). Steeper LAO views also increased operator dose. LAO 90 degrees produces 8 times the dose of LAO 60 degrees and 3 times the dose of LAO 30 degrees. Fluoroscopy produced more radiation than cine during angioplasty, by a factor of 6:1. Reducing the steepness of angulation reduces operator radiation dosage.

Peripheral Vascular Angiography (See also Chapter 14)

Renal Arteriography

Selective renal arteriography or arteriography obtained from aortic flush is used to evaluate the renal artery origins and vasculature. Remember, for renal artery identification during aortography, the origins of the arteries usually arise at the L1 vertebra (just below the T12 ribs). Selective renal arterial injections provide the most detail. The LAO projection often provides the best view of the renal artery ostia in a majority of patients. Acute angled takeoffs of the renal artery may require specially shaped catheters or a brachial arterial approach from above. Atherosclerotic disease of the renal artery usually involves the proximal one-third of the renal artery and is seldom present without abdominal atherosclerotic plaques. A renal artery stenosis artery is rarely the sole determinant for surgery or angioplasty. Refractory hypertension and determination of the renin-angiotensin levels are usually the indicators for an interventional (angioplasty or stent) procedure. Renal artery fibromuscular dysplasia may occur and appear as atherosclerotic disease. This finding is often present in middle-aged women in whom other vessels are involved, most commonly cerebral or visceral arteries. In contrast to atherosclerotic narrowing, the proximal one-third of the main renal artery is usually free of disease.

Aortography of the thoracic and abdominal aorta is used to assess disease, dissections, and course of the vessel to perform and plan interventions. In high-risk PCI, abdominal aortographic is useful prior to insertion of IABP or LV support devices.

Lower Extremity Angiography

Angiography of the lower extremities is part of peripheral vascular interventions, discussed in Chapter 11. Based on clinical signs and symptoms of arterial insufficiency to the legs, suspected obstructions of the vessel are initially screened with noninvasive studies (i.e., ankle brachial index). Angiography is performed with small-diameter (5F)

catheters and reduced contrast volumes (10–20 mL over 1–2 sec) which are injected, panning down and following the artery course to the most distal locations. Angulated views may be necessary to open bifurcations and overlying vessels that obscure the vessel origin. Panning down to the ankle must be tested before obtaining final views. Digital subtraction techniques are commonly available in modern laboratories. Nonionic contrast agents are less painful than ionic media for peripheral angiography.

One major challenge encountered with femoral-iliac angiography is the contralateral (opposite leg) approach, crossing over the aortic bifurcation of the iliac vessels, especially in patients with high bifurcation or prior aorto-bifurcation graft. To enter the opposite iliac artery, a right Judkins or internal mammary artery graft catheter or other special catheters (crossover, Simmons catheter, etc.) is advanced with a guidewire over the bifurcation and down into the opposite femoral artery. The wire is passed into the selected artery. The catheter may be advanced and exchanged (over a long 300-cm wire) for an appropriate angiographic or balloon dilatation catheter, as required.

The area most frequently involved in peripheral atherosclerotic disease is the distal superficial femoral artery at the abductor canal (Fig. 3-7). The calf (tibial), and knee (popliteal) arteries are the next most commonly involved vessels after the superficial femoral artery. Disease in the deep femoral artery (femoral profunda) is rare. Pathways of collateralization are often rich and varied in patients with chronic distal femoral artery disease, especially in total occlusion of the superficial femoral artery that reconstitutes at or below the knee, close to the branching trifurcation of the tibial and deep peroneal arteries. Determining the level of reconstitution of collateralized vessels and distal runoff is crucial in determining the feasibility of revascularization. Magnified images focusing on the area of interest are frequently needed.

Diagrams and nomenclature for additional angiographic studies are shown in Figures 3-8 through 3-12; see also Chapter 11.

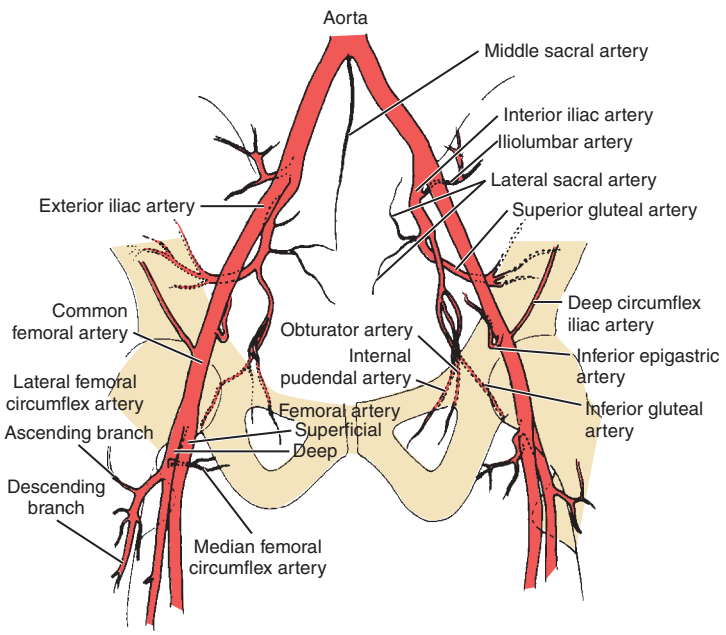


Figure 3-8 Pelvic and proximal femoral arterial branches. (From Johnsrude IS, Jackson DC, Dunnick NR. *A practical approach to angiography,* 2nd ed. Boston: Little, Brown, 1987.)

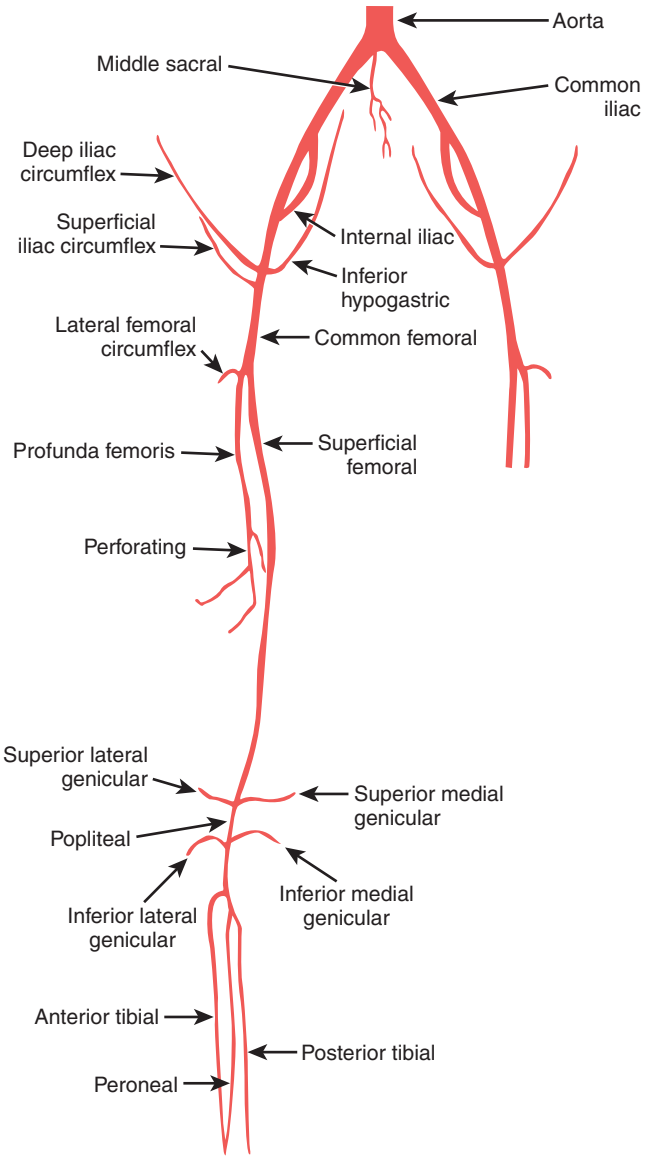


Figure 3-9 Lower extremity vascular anatomy. (From Medical Learning Incorporated, with permission.)

Pacemakers During PCI

The routine use of pacemakers for PCI is not required. Cardiac pacemakers may be used prophylactically during PCI to reduce the hemodynamic compromise of heart block and are needed to rescue patients after the development of conduction abnormalities associated with hypotension. External pacing patches are useful for emergency pacing when a temporary pacing wire cannot be immediately positioned. When using pacing patches, sedate the patient, since each electrical stimulation cause contraction of chest muscles as well as heart muscle and may be painful.

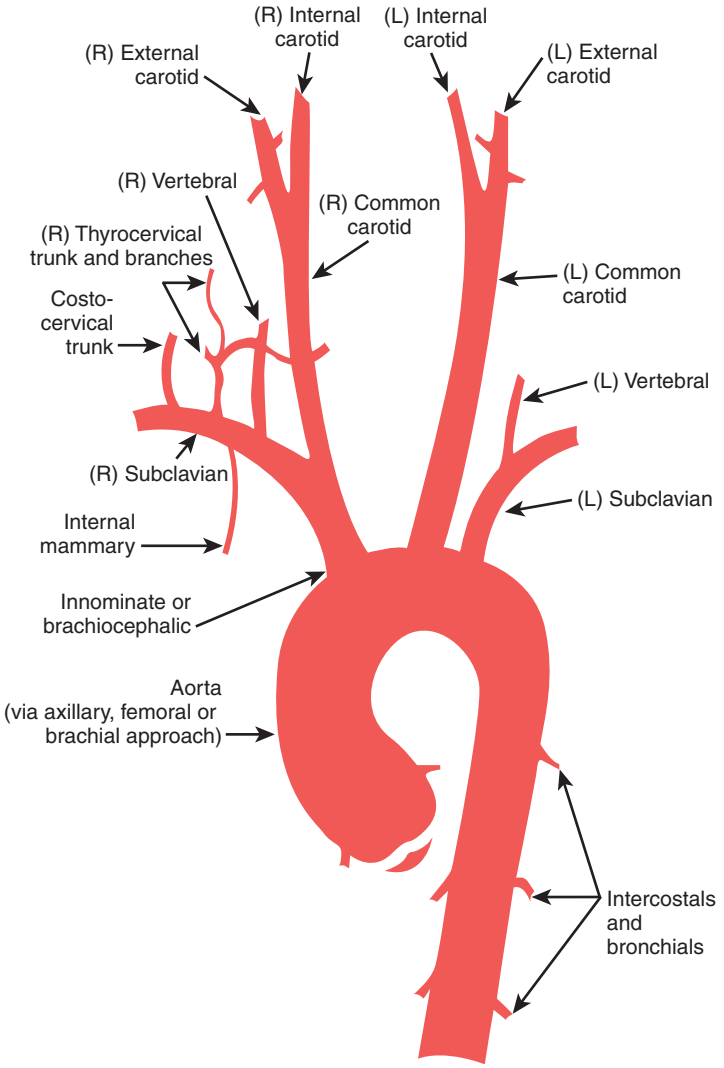


Figure 3-10 Ascending aorta and head and neck vessels. (From Medical Learning Incorporated, with permission.)

Indications

1. Previously demonstrated high-degree conduction block
2. Symptomatic bradycardia (after contrast or angiography of RCA)
3. Acute myocardial infarction with trifascicular block
4. Prophylactic use for rotational atherectomy and thrombectomy procedures, especially involving the RCA
5. Transluminal alcohol septal artery ablation in hypertrophic obstructive cardiomyopathy (HOCM) patients

1. Gastroduodenal
2. Superior pancreaticoduodenal
3. Inferior pancreaticoduodenal
4. Dorsal pancreatic
5. Pancreatic magna

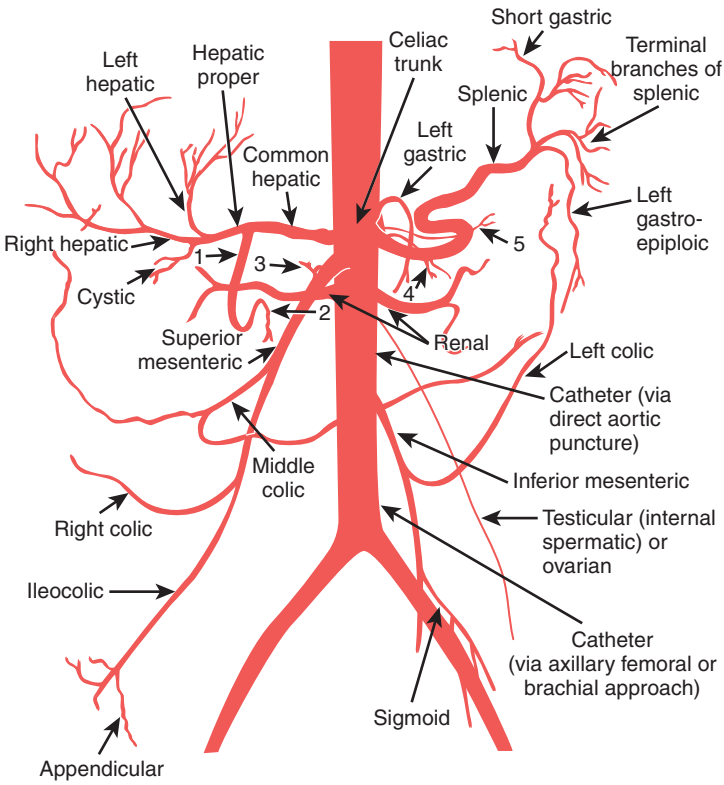
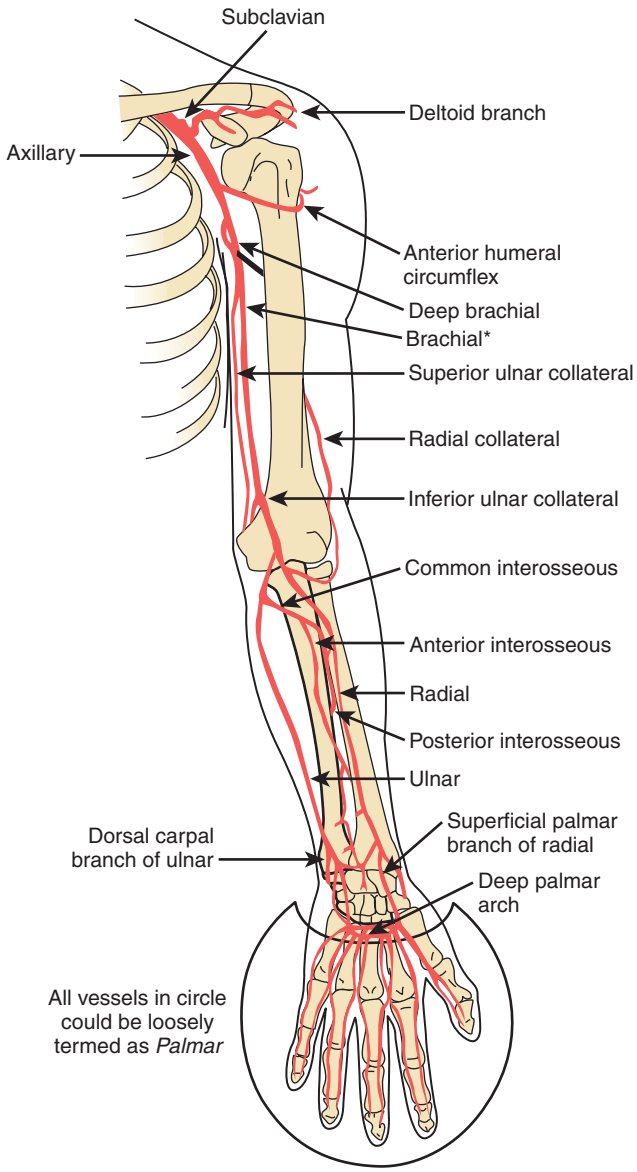


Figure 3-11 Commonly accessed arteries of the abdomen. (From Medical Learning Incorporated, with permission.)

Atropine may be used to prevent bradycardia but a pacemaker should be on standby for patients who experience severe bradycardia during coronary injections.

Temporary transvenous pacemaker placement can be achieved through the internal jugular, subclavian, brachial, or femoral vein route. The easiest access is usually the vein next to the arterial entry site. Right ventricular pacing is best accomplished with a 5 F balloon-tipped pacing catheter because there is a reduced incidence of perforation of the thin free wall or apex of the right ventricle when the balloon is inflated.

Cutaneous patch pacemakers are also effective until secured pacing routes can be established. Muscle contractions induced by the cutaneous pacing patches are uncomfortable so the patient should be well sedated.



*Level of lower margin of teres major muscle is site (landmark) for where the axillary artery by name changes into the brachial artery.

Figure 3-12 Vascular anatomy of the upper extremity. (From Medical Learning Incorporated, with permission.)

Suggested Readings

Balter S, Moses J. Managing patient dose in interventional cardiology. *Catheter Cardiovasc Interv* 2007;70:244–249.

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4

Complications of Percutaneous Coronary Interventions

RYAN BERG · MICHAEL J. LIM

Percutaneous coronary intervention (PCI) is associated with rare but serious complications. Most of the complications are generic to all diagnostic coronary angiography procedures and some are specific to coronary intervention. Events like death, myocardial infarction (MI), and bleeding occur at higher rates for interventional procedures since there is prolonged procedural time, complexity, and the use of anticoagulation (see Tables 4-1 and 4-2). It is critical to understand the possible complications of PCI in order to provide proper informed consent to the patient. It is also critical to be vigilant and to recognize potential complications at an early stage to try to reverse the adverse outcome, as the most common cause of all post-PCI deaths is from a procedural complication rather than from a preexisting cardiac condition. Fortunately, death is very rare with diagnostic angiography (<0.1%). The mortality rate increases 13 times with the addition of the complexity of coronary intervention to 1.3% (see Table 4-3).

Complications of PCI can occur at any step of the procedure, from the administration of sedation to the transfer as the patient leaves the laboratory. This chapter will discuss many of the possible complications in the order that they might be encountered during the procedure.

Table 4-1

Event Rates of Diagnostic Versus PCI Complications

Complication	Event Rate Diagnostic Procedure (%)	Event Rate Interventional Procedure (%)
Death	0.1	1.3
Significant bleed	0.5	5–12
AV fistula	0.75	1.1
Pseudoaneurysm	0.2	1–2
Contrast-induced nephropathy	5	8–57
Periprocedural MI (>3xULN cardiac enzyme)	0.1	8
Air embolism	0.1–0.3	0.1–0.3
Cerebrovascular accident	0.3	0.3
Ventricular arrhythmia	0.4	0.84
Coronary dissection	.03–0.46	29–50
Aortic dissection	<.01	.03
Infection/bacteremia	.11	0.64
Anaphylactoid reaction to contrast	0.23	0.23
Cholesterol embolization	0.8–1.4	0.8–1.4

AV, arteriovenous; *MI,* myocardial infarction; *ULN,* upper limits of normal.

Table 4-2

Complications Specific to PCI	
Complication	**Event Rate (%)**
No-reflow phenomenon	2
Stent thrombosis	2
Vessel perforation	0.84
Stent embolization	0.4–2
Need for emergent bypass surgery	0.15–0.3
Wire fracture	0.1
Stent infection	<.1 (case reports only)

Vascular Access

The first part of any PCI begins with vascular access. Using the femoral access, the major complications are femoral artery dissections (Fig. 4-1A, B), pseudoaneurysm, arteriovenous (AV) fistula, and retroperitoneal bleeding. As seen in Table 4-1, the incidence of these complications is increased compared to a strictly diagnostic procedure. All arterial complications are markedly reduced using the radial artery access.

A femoral artery pseudoaneurysm represents failure of sealing of the initial arterial puncture site, allowing arterial blood to flow into the surrounding tissue. This forms a pulsatile hematoma that acts as the covering roof of the aneurysm (see Fig. 4-1A, B). Pseudoaneurysms are late appearing, associated with local pain and swelling and diagnosed with femoral ultrasound with an excellent sensitivity of 94% to 97%. There are multiple risk factors for pseudoaneurysm (see Table 4-4).

Small pseudoaneurysms (<2 cm) often close spontaneously within 1 month. In larger pseudoaneurysms, or in small ones that fail to close, active treatment is necessary. The two most common treatment methods are ultrasound guided compression or thrombin injection. In some hospitals, ultrasound guided compression is not offered because of increased stress-related wrist injury to the ultrasound technician. Other advantages of thrombin injection over ultrasound compression are seen in Table 4-5.

Thrombin injection can be performed by diluting 1000 U into a 1 mL syringe with normal saline (final concentration of 100 U per 0.1 mL) and injected with direct ultrasound visualization through a long 22-gauge needle until thrombus is formed in the pseudoaneurysm cavity and Doppler-detected flow is abolished (see Fig. 4-2A, B). Rarely, in very large pseudoaneurysms and those resistant to thrombin injection, vascular surgery is required.

Another complication of vascular access is AV fistula formation (Fig. 4-2A, B). This is recognized on physical exam by a palpable thrill

Table 4-3

Modes of Death During PCI	
Mode of Death	**Event Rate (%)**
Low output failure	66.1
Ventricular arrhythmias	10.7
Stroke	4.1
Preexisting renal failure	4.1
Bleeding	2.5
Ventricular rupture	2.5
Respiratory failure	2.5
Pulmonary embolism	1.7
Infection	1.7

Adapted from Table 1, page 633 of Malenka DJ, O'Rourke D, Miller MA et al. Cause of in-hospital death in 12,232 consecutive patients undergoing percutaneous transluminal coronary angioplasty. Am Heart J 1999; 137(4):632-638.

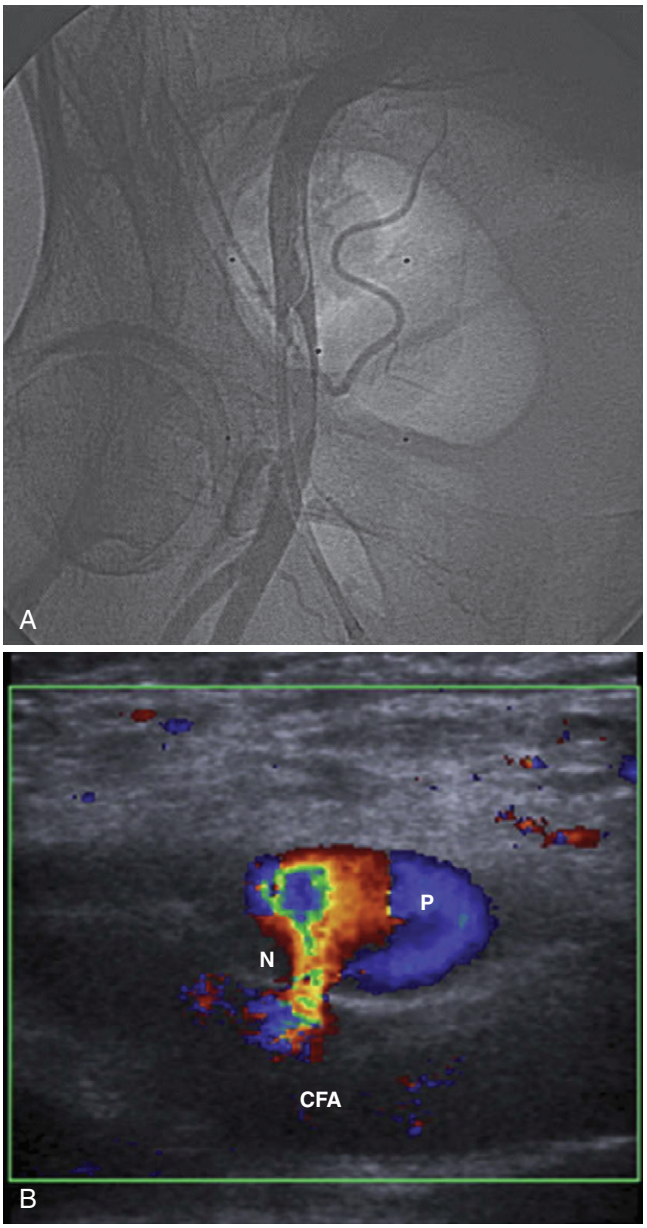


Figure 4-1 **A,** Cineangiogram frame of femoral artery dissection. This problem may be associated with limb ischemia or bleeding. It may require surgery but more often can be treated by contralateral access and implantation of iliac stent. **B,** Ultrasound picture of a pseudoaneurysm (*P*) arising from the common femoral artery (*CFA*). The circular color object is the hematoma which is fed by blood flow from the artery through the characteristic narrow neck (*N*). (From Ahmad F, Turner SA, Torrie P, *et al.* Iatrogenic femoral artery pseudoaneurysms—a review of current methods of diagnosis and treatment. *Clin Radiol* 2008; 63:1310-1316, Fig. 1.)

or an audible continuous bruit. Unlike pseudoaneurysms, conservative treatment with watchful waiting is the most common treatment modality (90%). One third of persistent AV fistulae will close during the first 12 months. Most persistent AV fistulae are asymptomatic and do not require repair. Rarely, they can be symptomatic (moderate pain) and, in large patient series, about 10% of AV fistulae will ultimately require surgical repair.

Table 4-4

Risk Factors for Pseudoaneurysm Formation
Procedural Factors
Catheterization of both artery and vein
Cannulation of the superficial femoral or profunda femoris rather than common femoral
Inadequate compression post procedure
More anticoagulation used
Patient Factors
Obesity
Hemodialysis
Calcified arteries

AV fistulae produce low shunt blood flow volumes (160–510 mL/min) compared to most large intracardiac (e.g., left to right) shunts or dialysis shunts (1000 mL/min). AV shunt flows must exceed 30% of the cardiac output to produce symptoms, and therefore it is quite rare to have a truly symptomatic shunt from a femoral AV fistula. The main risk factor for development of an AV fistula is a low arterial puncture, responsible for almost 85% of all AV fistulae.

Infection

A rare complication of groin access is systemic infection. The Society for Coronary Angiography and Intervention has detailed infection control guidelines for the cardiac catheterization laboratory. Proper sterile technique, including hand washing, use of hats, masks, gown, and gloves, has limited bacterial infections to occur in only 0.64% of interventional cases with septic complications in only 0.24% of cases. Routine antibiotic prophylaxis is *not* recommended before cardiac catheterization. However, if there is any concern for contamination of the femoral sheath (transport between rooms, patient touching site, changing out sheaths in a delayed procedure), it is standard to give 1 gram of cephalexin as a prophylactic measure. If the patient is allergic, 1gram of vancomycin can be given alternatively.

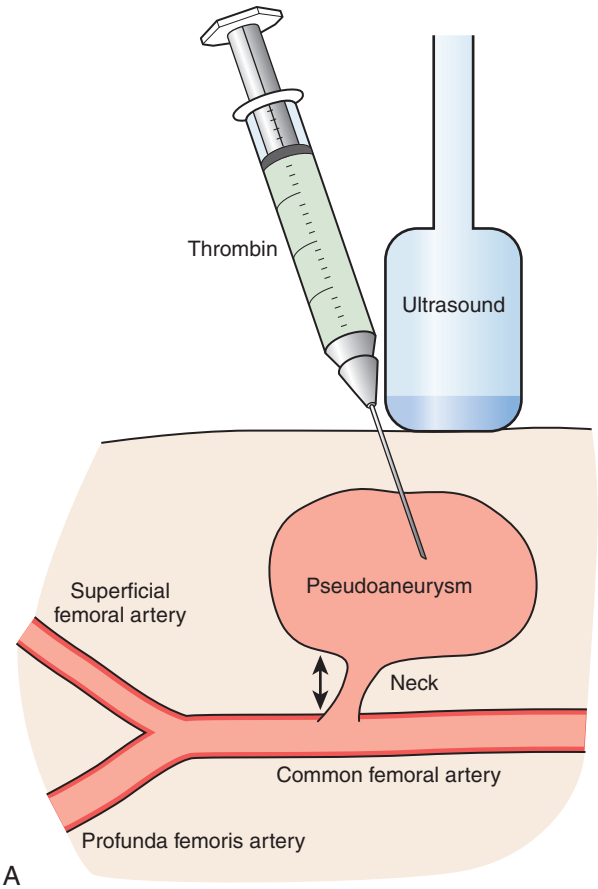
An equally concerning infectious complication is the exposure of the physicians or staff to the patient's potential pathogens. Universal precautions are to be followed by everyone in the catheterization laboratory. If there is an occupational exposure, proper management per your hospital guidelines should be followed. See Table 4-6 for U.S. Public Health Service guidelines.

Bleeding

The last and most dangerous complication of groin access is major femoral bleeding. Large femoral hematomas have an incidence of 2.8% compared to a 0.3% incidence of retroperitoneal bleeds. A retroperitoneal hematoma or a significant femoral hematoma (>5 cm) often

Table 4-5

Advantages of Thrombin Injection Compared With Ultrasound Compression
Greater technical success (96% vs. 74%)
Less painful to the patient and technician
No conscious sedation required
Effective in patients on anticoagulation
Can be used in pseudoaneurysms above the inguinal ligament



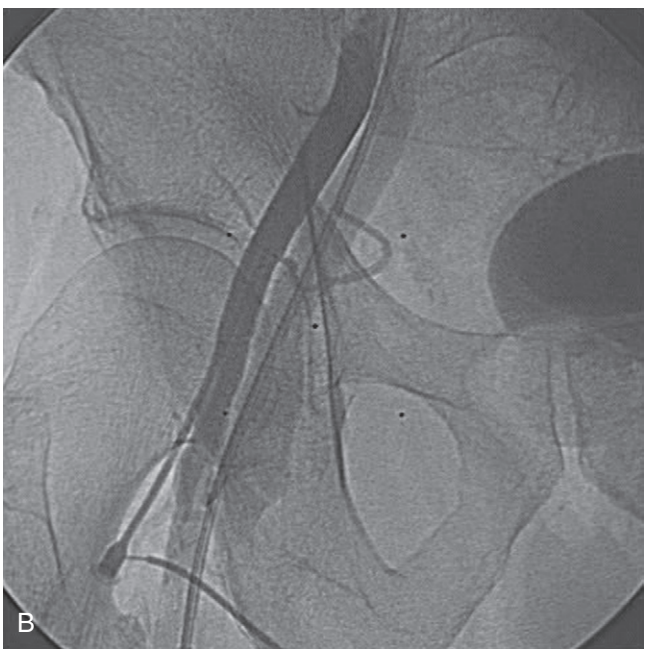


Figure 4-2 **A,** Schematic representation of the technique utilized to inject thrombin into a pseudoaneurysm under ultrasound guidance. (From Ahmad F, Turner SA, Torrie P, *et al.* Iatrogenic femoral artery pseudoaneurysms—a review of current methods of diagnosis and treatment. *Clin Radiol* 2008; 63:1310, Fig. 3.) **B,** Cineangiogram of arteriovenous fistula. Contrast visualized in the vein returning cranially indicates a communication with the artery, i.e., a fistula. Treatment is described in the text.

Table 4-6

Management of Occupational Exposure to Hepatitis B Virus, Hepatitis C Virus, and HIV

I. Definition: Direct contact with blood or body fluids (including percutaneous injury), contact of mucous membranes, or skin contact, especially if abraded.
II. Procedure
  A. Clean site of exposure with soap and copious amounts of water; flush mucous membrane with large quantities of water.
  B. Victim should report incident promptly, including patient/source information.
  C. Provide wound care and review with victim tetanus and hepatitis B prophylaxis information.
  D. Counsel and obtain consent for HIV testing from both victim and patient/source.
  E. Order the following laboratory specimen with appropriate consent obtained:
    1. Victim: hepatitis C antibody, hepatitis B surface antigen, HIV
    2. Patient: hepatitis B surface antigen and core antibody, hepatitis C antibody, ALT, RPR, HIV
  F. Review hepatitis B vaccination and response status of victim and follow postexposure prophylaxis to hepatitis B protocol
  G. If patient is hepatitis C positive or has elevated ALT:
    1. Follow postexposure prophylaxis to hepatitis B protocol.
    2. Follow up for anti-HIV therapy per protocol.
    3. Schedule hepatitis C and HIV testing for 6 weeks, 3 months, and 6 months.

ALT, alanine aminotransferase; *HIV,* Human Immunodeficiency Virus; *RPR,* rapid plasma reagin.
Adapted from Table 2, page 85 of Chambers C, Eisenhauer M, McNicol L, *et al*. Infection control guidelines for the cardiac catheterization laboratory: society guidelines revisited. *Catheter Cardiovasc Interv* 2006;67:78–86.

requires blood transfusions and prolonged hospitalization. More significant bleeds can require surgery, and significant bleeding in relation to PCI has been shown to correlate with mortality. Significant risk factors for major femoral bleeding are listed in Table 4-7.

The bleeding complication of most concern is a retroperitoneal hematoma, as large amounts of blood can fill the pelvic cavity and shock can develop rapidly. If a retroperitoneal bleed is suspected (see Table 4-8), volume (crystalloid solutions) should be given and blood should be ordered immediately for transfusion as soon as available. A vascular surgeon should also be consulted immediately. If the patient remains hemodynamically unstable despite volume resuscitation, surgery or endovascular repair (covered stent placement) may be needed; this occurs in approximately 16% of patients. However, the majority (84%) of cases can undergo a conservative "watchful waiting" strategy, as the hematoma usually stabilizes from tamponade of the initial site of extravasation. A computed tomography (CT)

Table 4-7

Significant Risk Factors for Major Femoral Bleeding

Risk Factor	Odds Ratio
Age >75 vs. <55	2.59
Heparin use postprocedure	2.46
Severe renal impairment	2.25
Age 65–74 vs. <55	2.18
Female patient	1.64
Closure device use	1.58
Sheath size 7F–8F vs. <6	1.53
GP IIb/IIIa use	1.39
Longer procedure duration	1.2

Adapted from Doyle B, Ting HH, Bell MR, *et al.* Major femoral bleeding complications after PCI. *JACC Cardiovasc Interv* 2008;1(2):202–209.

Table 4-8

Classical Signs and Symptoms of Retroperitoneal Bleed
Hypotension
Bradycardia
Back/flank pain
Groin pain
Abdominal pain
Transient response to fluid loading
Grey Turner sign (bruising along flank) [late appearing]
Cullen sign (bruising around umbilicus) [late appearing]

scan will be confirmative of the clinical diagnosis and should only be ordered once the patient is stable. Vascular surgeons use the CT scan as a baseline study and as a method to localize the origin of the bleed (if radiographic contrast media is used). Most retroperitoneal hematomas are caused by bleeding from the external iliac artery above the inguinal ligament or inferior epigastric artery. Rarely, bleeding below the inguinal ligament can track between tissue planes and extend into a retroperitoneal accumulation. Bleeding might also rarely extend to the scrotum through extension along the spermatic cord. Most cases of scrotal hematoma can also be managed conservatively with elevation and ice. However, rarely, large tense scrotal hematomas can cause significant pain and may compromise the viability of the scrotal skin and/or testicle which would require urgent surgical exploration (Fig. 4-3).

Complications of Vascular Access Closure Devices

Many arterial access sites will now be closed in the laboratory with percutaneous vascular closure devices. Hemostasis success rates are less than 100%. Each device has failure modes particular to its mechanism of action. Suture fractures or failure to deliver a knot (Prostar, Perclose), clip failure (StarClose), or collagen introduction or emboli into the vessel (Angio-Seal), or any failure to seal the puncture site can cause femoral or retroperitoneal bleeding. All vascular complications,

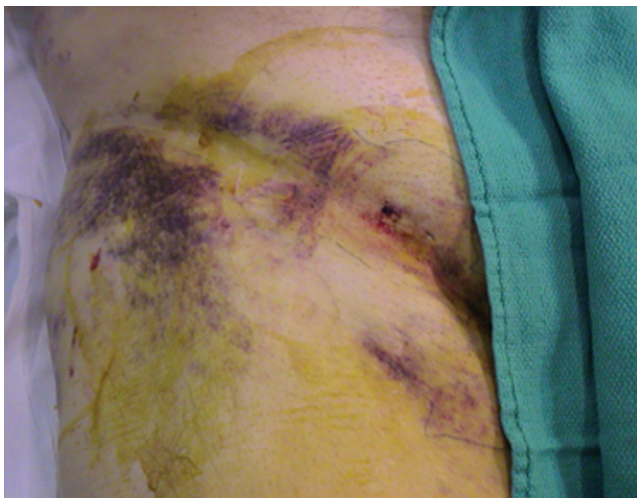


Figure 4-3 Picture of a patient following a cardiac catheterization utilizing femoral access who developed a large hematoma. (Courtesy of Dr. Zoltan Turi.)

including pseudoaneurysm, bleeding and hematoma, infection, arterial stenosis or occlusion, and venous thrombosis, can occur, with an incidence of approximately 1% to 5%.

Compared to manual compression, percutaneous closure device complications tend to have a greater incidence of pseudoaneurysms not amenable to ultrasound compression therapy, a greater loss of blood and need for transfusions, a greater incidence of arterial stenosis or occlusion, the need for more extensive surgical repair, and a greater incidence of groin infections. Thus, patients treated with vascular closure devices merit as much, if not more, attention to vascular complications than those treated with manual compression.

Atheroembolism

After vascular access is obtained, the guide catheter is advanced over a guidewire along the aorta to finally seat in the coronary artery of interest. The guidewire protects the vessels from the guide catheter scraping against the aortic wall causing atheroembolism. This is even more common in larger diameter guide catheters. The guidewire itself can also cause atheroembolism. To minimize atheroembolism, always aspirate blood from the catheter to clear any debris that might have been picked up in transit. If a guide catheter is connected to a Y connector during advancement, the valve should be cleared before proceeding.

Peripheral atheroembolism with obstruction of small arteries and arterioles by cholesterol crystals is known to produce the cholesterol embolization syndrome (CES), a rare occurrence (incidence of 0.75%–1.4%) using the above precautions. Cholesterol emboli are diagnosed by one of three cutaneous signs (see Table 4-9 and Fig. 4-4) and an elevated eosinophil count. In-hospital mortality is as high as 16% in those patients with definite CES, as multiorgan embolization often can lead to multiorgan failure.

Atheroembolism can also cause a cerebral vascular accident (CVA) or transient ischemic attack (TIA). The overall incidence of TIA (.04%) or CVA (0.25%) is quite low after PCI. There are various multivariate predictors of in-hospital CVA (see Table 4-10).

The most common indicator of a perioperative TIA or CVA is motor or speech deficits. In-hospital death can occur in up to 25% of those with a CVA, but increased mortality is not expected with a TIA. Management follows recommendations of the neurologic consultation. If the stroke occurs during the procedure, consideration should be given for an emergent neurointervention with resultant cerebral angiography and intervention if an ischemic stroke with arterial occlusion is found. If the stroke occurs postprocedure, confirmed by advanced imaging (Fig. 4-5), then thrombolysis can be considered (after hemorrhagic stroke has been ruled out).

Complications Related to Guide Catheters, Balloons, Stents, and Intravascular Devices

The guide catheter itself can cause coronary dissection with or without extension to the aortic root. Guide catheter–related dissection is a rare event with a reported incidence of 0.03% to 0.3%. The mechanism of

Table 4-9

Cutaneous Signs of Cholesterol Embolization Syndrome
Livedo reticularis
Blue toe syndrome (also known as purple toe syndrome or “trash” foot)
Digital gangrene

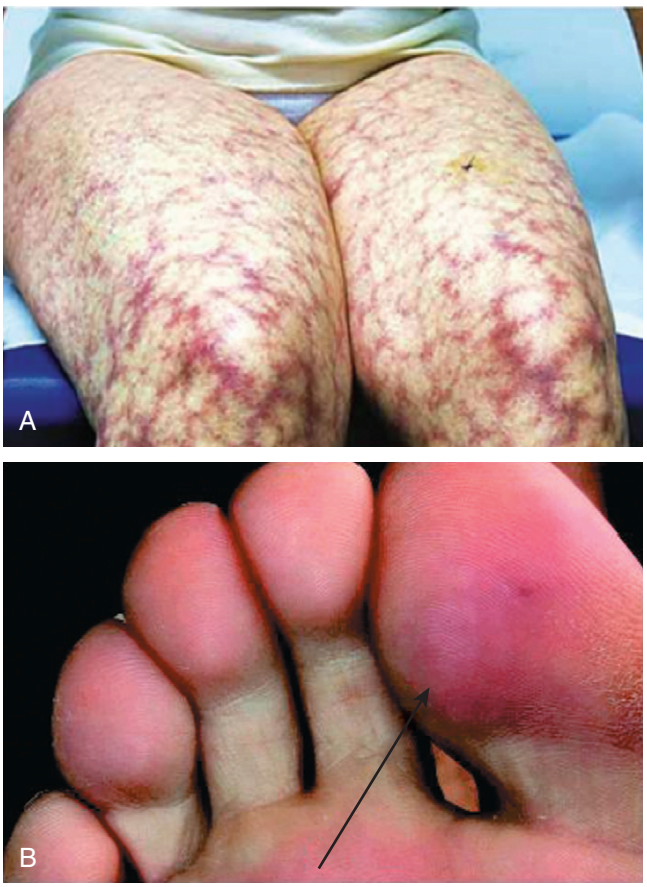


Figure 4-4 **A,** Picture showing a patient with livedo reticularis on both legs secondary to the "showering" of emboli after a cardiac catheterization. (From Kauke T, Reininger A. *N Engl J Med* 2007;356:284.) **B,** Picture of a patient's foot depicting the typical findings of cholesterol emboli to the great toe (*arrow*) following cardiac catheterization. (From Venzon R, Bromet D, Schaer G. Use of Corticosteroids in the Treatment of Cholesterol Crystal Embolization after Percutaneous Transluminal Coronary Angioplasty. Journal of Invasive Cardiology 2004;16(4):222-223.)

the dissection is likely due to mechanical trauma to the intima of the vessel (either normal or with plaque) from a catheter that is wedged into the wall rather than lying coaxial in the vessel lumen. A jet of contrast from an abnormally seated catheter can aggravate or produce a coronary dissection. Dissection of the right coronary artery from guide catheter trauma is more common than left main dissection because of

Table 4-10

Independent Predictors of In-Hospital CVA

Predictor of CVA	Odds Ratio
Thrombolytics prior to PCI	4.7
Creatinine clearance <40 mL/min	3.1
Urgent or emergent PCI	2.7
Unplanned intra-aortic balloon pump	2.3
IV heparin prior to PCI	1.9
Hypertension	1.9
Diabetes	1.8

CVA, cardiovascular accident; *PCI,* percutaneous coronary intervention.
Adapted from Dukkipati S, O'Neill WW, Harjai KJ, *et al.* Characteristics of cerebrovascular accidents after percutaneous coronary interventions. *J Am Coll Cardiol* 2004;43(7):1161–1167.

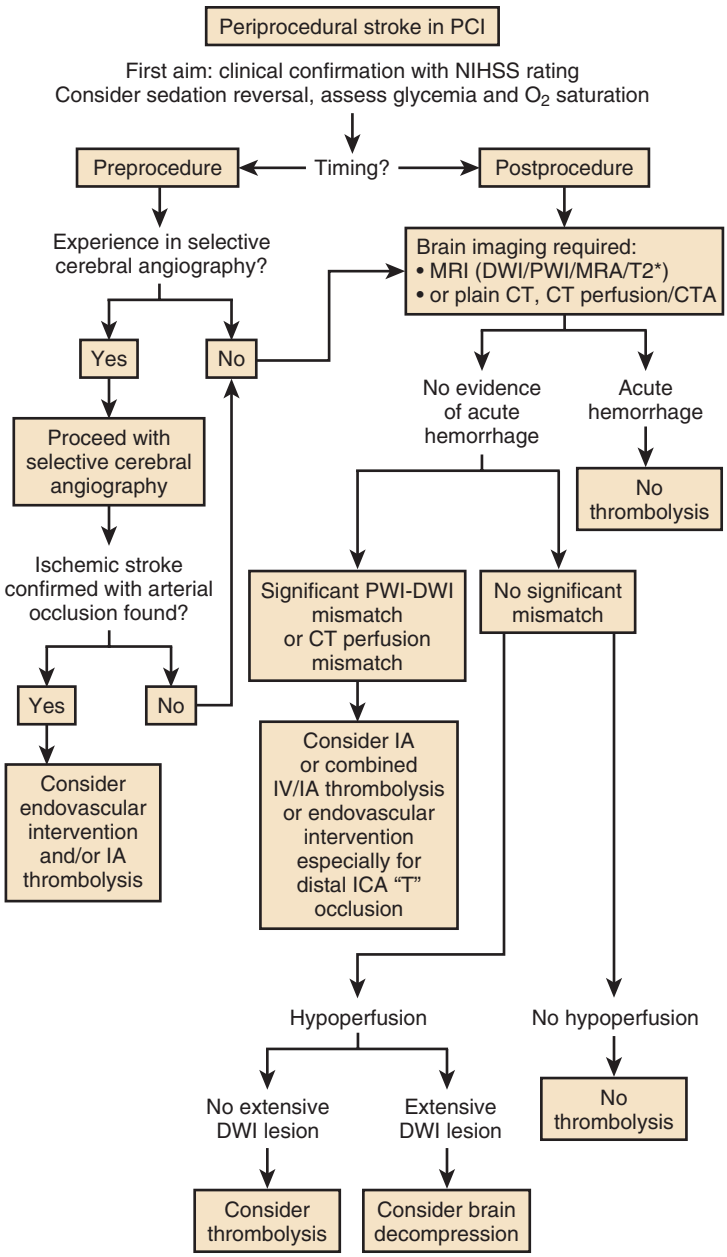


Figure 4-5 Suggested algorithm for the workup and treatment of an ischemic stroke following a catheterization procedure. *CT,* computed tomography; *CTA,* computed tomography angiography; *DWI,* diffusion-weighted imaging; *IA,* intra-arterial; *ICA,* internal carotid artery; *IV,* intravenous; *MRA,* magnetic resonance angiography; *MRI,* magnetic resonance imaging; *PWI,* perfusion-weighted imaging. (Adapted from Hamon M, Baron JC, Viader F, *et al.* Periprocedural stroke and cardiac catheterization. *Circulation* 2008;118:678–683.)

relative size differences in the ostia. The Amplatz left guide catheters are the most likely to dissect the coronary artery; this is due to its predilection to dive deeply into the artery. Stenting the dissected area remains the standard of treatment. A guide catheter ostial or proximal dissection should be fixed before proceeding to the intended PCI lesion. The rationale is that if the dissection is not fixed, it can propagate forward and cause abrupt vessel closure or propagate backward and cause aortic dissection.

Table 4-11

Classification of Coronary Dissection	
Type of Dissection	**Description**
Type A	Luminal haziness
Type B	Linear dissection
Type C	Extraluminal contrast staining
Type D	Spiral dissection
Type E	Dissection with reduced flow
Type F	Dissection with total occlusion

More commonly, coronary dissection is caused by balloon angioplasty trauma. Although microscopic dissections occur with every balloon angioplasty procedure, larger angiographically visible dissections are present in only 30% to 50% of all angioplasty procedures. In the era before stenting, coronary dissection was a significant risk factor for acute or abrupt vessel closure, a rare phenomenon in modern PCI procedures with stents easily sealing the tissue flaps. The classifications of coronary dissections are provided in Table 4-11 and Fig. 4-6.

The incidence of aortic dissection caused by guide catheter trauma is very rare (0.02–0.07%) (Fig. 4-7). Table 4-12 shows a classification scheme for extension of an aortic dissection. Almost all cases of retrograde extension of dissection are from the right coronary artery although there are a couple of case reports of similar dissection from the left main. Class I and II lesions have a good prognosis and can be treated by stenting of the coronary dissection with close clinical follow-up. It is reasonable to follow the evolution of the dissection with imaging modalities (CT or TEE). If the patient remains stable over the next 24 to 48 hours of hospitalization, he or she can be safely discharged without the expectation for further complication. To reduce the chance of extension, the systolic blood pressure must be optimally controlled.

Dissection type	Description	Angiographic appearance
A	Minor radiolucencies within the coronary lumen during contrast injection with minimal or no persistence after dye clearance.	
B	Parallel tracts or double lumen separated by a radiolucent area during contrast injection with minimal or no persistence after dye clearance.	
C	Extraluminal cap with persistence of contrast after dye clearance from the coronary lumen.	
D	Spiral luminal filling defects.	
E+	New persistent filling defects.	
F+	Those non-A–E types that lead to impaired flow or total occlusion.	
+ May represent thrombus.		

Figure 4-6 Types of coronary artery dissections: NHLBI classification system. (From Safian R, Freed M, eds. *The manual of interventional cardiology*, 3rd ed. Birmingham, MI: Physicians' Press, 2001: 389.)

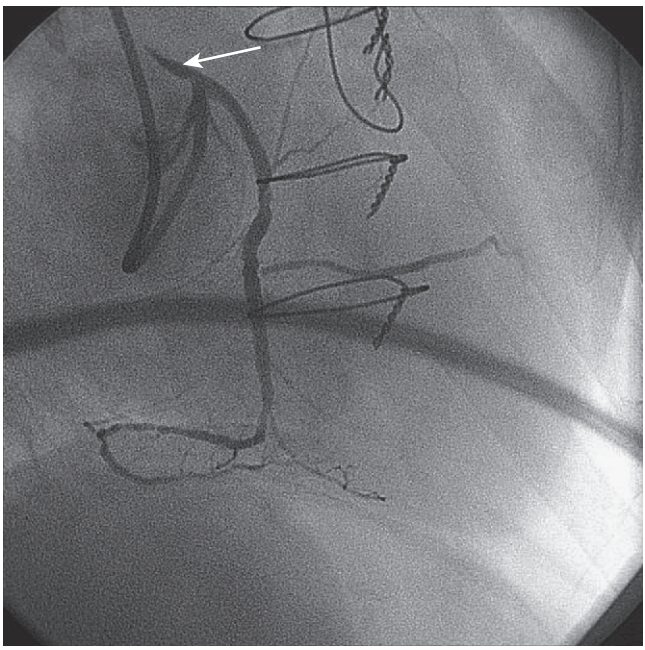


Figure 4-7 Angiogram of an anomalous right coronary artery following the placement of a stent. The arrow is pointing to a contrast stain extending upward from the ostium of the artery representing a dissection of the aorta caused by the guide catheter.

Table 4-12

Classification of Coronary Dissection With Retrograde Extension Into the Aortic Root

Classification	Extent of Aortic Involvement in the Dissection
Class I	Involving the ipsilateral cusp
Class II	Involving cusp and extending up the aorta <40 mm
Class III	Involving cusp and extending up the aorta >40 mm

However, antiplatelet therapy should not be suspended with a recently placed coronary stent. Class III lesions generally should be treated surgically and are associated with a high mortality rate.

Contrast Media Complications

Intravascular radiographic contrast media (RCM) can be associated with anaphylactoid reactions and acute renal failure. Fortunately, anaphylactoid reactions are rare, occurring in only 0.23% of procedures. Table 4-13 lists the severity classification for contrast-induced anaphylactoid reactions.

Table 4-13

Severity Classification for Contrast-Induced Anaphylactoid Reactions

Minor	Moderate	Severe
Urticaria (limited) Pruritus Erythema	Urticaria (diffuse) Angioedema Laryngeal edema Bronchospasm	Cardiovascular shock Respiratory arrest Cardiac arrest

Anaphylactoid Reaction

An anaphylactoid reaction is different from an anaphylactic reaction. An anaphylactic reaction is an IgE-mediated hypersensitivity reaction requiring prior sensitization of the patient to a given antigen. An anaphylactoid reaction does not require prior sensitization and is not antibody mediated. Rather, it is an immediate hypersensitivity reaction caused by direct mast cell activation and/or activation of the kinin and complement cascades. As seen from Table 4-13, the symptoms of the reactions can be similar. Risk factors for an allergic reaction to RCM include prior RCM reaction (up to 60% chance of repeat reaction) and a history of atopy (asthma, allergic rhinitis, drug allergies, food allergies). Shellfish allergy simply is a marker for an atopic individual and therefore is a slightly higher risk of a RCM allergic reaction. Patients are no more likely to have an anaphylactoid reaction than patients with other food allergies. Shellfish allergy involves tropomyosin proteins as the antigen, having nothing to do with iodine content in various shellfish.

Individuals at risk of an anaphylactoid reaction require premedication. Prednisone 60 mg should be given the night before the procedure and the morning of the procedure. Benadryl 50 mg IV should also be given up to 1 hour before the procedure. If the first prednisone dose is missed, the glucocorticoid regimen loses its effectiveness. H1 antihistamines have not been shown conclusively to reduce the risk of contrast-mediated reactions. Low osmolar or iso-osmolar contrast agents are used which will further decrease the chance of an anaphylactoid reaction as compared to the obsolete high osmolar contrast agents.

Treatment of an anaphylactoid reaction is dependent upon the severity of the reaction (see Table 4-14). For the most severe reactions,

Table 4-14

Treatment of Anaphylactoid Reactions in the Cardiac Catheterization Laboratory

Urticaria	Bronchospasm	Facial/Laryngeal Edema	Hypotension/Shock
Diphenhydramine 25–50 mg IV	Oxygen	Oxygen	Epinephrine bolus until blood pressure (BP) is maintained; then start infusion (as described previously)
	Albuterol Inhaler/ nebulizer	Emergent anesthesia consult for potential intubation. Tracheostomy tray should be available.	1 liter normal saline bolus rapidly (pressure bag). Repeat as necessary.
	Diphenhydramine 50 mg IV	Diphenhydramine 50 mg IV	
	Hydrocortisone 200–400 mg IV or methylprednisolone 125 mg IV	Epinephrine bolus/drip (as described under bronchospasm)	Diphenhydramine 50–100 mg IV
	For severe reaction Epinephrine bolus 10 mcg/ min as needed. An infusion of 1–4 mcg/ min might be needed as well.		Hydrocortisone 400 mg IV or methylprednisolone 125 mg IV

bolus epinephrine is prepared by mixing 0.1 mL of a 1:1000 solution or 1 mL of a 1:10,000 solution diluted in 10 mL syringe with saline, producing a final concentration of 10 mcg/mL. If a patient has recently taken beta blockers, he or she might not have an adequate response to epinephrine. In this case, glucagon 1 to 2 mg IV over 5 minutes, then infusion 5 to 15mcg/min, can be given to help reverse the effect of the beta blockade (by activating cyclic adenosine monophosphate [AMP] at a site independent from beta adrenergic agents).

Contrast-Induced Nephropathy (CIN)

Intravascular contrast media also can put the patient at risk for acute renal failure following PCI. This contrast-induced nephropathy (CIN) is likely caused by acute tubular necrosis. Mehran *et al.* developed a validated risk scoring system in order to predict the likelihood of developing CIN (see Fig. 4-8). CIN is typically defined as a relative increase in serum creatinine of >25% or an absolute increase >0.5 mg/dL. While it is not uncommon to develop transient increases in serum creatinine, it is rare to need temporary dialysis and even rarer to need permanent dialysis following CIN. The time course of CIN demonstrates an increase in creatinine starting in 12 to 24 hours for most patients, but it may take as long as 48 to 96 hours to peak. Most cases show a return to baseline creatinine by days 3 to 5 but can take up to 7 to 10 days. Serum creatinine should be routinely obtained at 48 to 72 hours following contrast administration in a high-risk patient.

In high-risk patients, CIN prevention consists of two principles: adequate hydration and limitation of the volume of contrast administered. The use of iso-osmolar contrast agents, sodium bicarbonate intravenous fluids, or n-acetylcysteine (600–1200 mg PO bid × 4 doses) are also purported to be effective, but the supporting data for each are weak. All other potential therapies, including diuretics, mannitol, dopamine, fenoldopam, or theophylline, have not been consistently proven to work for preventing CIN and should *not* be used.

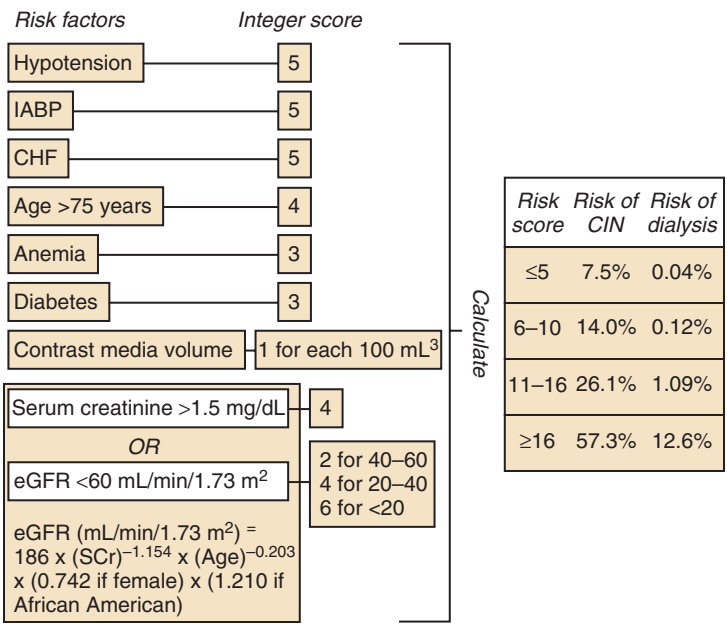


Figure 4-8 Risk score developed by Mehran *et al.* to predict the likelihood of developing postprocedural contrast-induced nephropathy (CIN). *CHF,* congestive heart failure; *eGFR,* estimated globular filtration rate; *IABP,* intra-aortic balloon pump.

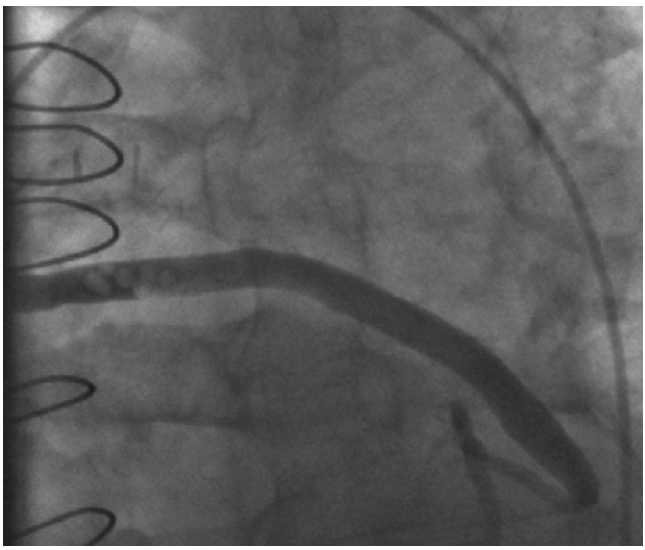


Figure 4-9 Angiogram obtained during a diagnostic catheterization depicting the injection of contrast into a vein graft to the obtuse marginal branch. On close inspection, several round objects can be seen in the proximal portion of this graft that represent air bubbles injected from the guide catheter.

Air Embolization

Another potential complication of coronary angiography and contrast media injection is air embolization (Fig. 4-9). This is always an iatrogenic complication due to failure to clear the air from the injection manifold system. Automatic contrast injection systems have a much lower rate of air embolism because of built-in air detection sensors. However, these systems do not fully eliminate the incidence of air embolism despite their inherent safety mechanisms and are not a replacement for good manifold technique of aspiration and visual inspection for bubbles. Treatment of coronary air embolism consists of immediate initiation of 100% oxygen by facemask. The oxygen helps to minimize ischemia and produces a diffusion gradient favoring reabsorption of the air. If large bubbles persist, the air can be aspirated by various aspiration catheters.

Arrhythmias

Another general complication of PCI that might occur at any time during the procedure is arrhythmia (either tachycardia or bradycardia). Unstable tachycardias like ventricular tachycardia or ventricular fibrillation are more commonly seen in the setting of an acute myocardial infarction. Bradycardia is most often seen in RCA occlusions; use of rotational atherectomy, especially in the RCA; or use of rheolytic thrombectomy catheters. Treatment of arrhythmias should follow standard Advanced Cardiovascular Life Support (ACLS) protocols. In general, for unstable patients, it is always good practice to electrically cardiovert tachycardic arrhythmias. For unstable bradycardia, atropine can be given and transcutaneous pacing can be initiated. These measures can buy time to set up for temporary transvenous balloon flotation pacemaker placement. Transvenous pacemakers should be placed prophylactically for cases of rotational atherectomy in the RCA and in all cases of rheolytic thrombectomy. If transvenous pacing is not readily available, guidewire pacing (connecting the negative lead to guidewire and positive lead to patient) may be used, as it has been shown to be effective.

No Reflow

An acute cessation of coronary flow during PCI can occur as a result of abrupt occlusion or a consequence of distal failure of outflow. This observation, termed the *no-reflow phenomenon*, is used by some authors only in conjunction with microembolization, whereas others reserve the term for myocardial blush grades of 0 or 1 (regardless of coronary TIMI flow) in the setting of a primary PCI.

Regardless, the differential diagnosis of no reflow includes severe spasm, dissection, in situ thrombus, plaque rupture, or distal microembolization. If no reflow is due to thrombus or new plaque rupture, then manual catheter aspiration is appropriate. Additional anticoagulation with IIb/IIIa inhibitors should be started. Rechecking activated clotting time (ACT) levels is prudent. Additional angioplasty and stenting might be necessary.

If no reflow is due to dissection, additional stenting is necessary. If no reflow is due to severe spasm, intracoronary nitroglycerin doses at a concentration of 100 mcg/mL are given until the vasospasm is relieved. Although intracoronary nitroglycerin can help relieve vasospasm, it has not been shown to be effective in relief of the no-reflow phenomenon from distal microembolization. See Table 4-15 for a list of medications that are effective in the no-reflow phenomenon. Often, several grams of these agents given in small 100mcg intracoronary boluses will be necessary.

No reflow from embolization to the microvasculature is most commonly seen in interventions on saphenous vein grafts and acute myocardial infarctions. Prophylactic distal filters or proximal protection with the Proxis device can help reduce the embolic burden and prevent no reflow.

Coronary Perforation

The incidence of coronary perforation is 0.84% of PCI cases. Coronary perforation can be caused by a wire "exiting" the vessel or by a tear (dissection) in the vessel from balloon angioplasty, stenting, or rotational atherectomy. Table 4-16 shows the classification of coronary perforations.

Class I and II perforations are usually managed conservatively without any specific treatment. Class III perforations are associated with rapid development of tamponade (63%), the need for urgent bypass surgery (63%), and a high mortality rate (19%). To minimize the chance of wire perforation, hydrophilic tipped or stiff wires that are used to get through difficult lesions should be exchanged for workhorse wires with softer hydrophobic tips. If a *distal* perforation from a wire tip occurs,

Table 4-15

Pharmacologic Management of No-Reflow Microembolization Syndrome

Medicine	Dose
Adenosine	100 mcg/mL 1–2 mL bolus, reassess flow and hemodynamics
Nitroprusside	100 mcg/mL 1–2 mL IC bolus, reassess
Verapamil	100 mcg/mL 1–2 mL IC bolus, reassess

Table 4-16

Classification of Coronary Perforations

Class	Description
I	Intramural crater without extravasation
II	Pericardial or myocardial blush/staining
III	Perforation >1 mm in diameter with contrast streaming or cavity spilling

the initial first step should be balloon tamponade of the vessel at the perforation site. Prolonged (several minutes) inflations with test deflations can be tried over an hour. After every balloon inflation, a puff of contrast should be given to evaluate the status of the perforation. If balloon tamponade is not successful, the operator must consider distal coil placement. Anticoagulation should *not* be immediately reversed with the wire and balloon in the vessel during the attempted perforation occlusion. Immediate reversal could lead to thrombosis throughout the whole vessel, an event that leads to a higher degree of mortality than the perforation itself. Reversal of anticoagulation should be performed after the equipment is removed from the coronary vessel. Discontinue glycoprotein IIb/IIIa inhibitor after a perforation is visualized.

Covered stents are usually not helpful for distal wire perforations because of the tapered vessel size at their end. However, if a branch of a main vessel is leaking, the perforation can be excluded with a covered stent. For larger perforations, a covered stent placement with a polytetrafluoroethylene (PTFE)-covered stent is the standard of care.

If the perforation occurred after balloon and stent placement, the balloon should be immediately reinflated to stop further extravasation of blood into the pericardial space. At this point, a pericardial drain can be placed to relieve or protect against tamponade while definitive measures are taken to treat the perforation. Bivalirudin should be discontinued, as it will take up to 2 hours to decrease the anticoagulation status to a normal level.

To place a covered stent, obtain contralateral access and, using a second guide catheter, intubate the perforated artery. The first guide catheter can be slightly backed out to allow intubation by the new guide. A 7 F guide is recommended by the package insert to deliver the covered stents, although anecdotally, they have been delivered through 6 F guiding catheters as well. Once the second guide is in place, a second guidewire should be used and placed up to the proximal edge of the inflated balloon. The balloon is then briefly deflated as the wire passes down to the distal vessel and then the balloon is immediately reinflated. Next, a covered stent is placed over the second guidewire to the proximal edge of the inflated balloon. The balloon is deflated, and the balloon and first wire are removed as the covered stent is positioned and immediately deployed. Deployment should be done at higher atmospheres to ensure good apposition of the covered stent. If additional access is not available, a quick exchange of balloon for covered stent can be used as well. However, this allows at least 30 to 60 seconds of free coronary flow into the pericardial space, so a pericardial drain must already be in place. As a little as 100 mL of an acute effusion can cause chamber compression and hemodynamic collapse. Once the covered stent is deployed and the coronary wire removed, heparin can be immediately reversed. The pericardial drain should be left in place overnight as a precautionary measure.

Retained PCI Equipment Components

Rarely, fragments of interventional equipment may be broken and remain in a coronary artery. This may occur with guidewire tips from both fixed-wire and movable, over-the-wire balloon systems, or distal fragments of various other catheters. These retained intravascular fragments carry the risk of coronary artery occlusion, distal embolization of clot, vessel perforation, infection, and ischemic complications. Dislodgement of stents from the delivery balloons has also been a source of retained interventional equipment.

Removal of intravascular fragments and foreign bodies should be done immediately to avoid the complications mentioned above, as well as incorporation of this material after several days during which the

objects become coated and interred within the vessel. There are several techniques for removal of retained intravascular foreign bodies. Baskets, forceps, and snares are available and are manufactured in sizes appropriate for placement within the coronary arteries. Guidewire fracture has an incidence of 0.1%. Most cases of wire fracture have been reported with the rotational atherectomy wires.

There are multiple options for dealing with a retained wire fragment. A small wire fragment may be left in place and allowed to endothelialize, as a stent would. Dual antiplatelet therapy should be given if a wire is just left in place.

For a wire fragment more centrally located in the vessel lumen, a stent can be deployed to trap the wire in place and avoid any possibility of further migration.

For a very long wire fragment extending into the guiding catheter, a balloon can be advanced to the end of the guide catheter and inflated, thereby trapping the wire against the side of the guide. At this point, the guide, balloon, and retained wire can be removed all at once.

For a longer wire fragment that does not extend into the guide, removal with a microsnare catheter may be the best choice. An over-the-wire balloon can be delivered next to a visible end of a retained guidewire (usually only the distal end is visible). A microsnare is then placed through the lumen of the over-the-wire balloon and is used to lasso the retained wire. It can then be pulled into the guiding catheter and subsequently removed. If a microsnare (Fig. 4-10A, B) is not readily available, using a two-wire technique, you can effectively ensnare a retained wire. This method is accomplished by placing two new guidewires next to the retained fragment. A single torquing device is placed over both wires and the Y connector is left slightly open as the torquing device is spun in one direction. This allows the two wires to form a double helix around each other, and this helix will propagate distally and eventually ensnare the retained wire. All wires are then pulled back into the guide at once (see Fig. 4-11).

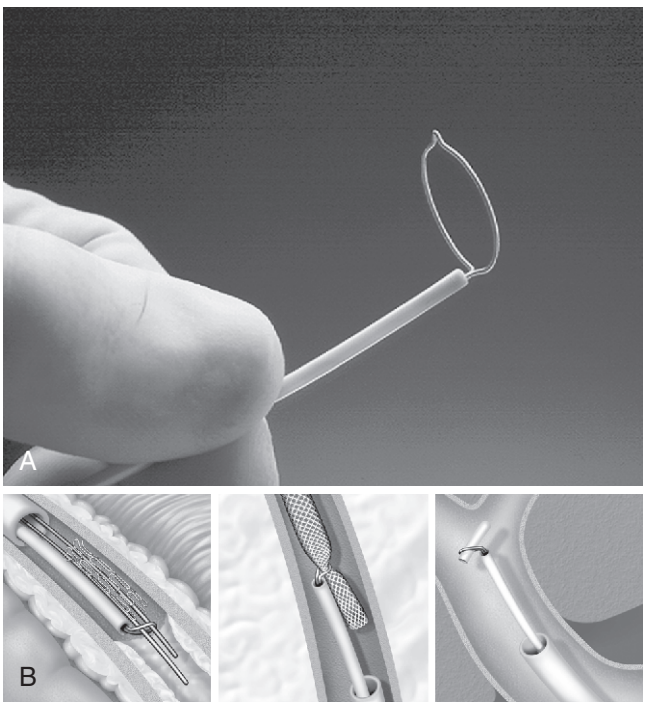


Figure 4-10 **A,** Microvena snare for retrieval of intracoronary equipment fragments. **B,** *Left panel,* Loop snare is used to capture a stent on second wire. *Middle,* Loop snare can be used to capture free stent. *Right panel,* loop snare can capture catheter fragments. (Courtesy Microvena Company, Minneapolis, MN.)

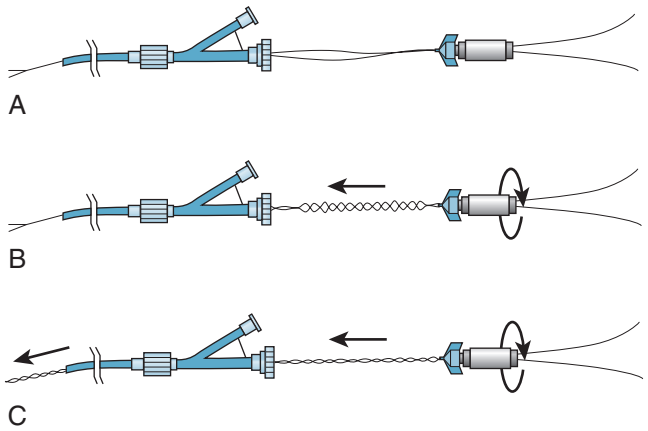


Figure 4-11 **A,** Diagram showing two guidewires entering single Y connector through a single torquing device. **B,** The wires are torqued together forming a helix. **C,** The helix propagates distally and can be used to ensnare a trapped wire fragment. (From Gurley J, Booth D, Hixon C, et al. Removal of Retained Intracoronary Percutaneous Transluminal Coronary Angioplasty Equipment by a Percutaneous Twin Guidewire Method. Catheterization and Cardiovascular Diagnosis. 1990; 19:251-256.)

Another rare complication is stent dislodgement and embolization with an incidence of approximately 0.4%. Stent dislodgement most often occurs in tortuous, calcified vessels. Management options include retrieval, deployment in place, or crushing against the wall of the vessel with a balloon or new stent. Ideally, retrieval should be tried first so that the stent is not placed in an unintended position. Mortality rates as high as 17% have been reported for stent embolizations that are unsuccessfully managed (usually requiring emergent surgery), but they are as low as 0.9% in patients who have successful retrieval of a stent.

Retrieval methods are similar to those discussed with fractured wire retrieval. Microsnares or dual wires can be used to ensnare and remove the loose stent. Additional methods include advancing a small balloon over the same wire that the undeployed stent is floating on, inflating the balloon past the stent, and then pulling back the balloon, which should shift the free stent into the guide. If the stent is dislodged in a large proximal vessel, retrieval with myocardial biopsy forceps can be considered as well. If retrieval is not possible, then "playing the stent where it lies" (i.e., deploying or crushing the stent at that site) is the best option. To attempt to place the stent in its position, a small balloon of similar or longer length than the stent is positioned across the profile of the stent. Initially, this can be attempted with a small 1.5-mm balloon blown up to 1 to 2 atm; this might be enough to capture the stent and move the system as a whole to a more desirable spot (to the initial lesion or at least out of the left main). If it cannot be moved, the balloon should be deployed at full atmospheres to dilate the stent as much as possible. A second undeflated balloon equal to the vessel diameter can then be placed to ensure adequate stent apposition. Rarely, a small diameter balloon will not recross the stent. In this case, a second wire is placed down next to the embolized stent, and another stent is placed adjacent to the embolized stent and is used to crush the loose stent against the arterial wall. In over 50% cases of embolization, the stent might be embolized to the peripheral arteries. In these cases, snares or forceps can be used to retrieve the stent if it can be visualized in the periphery.

Stent Thrombosis

Stent thrombosis is a rare but devastating complication of PCI. Mortality rates are reported from 25% to 40%. Stent thrombosis is defined as acute (<24 hours), subacute (within 30 days), late (between 1 month

Table 4-17

Academic Research Consortium Criteria for Stent Thrombosis	
Definition	**Criteria**
Definite stent thrombosis	Angiographic confirmation of thrombus that originates inside or within 5 mm of the stent which is associated with symptoms, electrocardiogram (ECG) changes, or biomarker elevation, or pathologic confirmation of stent thrombosis determined at autopsy, or from tissue obtained following thrombectomy
Probable stent thrombosis	Unexplained death occurring with 30 days after the index procedure, or a myocardial infarction occurring at any time after the index procedure that was documented by ECG or imaging to occur in an area supplied by the stented vessel in the absence of angiographic confirmation of stent thrombosis or other culprit lesion
Possible stent thrombosis	Unexplained death occurring more than 30 days after the index procedure

and 1 year) or very late (>1 year). In an attempt to standardize the definition of stent thrombosis, the academic research consortium divided the criteria for stent thrombosis into definite, probable, or possible (see Table 4-17).

Both bare metal stent and drug-eluting stent thrombosis occurs most commonly in the acute or subacute time frame. Drug-eluting stents, however, also have a higher risk of thrombosis in the late and very late period, due to incomplete endothelialization; this provides a strong argument for continuing dual antiplatelet therapy for at least 1 year after drug-eluting stent implantation. Premature discontinuation of dual antiplatelet therapy is the greatest risk factor for stent thrombosis. Other risk factors are listed in Table 4-18.

Almost one third of patients in whom antiplatelet therapy is discontinued prematurely are at risk of stent thrombosis. Because drug-eluting stents require a longer duration of dual antiplatelet therapy, it is crucial to decide before the diagnostic angiogram if the patient is an appropriate candidate for long-term dual antiplatelet therapy. If a patient cannot afford or cannot take long-term dual antiplatelet therapy, or if the patient requires surgery in the next 12 months that would necessitate discontinuation of antiplatelet therapy, consider bare metal stent use. Similarly, if the patient currently requires long-term Coumadin, or if the patient has a history of major bleeding episodes, he or she may not be a candidate for long-term dual antiplatelet therapy, and bare metal stent placement should be employed.

Stent Infection

The rarest complication of PCI is stent infection. There are fewer than 20 case reports of intracoronary stent infection in the literature which include both drug-eluting stents and bare metal stents. In some cases

Table 4-18

Risk Factors for Stent Thrombosis
Premature discontinuation of antiplatelet therapy
Incomplete stent expansion
Greater stent length
Subtherapeutic periprocedural anticoagulation
Cocaine use
Prior brachytherapy
Postprocedure TIMI flow grade <3
Treatment of bifurcation lesion

TIMI, thrombolysis in myocardial infarction.

Table 4-19

Risk Factors for Bacteremia After Cardiac Catheterization

Avoidable Risk Factors
Difficult vascular access
Multiple skin punctures
Repeated catheterization at the same vascular access site
Extended duration of the procedure
Use of multiple PTCA balloons
Deferred removal of the arterial sheath
Unavoidable Risk Factors
Presence of congestive heart failure
Patient's age >60

PTCA, percutaneous transluminal coronary angioplasty.
Adapted from Kaufman B, Kaiser C, Pfisterer M et al. Coronary stent infection: a rare but severe complication of percutaneous coronary intervention. *Swiss Med Wkly* 2005;135:483-487.

mycotic aneurysms are formed at the site of stenting, but other cases present with persistent bacteremia. *Staphylococcus aureus* is the most common microorganism implicated. Stent infection presents within 4 weeks after stent implantation with fever and bacteremia. Typical findings of chest pain, ECG changes, and troponin elevation might be absent. A high degree of suspicion should accompany any fever occurring within 1 month of PCI. Confirmation of the diagnosis may be difficult with imaging. Besides antibiotic therapy, most cases (>60%) will require surgery. In general, there is up to a 40% mortality rate with stent infection. Strict infection control measures (as discussed in Kern (2011) *The Cardiac Catheterization Handbook*, 5th edition) must be adhered to in the catheterization laboratory. Risk factors for bacteremia associated with cardiac catheterization are shown in Table 4-19.

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5

Antithrombotic and Antiplatelet Therapy for Percutaneous Coronary Interventions

MORTON J. KERN · ARNOLD H. SETO · CHARLES M. PARISE

Familiarity with commonly used antithrombotic and antiplatelet agents is required in the management of interventional cardiology patients. This chapter outlines recommendations and uses of various antithrombotic and antiplatelet agents. Antithrombotic and antiplatelet agents for percutaneous coronary intervention (PCI) are summarized in Table 5-1, and recommendations from the ACC/AHA are summarized in Table 5-2.

Anticoagulants

Heparin

Heparin is given to PCI patients in doses between 40 and 70 U/kg intravenously. Unfractionated heparin (UFH) is a glycosaminoglycan widely used as an anticoagulant. It acts by accelerating the activity of antithrombin III (AT III), a molecule that breaks down the procoagulant factor IIa (thrombin) and factor Xa by forming a complex with AT III and thrombin. Figure 5-1 diagrams the coagulation cascade and role

Table 5-1

Antithrombotic and Antiplatelet Agents for PCI Intervention

Antithrombotic Therapy
• Heparin (unfractionated)
• Low-molecular-weight heparin
• Direct thrombin inhibitor
— Polypeptide inhibitors (hirudin [Lepirudin], bivalirudin [Angiomax])
— Low-molecular-weight inhibitors (argatroban [Acova])
Antiplatelet Therapy
• Cyclooxygenase inhibitors (aspirin)
• Adenosine diphosphate (ADP) receptor inhibitors (clopidogrel [Plavix], prasugrel [Effient], ticlopidine [Ticlid])
• Phosphodiesterase inhibitors (cilostazol [Pletal])
• Glycoprotein IIb/IIIa receptor inhibitors (abciximab [ReoPro], eptifibatide [Integrilin], tirofiban [Aggrastat])
• Adenosine reuptake inhibitors (dipyridamole [Persantine])
• CPTPs (cyclo-pentyl-triazolo-pyrimidines) [Ticagrelor (Brilinta)]
• Platelet glycoprotein IIb/IIIa antagonists
— Abciximab
— Eptifibatide
— Tirofiban

Table 5-2

ACC/AHA Recommendations for Pharmacologic Management of Patients Undergoing PCI Intervention

Drug	Unstable Angina/NSTEMI	STEMI	Comments
Aspirin	I	I	
Clopidogrel	I	I	Loading dose of 300–600 mg recommended prior to PCI.
Prasugrel	I	I	
Unfractionated heparin	I	I	
Low-molecular-weight heparin	I	I	
Bivalirudin	I	I	Especially for patients at high risk of bleeding.
Fondaparinux	I	I	Requires an additional antithrombin during PCI. Preferred for conservative strategy.
Glycoprotein IIb/IIIa inhibitors	IIa	IIa	IIa in selected patients without preloading clopidogrel, or with significant thrombus burden; IIb otherwise.

ACC, American College of Cardiology; *AHA,* American Heart Association; *NSTEMI,* non-ST-segment elevation myocardial infarction; *PCI,* percutaneous coronary intervention; *STEMI,* ST-segment elevation myocardial infarction.

of antithrombins. In contrast, low-molecular-weight heparin (LMWH) is too small to participate in this ternary complex and exerts its effect primarily on factor Xa levels. Both UFH and LMWH are unable to significantly interact with thrombin that is already bound to clot. For this reason adjunctive antiplatelet agents (e.g., aspirin, thienopyridines, and glycoprotein IIb/IIIa receptor antagonists) are typically required for PCI procedures.

The half-life of UFH is 1.5 hours, allowing for greater control of the anticoagulant effect. Discontinuation of a UFH IV drip can normalize the clotting cascade in a few hours. If there is a need to discontinue the anticoagulant effect of UFH emergently, protamine sulfate can be given, which forms an ion pair with UFH, neutralizing it. Protamine dosage for UFH reversal is 1 to 1.5 mg IV per 100 units of remaining active UFH, based on the time course of UFH administration (max 50 mg/dose at 5 mg/min). Although most of the protamine sulfate used today is recombinant, caution should be used in patients with fish allergies, as some proportion may still be derived from fish sperm. Typical protamine allergic reactions can include hypotension and bronchoconstriction due to histamine release. A slow IV infusion, while closely monitoring the patient, may mitigate the severity of the reaction. Care should also be observed in diabetic patients taking protamine-containing insulin preparations (e.g., NPH insulin), as they are at increased risk for severe protamine reactions, including anaphylaxis.

Summary of Heparin Mode of Action

1. Heparin is a mixture of glycosaminoglycans (mucopolysaccharides) that combine with a plasma protein called antithrombin III (AT III) to make the AT III a highly effective inhibitor of thrombin and several other clotting factors.
2. Heparin requires the presence of AT III to be effective.

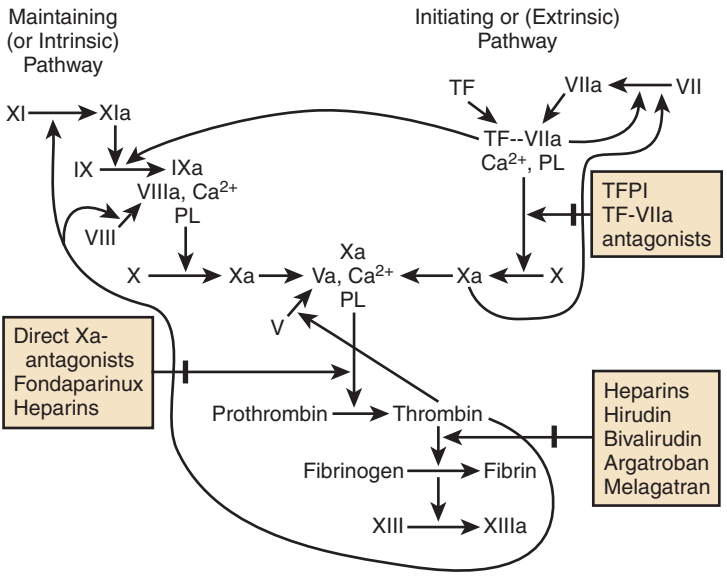

Figure 5-1 Diagrams of the coagulation cascade and role of antithrombins. (Adapted from Wiley-Liss, Inc., a subsidiary of John Wiley & Sons, Inc. from Conde ID, Kleiman NS. Arterial thrombosis for the interventional cardiologist: from adhesion molecules and coagulation factors to clinical therapeutics. *Catheter Cardiovasc Interv* 2003;60:236–246.) and Garg R, Uretsky BF, Lev EL. Anti-platelet and anti-thrombotic approaches in patients undergoing percutaneous coronary intervention. *Catheter Cardiovasc Interv* 2007;70:388–406.

3. Unfractionated heparin (UFH) is a heterogeneous polysaccharide that binds to antithrombin to inhibit thrombin and factor Xa.

Monitoring

Heparin therapy is usually monitored by the activated clotting time (ACT), which is the time for whole blood to form a firm clot. When blood levels of heparin have been measured directly, antithrombotic efficacy occurs between 0.2 and 0.4 U/mL. It is common practice to maintain the Hemochron ACT at 300 to 350 seconds and the HemoTec ACT at 250 to 300 seconds, although some interventionalists may prefer higher values. When used with glycoprotein IIb/IIIa antagonists (abciximab, eptifibatide, tirofiban), the recommended heparin bolus is reduced to 40 U/kg to achieve a target ACT of between 200 and 250 seconds. The activated partial thromboplastin time (aPTT) is not used in the catheterization laboratory as it saturates at the doses of heparin used for PCI.

Indications

1. Angina for PCI, unstable angina, acute myocardial infarction
2. Following anterior wall myocardial infarction, 7 to 10 days until warfarin (Coumadin) increases international normalized ratio (INR) to therapeutic levels
3. Prevention and treatment of deep venous thrombosis
4. Treatment of pulmonary embolism

Side Effects

Heparin-Induced Thrombocytopenia (HIT). Heparin can cause an immune-mediated thrombocytopenia that can lead to thrombosis, stroke, loss of limb, or other ischemic events (e.g., heparin-induced

Table 5-3

Heparin-Induced Thrombocytopenia

	Type I Heparin-Induced Thrombocytopenia	Type II Heparin-Induced Thrombocytopenia
Incidence	10%	Rare
Mechanism	Direct platelet aggregating effect of heparin	Autoantibody (IgG or IgM) directed against platelet factor IV–heparin complex
Onset	Early (1–5 days)	Later (>5 days); may occur sooner if prior heparin exposure
Platelet count	50,000–150,000/mm^3	<50,000/mm^3
Duration	Transient; often improves even if heparin is continued	Requires discontinuation of all heparin; gradual recovery in platelet count over 1–5 days in most patients
Clinical	Benign	Recalcitrant venous and arterial course thromboses and thromboembolism; may be fatal
Heparin	Unfractionated or low-molecular-weight heparin	Argatroban and lepirudin are FDA-approved

may be continued

Modified from Safian R, Grines C, Freed M. *The new manual of interventional cardiology*. Birmingham, MI: Physicians' Press, 1999.

thrombocytopenia with thrombosis [HITT]). If heparin is given after the procedure, monitor platelet count daily. If platelets fall below 100,000 or by more than 50%, discontinue heparin and consider the possible etiologies of thrombocytopenia.

There are two types of heparin-induced thrombocytopenia (HIT) (Table 5-3). Type I HIT (HIT-1) is due to direct (non–immune-mediated) platelet activation, with mild thrombocytopenia and a benign clinical course. Type II HIT (HIT-2) is due to immune-mediated platelet activation, with moderate or severe thrombocytopenia and serious thromboembolic complications. Platelet transfusions should not be used to treat HIT due to increased risk of thrombotic complications. Anticoagulation to prevent thrombosis is the main treatment of HIT-2 patients; typical drugs are the direct-acting thrombin antagonists, lepirudin and argatroban. Compared with UFH, LMWH carries a reduced risk of HIT.

Minor Bleeding (Puncture Site, Gums, etc.). Discontinue heparin. Monitor vital signs, aPTT, hemoglobin, hematocrit, platelet count, ACT.

Major Bleeding (Retroperitoneal, Gastrointestinal). After bolus only, give protamine sulfate (1% solution) at 1 mg/100 U heparin or approximately 25 mg slow IV infusion over 10 minutes. Monitor vital signs, aPTT, hemoglobin, hematocrit, platelet count, ACT. Give blood transfusions as necessary according to transfusion guidelines. Assess site of bleeding and need for therapeutic interventions.

For patients receiving intravenous heparin infusion, discontinue infusion. Give protamine sulfate (1% solution) at 1 mg/100 U heparin or approximately 25 mg slow IV infusion over 10 minutes. Repeat ACT in 20 minutes.

For patients receiving large doses (>5000 U) of subcutaneous heparin, give protamine sulfate (1%) solution (1 mg/100 U heparin) slow IV infusion over 10 minutes. Repeat aPTT/ACT in 20 minutes and 1 hour. It may be necessary to repeat the protamine sulfate infusion after 1 hour because of the slow absorption of subcutaneous heparin. Observe for protamine reaction. Use protamine only when severe bleeding warrants it. Have resuscitation equipment available. Morphine (2–4 mg IV) is helpful for chills.

Use of Heparin as a Bridge to Warfarin Therapy

1. Give heparin 40–70 U/kg IV bolus followed by 1000–1700 U/hr IV infusion.
2. Obtain ACT at 4–6 hr and keep aPTT at 50–90 sec.
3. Start warfarin on day 1 at no more than 10 mg a day.
4. Obtain INR and platelet count.
5. Give heparin and warfarin jointly with heparin for 3 to 5 days, and until INR is between 2.0 and 3.0, then stop heparin.
6. Continue warfarin at an INR of 2.0 to 3.0.

Low-Molecular-Weight Heparin

LMWHs are fractionated heparins with molecular weights between 3000 and 7000 daltons (UFH is 3000–30,000 daltons). The therapeutic dose of the most commonly used LWMH, enoxaparin, is 1 mg/kg subcutaneously every 12 hours. Patients requiring PCI require additional intravenous bolus doses of enoxaparin to ensure adequate anti-Xa activity for the procedure. Table 5-4 describes suggested doses for PCI.

LMWHs have features distinct from UFH, including:

1. More predictable anticoagulation effect
2. Lack of inhibition by platelet factor 4
3. Lack of need for monitoring
4. Lower risk of HIT
5. Subcutaneous bolus administration

Table 5-5 compares features of LMWHs with UFH.

Absorption and Clearance

Peak plasma anti-Xa levels are achieved 3 to 4 hours after subcutaneous dosing and are detectable for up to 12 hours. LMWH is eliminated via the kidneys and caution should be used for patients with creatinine clearance <30 mL/min. LMWH can be given intravenously or subcutaneously, but not intramuscularly. It has a half-life of 2 to 4 hours longer than UFH.

Monitoring

LMWH activity is measured using blood anti-Xa levels. Routine monitoring is not currently indicated in most cases and is not readily available in many catheterization laboratories. LMWHs have a very predictable antithrombotic effect, which makes monitoring and dose adjustment necessary only in obese patients (BMI >40) or patients with renal insufficiency.

Table 5-4

Suggested Dosing of Enoxaparin Prior to PCI

Preprocedure Enoxaparin	IV Bolus Enoxaparin Dose at Time of PCI
No prior enoxaparin	0.75 mg/kg IV
Prophylactic doses of enoxaparin only	0.5 mg/kg IV
One-two 1 mg/kg SQ doses, last <8 hrs prior	0.3 mg/kg IV
One-two SQ doses, last 8–12 hrs prior	0.3–0.5 mg/kg IV
Adequate (>3) SQ doses, last <8 hrs prior	No additional enoxaparin
Adequate (>3) SQ doses, last 8–12 hrs prior	0.3 mg/kg IV
Any doses, >12 hours	Can use alternative antithrombin

Table 5-5

Comparison of Low-Molecular-Weight and Unfractionated Heparin

Characteristic	Unfractionated Heparin	Low-Molecular-Weight Heparin
Composition	Heterogeneous mix of polysaccharides; molecular weight 3000–30,000	Homogeneous glycosaminoglycans; molecular weight 4000–6000
Mechanisms	Activates antithrombin III*; equivalent activity against factor Xa and thrombin; releases TFPI from endothelium; unable to inactivate clot-bound thrombin or FDP; inactivates fluid phase thrombin	Less activation of antithrombin III; greater activity against factor Xa than thrombin; releases TFPI for endothelium; unable to inactivate clot-bound thrombin or FDP; weaker inactivation of fluid-phase thrombin
Pharmacokinetics	Variable binding to plasma proteins, endothelial cells, and macrophages leads to unpredictable anticoagulant effects (less available to interact with antithrombin III); short half-life	Minimal binding to plasma proteins, endothelial cells, and macrophages leads to predictable anticoagulation; longer half-life
Laboratory monitoring	Unpredictable anticoagulant effects; use aPTT or ACT	Unable to use aPTT or ACT except in renal failure to body weight <50 kg or >80 kg; use anti-factor-Xa levels
Clinical uses	Venous thrombosis; unstable angina, acute myocardial infarction, ischemic stroke, PCI	Venous thrombosis in surgery and trauma patients, unstable angina, ischemic stroke. No advantage during PCI
Reversal	Protamine neutralizes antithrombin activity	Protamine neutralizes antithrombin activity but only partially reverses anti-factor-Xa activity
History of HIT-2	Should not be used in patients with a history of HIT-2	Should not be used in patients with a history of HIT-2
Cost	Inexpensive	10–20 times more expensive than unfractionated heparin

*Antithrombin III is now commonly referred to as antithrombin.
ACT, activated clotting time; *aPTT,* activated partial thromboplastin time; *FDP,* fibrin degradation product; *HIT,* heparin-induced thrombocytopenia; *PCI,* percutaneous coronary intervention; *TFPI,* tissue factor pathway inhibitor.
Modified from Safian R, Grines C, Freed M. *The new manual of interventional cardiology*. Birmingham, MI: Physicians' Press, 1999.

Clinical Use

LMWHs, especially enoxaparin, have been shown to be equally effective as UFH in the prevention of recurrent myocardial infarction and recurrent angina when used in the treatment of acute coronary syndromes. There is a trend toward increased bleeding when LMWHs are used as anticoagulation for PCI. This is especially true if there is switching between UFH and LMWH, as seen in the recent SYNERGY and STACKENOX trials. In contrast, in patients in whom a conservative strategy is planned, LMWH may have superior ischemic benefits compared to UFH.

The major issue with respect to increasing use of LMWHs for PCI is the uncertainty of plasma activity of the drug, whereas the ACT has been a long-time hallmark of UFH activity. Furthermore, protamine administration is currently thought to reverse only about 60% of the drug's anti-Xa level. Although the use of LMWH has gained some adherents, particularly in Europe, in the United States, where the early invasive approach predominates, LWMH is only occasionally utilized for PCI.

Fondaparinux

The synthetic pentasaccharide fondaparinux (Arixtra) selectively binds antithrombin and causes rapid and predictable inhibition of factor Xa. Due to its linear pharmacokinetics, it is administered as a once-a-day subcutaneous injection of 2.5 mg. It is renally excreted with a half-life of 17 hours. Fondaparinux has been compared with enoxaparin in the OASIS-5 and OASIS-6 trials, where it has been found to be non-inferior in ischemic end points while reducing bleeding. A significant increase in guide catheter thrombosis during PCI with fondaparinux has limited its use—the addition of an antithrombin (heparin or bivalirudin) during PCI is recommended to reduce this risk and does not appear to worsen the risk of bleeding.

Warfarin

Racemic sodium warfarin is a coumarin derivative, acting by inhibiting the gamma-carboxylation of glutamic acid residues in the clotting proteins II (prothrombin), VII, IX, and X. It is not used for PCI but often employed for patients with atrial fibrillation, mitral stenosis, prosthetic heart valves, cardiomyopathies, pulmonary embolus, or chronic deep vein thrombosis.

Oral absorption is rapid and nearly complete. Warfarin is cleared from the blood and taken up by the liver over several hours. Daily warfarin takes 4 to 7 days to produce a therapeutic INR. Large loading doses do not markedly shorten the time to achieve a full therapeutic effect.

General Recommendations for Warfarin Use

Initiate therapy with either the estimated daily maintenance dose (2–5 mg) or, if a larger initial dose is chosen, start with no more than 10 mg. Elderly or debilitated patients often require low daily doses of warfarin (2–3 mg). After any dose change or any new diet or drug interaction, 4 to 5 days of the therapy is required to reach a new antithrombotic steady state.

Indications

1. Long-term secondary prevention for stroke after myocardial infarction (lifetime in enteric-coated aspirin failures)
2. Atrial fibrillation (lifetime)
3. Mechanical heart valves (lifetime)
4. Tissue heart valves (4–6 weeks, then start enteric-coated aspirin)
5. Long-term treatment of pulmonary embolus/deep venous thrombosis (3–6 months).

Contraindications and Precautions

Pregnancy. Warfarin is contraindicated during any stage of pregnancy because of its teratogenic and fetopathic effects. Obtain a pregnancy test before starting women of childbearing potential on warfarin.

Purpura. This rare skin and subcutaneous necrosis has been seen in a few individuals during the first few weeks of therapy with warfarin. The condition seems to be linked to protein C deficiency.

Dietary and Drug Interactions With Warfarin. Patients taking warfarin should eat a diet that is constant in vitamin K. Minimize changes in intake of green leafy vegetables (spinach, greens, and broccoli), green peas, and oriental green tea. Conditions that interfere with vitamin K uptake or interfere with liver function will increase the warfarin effect.

Heart Failure. Expect a longer prothrombin time in patients with congestive heart failure, jaundice, hepatitis, liver failure, diarrhea, or extensive cancer or connective tissue disease.

Metabolic Alterations Can Affect the Prothrombin Time. Expect a longer prothrombin time in patients with hyperthyroidism or high fever and expect a shorter prothrombin time in patients with hypothyroidism.

Direct Thrombin Inhibitors

Direct thrombin inhibitors are polypeptide or low-molecular-weight inhibitors (Table 5-6). Polypeptide inhibitors such as hirudin and bivalirudin inactivate circulating thrombin at the active binding site and clot-bound thrombin at exosite 1. Low-molecular-weight inhibitors such as argatroban inactivate circulating thrombin at the active binding site but do not inactivate clot-bound thrombin.

Unlike heparin, hirudin and bivalirudin do not require antithrombin for anticoagulant effect, form highly stable noncovalent complexes with circulating and clot-bound thrombin, and are not inhibited by platelet factor 4. Fewer ischemic and bleeding complications have been reported with bivalirudin in high-risk patients with postinfarction angina. A higher incidence of intracranial hemorrhage has been reported in three trials combining hirudin and thrombolytic therapy (GUSTO IIa, TIMI 9A, HIT-III).

In the United States, lepirudin and argatroban are approved for use in HIT. In such patients, lepirudin is administered as an initial bolus of 0.4 mg/kg (maximum 44 mg) over 15 to 20 seconds, followed

Table 5-6

Direct Thrombin Inhibitors

Polypeptide Inhibitors
Hirudin (lepirudin)*,†
Bivalirudin
Low-Molecular-Weight Inhibitors
Noncovalent
Argatroban†
Napsagatran
Inogatran
Melogatran
Reversible-covalent
Efegatran
Boro-arginine derivatives

*Derived from medicinal leech saliva and available by recombinant DNA technology as lepirudin; †FDA-approved for patients with HIT-2 who require anticoagulation.

by a continuous infusion of 0.15 mg/kg/hr (maximum rate 16.5 mg/hr). Monitoring is accomplished using the same aPTT/ACT guidelines as for UFH. Case reports have documented the use of both agents during PCI in patients with suspected HIT.

Bivalirudin (Angiomax) is approved for procedural anticoagulation in unstable angina and acute myocardial infarction. The dose is a 0.75 mg/kg IV bolus followed by a 1.75 mg/kg/hr infusion. The infusion is reduced to 1 mg/kg/hr and 0.25 mg/kg/hr in patients with a creatinine clearance (CrCl) <30 mL/min and patients on hemodialysis, respectively. The short half-life of 25 minutes allows prompt sheath removal after discontinuation of a bivalirudin infusion. Compared with UFH with glycoprotein inhibitors, bivalirudin demonstrates equal efficacy with a reduced risk of bleeding in patients with unstable angina/non–ST-segment elevation myocardial infarction (UA/NSTEMI) (REPLACE-2 and ACUITY trials) and in ST-segment elevation myocardial infarction (STEMI) (HORIZONS-AMI). These trials mandated preprocedural clopidogrel administration; however, the bivalirudin infusion may be extended for up to 4 hours following the procedure if antiplatelet agents are delayed.

Table 5-7 compares UFH with direct thrombin inhibitors.

Antiplatelet Agents

Antiplatelet drugs decrease platelet aggregation and inhibit thrombus formation to prevent both acute and chronic stent thrombotic occlusion. These drugs are highly effective in the arterial circulation, where anticoagulants have reduced effect. Coupled with antithrombin drugs (e.g., heparin or bivalirudin), the antiplatelet drugs are the mainstay of PCI pharmacology. Antiplatelet agents are required for stenting and are very useful for primary and secondary prevention of thrombotic cerebrovascular or cardiovascular disease.

There are six classes of antiplatelet drugs. The antiplatelet agents have different mechanisms, different effects, and different within-class potency and thus can function synergistically. Several antiplatelet drugs

Table 5-7

Comparison of Unfractionated Heparin and Direct Thrombin Inhibitors

	Unfractionated Heparin	Direct Thrombin Inhibitors (Hirudin, Bivalirudin)
Effect on clot-bound thrombin, FDP	None	Inactivation
Effect on antithrombin	High-affinity interaction; inhibits thrombin and factor Xa	High-affinity interaction
Effect on factor Xa bound to platelets	None	Inactivation
Binding to endothelium and plasma proteins	High; results in less heparin availability to activate antithrombin	None
Binding to PF4	High affinity	None
Anticoagulant effects	Highly variable	Predictable
Laboratory monitoring	Essential	May be unnecessary with bivalirudin

Summary: Direct thrombin inhibitors have biologic pharmacokinetic advantages compared to heparin. The biologic advantage reflects their ability to inactivate clot-bound thrombin via exosite 1 (polypeptide inhibitors), whereas the pharmacologic advantages produce more predictable anticoagulant effects without the need for intensive laboratory monitoring (especially bivalirudin), by less binding to endothelial and plasma proteins. Bivalirudin may block procoagulant activity associated with eptifibatide and tirofiban.

FDP, fibrin degradation product; *PF4,* platelet factor 4.

Modified from Safian R, Grines C, Freed M. *The New manual of interventional cardiology*. Birmingham, MI: Physicians' Press, 1999.

are often given together while weighing the risk of bleeding against benefit of preventing thrombosis. The classes of antiplatelet drugs are:

- Cyclooxygenase inhibitors (aspirin)
- Adenosine diphosphate (ADP) receptor inhibitors (clopidogrel [Plavix], prasugrel [Effient], ticlopidine [Ticlid])
- Phosphodiesterase inhibitors (cilostazol [Pletal])
- Glycoprotein IIb/IIIa receptor inhibitors (abciximab [ReoPro], eptifibatide [Integrilin], tirofiban [Aggrastat])
- Adenosine reuptake inhibitors (dipyridamole [Persantine])
- CPTPs (cyclo-pentyl-triazolo-pyrimidines [Ticagrelor])

Aspirin

Aspirin acetylate irreversibly binds and inactivates platelet cyclooxygenase, inhibiting production of thromboxane A2 (TXA2), which is a potent inducer of platelet aggregation and vasoconstriction via the production of cyclic adenosine monophosphate. Platelet resistance to aspirin is rare. Doses range between 81 and 325 mg orally daily. After oral ingestion, rapid absorption occurs with peak plasma levels in 20 minutes. It is rapidly cleared, but its effects last for the lifetime of the platelet. The template bleeding time can be used to gauge aspirin's effect on platelet function, but this is rarely necessary.

Indications

1. Stable angina
2. Unstable angina
3. Acute myocardial infarction
4. Coronary angioplasty
5. Primary and secondary prevention of myocardial infarction
6. Carotid or primary cerebrovascular disease (stroke prevention)
7. Peripheral vascular disease
8. Atrial fibrillation (not as effective as warfarin; use when warfarin is contraindicated)
9. Prosthetic heart valves (adjunctive therapy with warfarin).

Aspirin should be used with caution in those with aspirin allergies (asthma) and active peptic ulcer disease or other bleeding predispositions.

Clopidogrel

Together with aspirin, the most commonly used antiplatelet agent is clopidogrel, a thienopyridine. This drug class affects the ADP-dependent activation of platelet aggregation and adhesion through the IIb/IIIa receptors (Fig. 5-2). The platelet IIb/IIIa receptor is a glycoprotein responsible for platelet linkage to fibrinogen and von Willebrand factor. These links result in platelet-platelet attachment (fibrinogen) and platelet-vessel wall adhesion (von Willebrand factor), respectively. Clopidogrel is rapidly absorbed with peak plasma level in 2 hours, has a plasma half-life of 6 to 8 hours, and achieves steady-state drug levels in 14 to 21 days.

An unidentified hepatic metabolite of clopidogrel interferes with platelet membrane function by inhibiting ADP-induced platelet-fibrinogen binding and platelet-to-platelet interactions. Platelets exposed to the active metabolite are inhibited for their lifetime, about 7 to 10 days. Patients with variants of the CYP2C19 allele are poor metabolizers of clopidogrel and exhibit resistance to its effect.

The dose of clopidogrel is a 300 to 600 mg PO load prior to or at the time of PCI, then 75 mg PO daily for 6 to 12 months. Because of the rare potential of neutropenia or thrombotic thrombocytopenic purpura

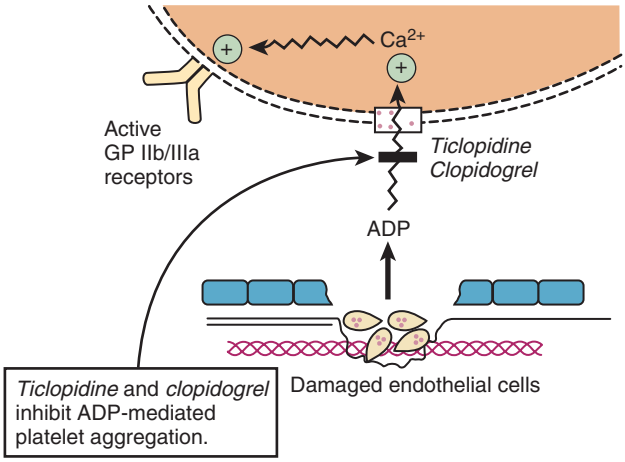

Figure 5-2 Thienopyridines block ADP receptors. *ADP,* adenosine diphosphate.

(TTP) with the previous thienopyridine ticlopidine, routine complete blood counts are recommended with this drug. However, no instances of TTP were seen in over 32,000 clopidogrel phase III trial patients, and TTP is estimated to occur in only 4 cases per million, making routine monitoring optional.

Indications

1. Prevention of stent thrombosis as part of a dual antiplatelet regimen
2. Prevention of myocardial infarction and stroke in patients who cannot take aspirin or fail aspirin therapy
3. Treatment of acute myocardial infarction with or without PCI
4. Stroke prevention in patients with risk factors or previous stroke

Prasugrel

Like clopidogrel, prasugrel is a pro-drug that is metabolized to an active metabolite before binding to a specific platelet receptor (P2Y12) to block platelet activity. Prasugrel is more efficiently metabolized than is clopidogrel, and more active metabolite is available, resulting in more effective platelet inhibition. The recent TRITON-TIMI 38 trial of patients with acute coronary syndrome undergoing PCI found that, compared to clopidogrel, prasugrel reduced recurrent myocardial infarction (10% vs. 7%; $P < 0.001$) and stent thrombosis (2.4% vs. 1.1%; $P < 0.001$). However, the benefit was associated with increased bleeding in the prasugrel group compared to clopidogrel group (2.4% vs. 1.8%; $P = 0.03$). Three risk factors were associated with excessive bleeding risk: age >75 years, weight <65 kg, and previous stroke or transient ischemic attack. The cost of prasugrel is currently comparable to clopidogrel and is economically feasible because of a lower rate of re-hospitalization involving PCI.

Ticagrelor

Ticagrelor is a direct-acting P2Y12 receptor antagonist in a chemical class called cyclo-pentyl-triazolo-pyrimidines (CPTPs). Unlike clopidogrel and prasugrel, ticagrelor binds reversibly with the P2Y12 receptor

and does not require hepatic metabolism to an active metabolite. Taken as a dose of 90 mg twice daily, ticagrelor was compared with clopidogrel in the large PLATO trial. Ticagrelor demonstrated reductions in the risk of myocardial infarction, cardiovascular death, and death from any cause, without increasing rates of bleeding.

Glycoprotein IIb/IIIa Receptor Blockers

The most potent antiplatelet agents are the glycoprotein IIb/IIIa receptor blockers (abciximab [ReoPro], eptifibatide [Integrilin], tirofiban [Aggrastat]), which are given only intravenously. These agents are highly effective as antiplatelet agents because they act on the final step in platelet activity, thereby inhibiting activation by any of the multiple upstream pathways. These agents are limited to the intra- and post-PCI procedure periods. Table 5-8 summarizes the use of glycoprotein receptor blockers for PCI.

Platelet Function Testing

Some patients with acute or subacute stent thrombosis have clopidogrel or aspirin resistance and may require platelet function testing. Although there is considerable literature on the subject of platelet function testing and resistance, the use of the point-of-care platelet function assays often results in ambiguous clinical decision making. Because thrombosis results from multiple pathways, treatment failure (e.g., subacute thrombosis) alone is not sufficient evidence of drug resistance.

Definition of Platelet Resistance

Drug resistance is the failure of the platelet to respond to an antiplatelet agent despite persistent activity of the antiplatelet agent. Platelets may respond to some stimuli but not to the "resistant" agent. The detection of nonresponsiveness to clopidogrel has been tested mostly by light transmission aggregometry studies using ADP. ADP causes platelets to aggregate (clump), reducing the transmission of light through a test tube. Early investigations suggested platelet resistance was an absolute change in aggregometry of <10%. This definition did not normalize for baseline activity and introduced some error into the assay. Various thresholds of normal platelet activity have been reported.

Platelet Function Assays

A large number of platelet function assays are available as commercial point-of-care testing systems (Table 5-9). The use of different point-of-care assays provides slightly different information on platelet function.

Evidence linking post-treatment platelet reactivity to long-term ischemic events is weak. Wide variations in response to therapy, ranging from 5% to 44% potential resistance are reported. Differences in the prevalence of platelet resistance between studies, dosing, definitions, laboratory methods, or insufficient incubation time has made a clear understanding of the significance of in vitro results difficult. Preliminary evidence suggests a potential threshold effect of platelet reactivity and associated increased risk of postdischarge ischemic events.

The major limitations of using platelet function testing to predict risk is that the measurement of platelet function in isolation fails to account for the multiplicity of additional clinical factors which may be significant contributors. None of the current studies using point-of-care platelet assays have assessed platelet-fibrin interactions, kinetics of thrombin generation, or measurements of platelet-fibrin clot strength, all contributing to thrombosis and important clinical events. At this time,

Table 5-8

Platelet Glycoprotein IIb/IIIa Antagonists for Percutaneous Coronary Intervention

	Abciximab	Eptifibatide	Tirofiban
Dose for PCI	0.25 mg/kg IV bolus plus 0.125 μg/kg/min (maximum 10 μg/min) IV infusion for 12 hr. Low-dose heparin and early sheath removal to minimize bleeding. For patients with unstable angina planning to undergo PCI within 24 hr, bolus plus infusion of abciximab (PCI dose) can be started up to 24 hr prior to PCI and continued at the same rate until 1 hr after the procedure.	*Acute coronary syndromes (PURSUIT dose)*: 180 μg/kg IV bolus plus 2.0 μg/kg/min IV infusion. If arrive in cath lab >4 hr after initiating therapy, no additional bolus is required. *Percutaneous intervention (ESPRIT dose):* 2 × 180 μg/kg/min IV bolus 10 min apart, plus 2.0 μg/kg/min IV infusion for 18–24 hr.	10 μg/kg IV bolus (over 3 min) immediately prior to PCI followed by an infusion of 0.15 ug/kg/min for 18-24 h. Patients with creatinine clearances <30 ml/min should receive half the usual infusion rate
Heparin (unfractionated)	Maintain ACT at 200–250 sec to minimize bleeding. Initial IV heparin dose based on ACT: ACT (sec) Heparin (bolus) <150 70 μ/kg 150–199 50 μ/kg >200 No additional Discontinue heparin immediately after PCI.	100 μ/kg bolus, titrate to ACT 300–350 sec. May also consider lower doses, as recommended for abciximab. In ESPIRIT, the recommended initial heparin dose was 60 μ/kg to achieve a target ACT of 200–300 sec.	100 u/kg bolus, titrate to ACT 300- 350 sec. May also consider lower doses, as recommended for abciximab
Aspirin	325 mg started at least 1 day prior to PCI and continued indefinitely; four chewable baby aspirin (325 mg total) for urgent intervention. For stents, add clopidogrel 300 mg oral load, then 75 mg PO daily for 2–4 weeks.	See abciximab.	See abciximab

ACT, activated clotting time; *PCI,* percutaneous coronary intervention, *PO,* per os (by mouth).
Modified from Safian R, Grines C, Freed M. *The new manual of interventional cardiology.* Birmingham, MI: Physicians' Press, 1999.

Table 5-9

Point-of-Care Platelet Function Assays

Platelet Function Assay	Mechanism	Method	Comments
VerifyNow Assay (Accumetrics, San Diego, CA)	Agonist-induced activated platelets bind to fibrinogen-coated polystyrene beads.	Whole blood added in mixing chamber with different receptor-coated beads causing agglutination; reflected light transmitted through the chamber is reduced. Assays for P2Y12, ADP, and IIb/IIIa are available.	Advantages: Automated cartridge-based bedside device, rapid assay for aspirin.
Plateletworks System (Helena Laboratories, Beaumont, TX)	Single platelet disappearance, expressed as platelet count after exposure to ADP.	Minimal sample preparation testing for platelet aggregation.	Sample preparation more time consuming.
PFA-100 Analyzer (Dade Behring, Marburg, Germany)	Adhesion and aggregation in whole blood under high shear conditions, exposed to collagen-epinephrine and/or collagen-ADP.	Whole blood put in citrated tubes, inserted through capillary collagen-coated membrane infused with ADP or epinephrine. Platelet formation and plugging is measured.	Advantage: Measures variety of platelet disorders. Disadvantage: Testing cartridge insensitive to clopidogrel. Device is used for research studies only.
Cone and Platelet Analyzer (DiaMed, Cressier sur Morat, Switzerland)	Measures interaction with platelets and shear forces.	Citrated whole blood is incubated with ADP. Tests the physiologic milieu of high shear stress. Microaggregate formation tested after exposure to clopidogrel.	Tests platelets more precisely than ex vivo. Limitations: No published studies demonstrating low-surface coverage associated with clopidogrel response.
Impedance Aggregometer (Chrono-Log, Havertown, PA)	Electrical impedance between two electrodes immersed in whole blood.	500 µL whole blood diluted and inserted into cuvette, which is incubated. Agonist added and resistance impedence computed.	A good correlation with optical aggregometry. Sample preparation 2 minutes, results available in 10 minutes. Limitation: No prospective studies.

ADP, adenosine diphosphate.

From Kern, M. Do we need platelet function testing in PCI intervention? *Cath Lab Digest* June 2009. http://cathlabdigest.com/articles/Do-We-Need-Platelet-Function-Testing-Percutaneous-Coronary-Intervention.

it is not justified to routinely look for platelet resistance in the clinical setting. The recent GRAVITAS study demonstrated that a protocol of routinely doubling the dose of clopidogrel in patients with clopidogrel resistance as defined by the VerifyNow assay was not associated with improved outcomes.

Platelet function testing may be helpful in a patient with recent subacute stent thrombosis. If clopidogrel or aspirin resistance is detected, a dose increase or change in the antiplatelet regimen would be indicated. Another useful scenario might be in a patient with a recently implanted stent who requires surgery that might be complicated by bleeding, and the risk of stent thrombosis after cessation of dual antiplatelet therapy (clopidogrel/aspirin) is high. If platelet function testing demonstrates minimally inhibited platelets on clopidogrel, one can proceed with surgery as needed. If platelet function is greatly impaired, then the timing of surgery must be balanced against the timing of clopidogrel withdrawal. Based on available data, daily clinical practice cannot yet be guided by point-of-care platelet function testing.

Thrombolytic Agents

Thrombolytic agents are proteins that convert a plasma proenzyme, plasminogen, to the active enzyme plasmin. Plasmin then solubilizes fibrin and degrades a number of other plasma proteins, most notably fibrinogen, ultimately producing clot lysis. All the currently available thrombolytic (fibrinolytic) agents are plasminogen activators. They all work enzymatically, directly or indirectly, to convert the single-chain plasminogen molecule to the double-chain plasmin (which has potent intrinsic fibrinolytic activity).

Tissue Plasminogen Activator (t-PA)

Derived by recombinant genetics from human DNA, t-PA is fibrin specific and activates plasminogen associated with fibrin directly by enzymatic action. The plasma half-life is 5 minutes, requiring an intravenous bolus and infusion.

TNKase (TNK-tPA)

TNK is a nonglycosylated deletion mutation of t-PA (contains 355 out of 527 of the amino acids that t-PA contains). It is given as a dose of 10 units and then again as 10-unit double bolus injection. Each bolus is given intravenously over 2 minutes. The second bolus is given 30 minutes after the first (supplied as a kit of two single-use vials). Dosing is based on weight, <60 kg, 30 mg IV over 5 minutes, maximum 50 mg; weight 60–69 kg, 35 mg IV, maximum 50 mg; weight >70 kg, 40 mg IV, maximum 50 mg.

Precautions and Contraindications (Table 5-10)

Bleeding is the major complication of thrombolytic therapy. Consequently, absolute contraindications include dissecting aortic aneurysm, pericarditis, stroke, or neurosurgical procedures within 6 months of known intracranial neoplasm.

Relative contraindications include major surgery or bleeding within 6 weeks, known bleeding diathesis, and severe uncontrolled hypertension.

Allergic reactions are associated most with anisoylated plasminogen streptokinase activator complex. t-PA also induces antibody production, which makes treatment with either of these agents less effective.

Table 5-10

Contraindications and Cautions for Thrombolytic Use in Myocardial Infarction

Contraindications

- Previous hemorrhagic stroke at any time, other strokes or cerebrovascular events within 1 year
- Known intracranial neoplasm
- Active internal bleeding (does not include menses)
- Suspected aortic dissection

Caution/Relative Contraindications

- Severe uncontrolled hypertension on presentation (blood pressure >180/110 mm Hg)*
- History of prior cerebrovascular accident or known intracerebral pathology not covered in contraindications
- Current use of anticoagulants in therapeutic doses (INR 2–3); known bleeding diathesis
- Recent trauma (within 2–4 wk) including head trauma or traumatic or prolonged (>10 min) CPR or major surgery (3 wk)
- Noncompressible vascular punctures
- Recent (within 2–4 wk) internal bleeding
- For streptokinase/anistreplase: prior exposure (especially within 5 days to 2 years) or prior allergic reaction
- Pregnancy
- Active peptic ulcer
- History of chronic severe hypertension

These contraindications and cautions are viewed as advisory for clinical decision making and may not be all-inclusive or definitive.
*Could be an absolute contraindication in low-risk patients with myocardial infarction.
INR, international normalized ratio; *CPR,* cardiopulmonary resuscitation.
Reproduced with permission from Ryan TJ, Antman EM, Brooks NH, *et al.* ACC/AHA guidelines for the management of patients with acute myocardial infarction: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Acute Myocardial Infarction). *J Am Coll Cardiol* 1999;34:890–911.

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6

Non-Balloon Coronary Interventional Techniques and Devices: Rotational Atherectomy, Thrombectomy, Cutting Balloons, and Embolic Protection Devices

MICHAEL S. KIM · ANDREW J. KLEIN · MORTON J. KERN

Introduction

Balloon angioplasty has given way to stenting as the primary modality of percutaneous coronary intervention (PCI). However, because the amount of atherosclerotic plaque in the artery may influence outcomes, physical removal of the plaque from inside the artery, called *atherectomy* (athero, "plaque"; ectomy, "cut"), was thought to improve the results of PCI. Although this promise was not fulfilled, two devices developed for this purpose remain in current practice: the high-speed rotational ablation catheter (Rotablator) and the directional atherectomy catheter (DCA).

None of the devices directed at plaque modification and removal can clear thrombus very well. Thus, additional non-balloon devices include thrombus aspiration catheters designed to treat arteries with significant amounts of thrombus complicating PCI and/or acute myocardial infarction (MI).

This chapter will focus on interventional devices that are commonly used as adjunctive therapy to balloon angioplasty and stenting in specific clinical scenarios. Specifically, this chapter will review the indications and techniques involved in performing rotational atherectomy, thrombectomy, and cutting balloon atherectomy and will describe embolic protection devices.

Rotational Atherectomy

The primary purpose of rotational atherectomy (RA) is to remove calcific atherosclerotic plaque (i.e., debulk) from vessels prior to stenting. The physical principle underlying RA is that of differential cutting, that is, the ability to selectively ablate or remove one material (i.e., plaque, calcium, etc.) while sparing and maintaining the integrity of a second material (i.e., normal elastic tissue) based on differences in substrate composition. As data comparing RA to balloon angioplasty demonstrate no consistent benefit of RA with regard to restenosis and/or target vessel revascularization (TVR) in the treatment of either de novo coronary disease or in-stent restenosis, the use of RA has diminished

greatly since its introduction in the late 1980s and has decreased even further in today's era of drug-eluting stent use.

Indications and Contraindications

While RA has been successfully utilized in a variety of clinical scenarios, in the contemporary practice of interventional cardiology, RA is most commonly used to facilitate stent delivery, particularly in lesions that are not easily dilatable because of the proliferation of fibrocalcific plaque. Heavily calcified lesions pose a particular technical challenge during PCI for two primary reasons:

1. The treatment of fibrocalcific plaques with balloon angioplasty often results in incomplete lesion dilation, which subsequently increases the risk of restenosis or acute/subacute stent thrombosis. Aggressive attempts to dilate resistant lesions with either high-pressure inflations or the use of noncompliant balloons carries the risk of vessel wall injury (i.e., dissection or perforation).
2. Non-dilatable lesions often inhibit the passage of balloons and stents, thereby limiting options for definitive revascularization. In these clinical situations, initial plaque debulking with RA may improve initial procedural success by improving arterial compliance, thereby facilitating more uniform and symmetric stent deployment while potentially allowing for increases in postprocedure minimal lumen diameter. Finally, while treating bulky lesions at or near a large branch vessel, preemptive use of RA may help minimize plaque shifting (i.e., the "snow-plowing" phenomenon) and alleviate the need for subsequent side branch intervention.

Although RA may assist in the delivery and deployment of interventional equipment (i.e., balloons and stents), there are specific clinical situations where its use should either be used with great caution or avoided altogether (Table 6-1).

Equipment

The Rotablator Rotational Atherectomy System (Boston Scientific Corporation, Natick, MA) is the only commercially available RA system (Figs. 6-1 and 6-2). The system consists of a nickel-plated brass elliptical burr (available in sizes of 1.25–2.5 mm in diameter) that is coated

Table 6-1

Indications and Contraindications to Rotational Atherectomy

Indicated	High-Risk	Contraindicated
• Single-vessel atherosclerotic coronary artery disease with a calcified plaque that can be passed with a guidewire • Low-risk, multivessel coronary artery disease • De novo lesion < 25 mm in length	• Severe, diffuse multivessel coronary artery disease • Unprotected left main PCI • Patients with compromised LV function (LVEF < 30%) • De novo lesion > 25 mm in length • Severely angulated (> 45 degrees) lesions • Last remaining conduit with compromised LV function • Angiographic evidence of thrombus	• Occlusions where a guidewire cannot be passed • Saphenous vein graft PCI • Angiographic evidence of significant dissection Type C or greater at the treatment site

LV, left ventricular; *LVEF,* left ventricular ejection fraction; *PCI,* percutaneous coronary intervention.

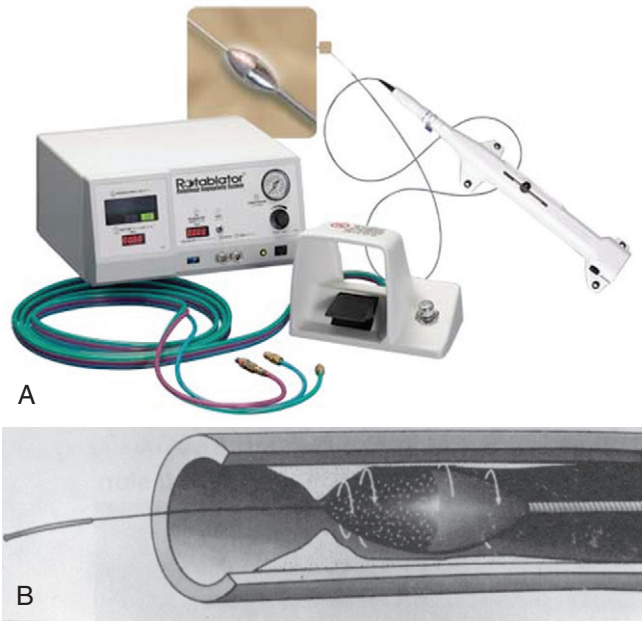

Figure 6-1 **A,** Rotablator Rotational Atherectomy System. **B,** Diagram of the rotational atherectomy burr. (Courtesy of Boston Scientific Corp., Natick, MA.)

on its leading edge with diamonds that are 20 to 30 microns in diameter. The burr is attached to a long, flexible driveshaft that is inserted through a guide catheter (6–10 F; see Table 6-2) over a 0.009-inch stainless steel guidewire (i.e., RotaWire). The RotaWire is available in both extra-support and floppy grades of stiffness. Whereas the floppy RotaWire is used in the majority of cases, the extra-support version may assist in advancing the device to very distal lesions. Finally, the Rotablator driveshaft itself is contained in a 4.3 F Teflon sheath and is connected to a turbine driven by compressed nitrogen gas. A continuous infusion of pressurized emulsifier solution (i.e., Rotaglide) with saline is infused through the drive shaft to aid lubrication and heat dissipation.

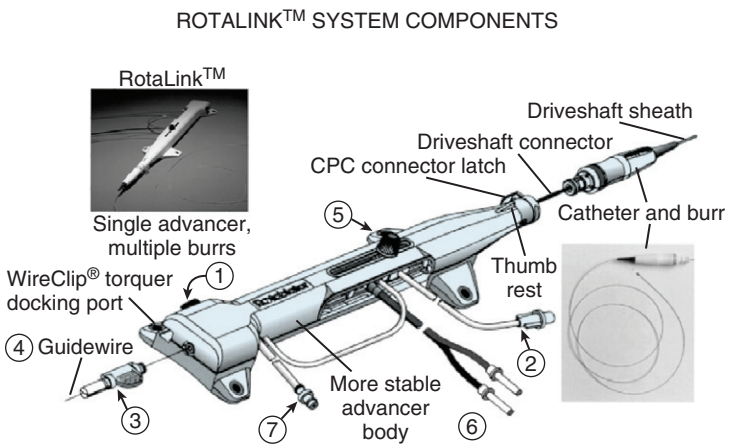

Figure 6-2 Rotablator advancer unit with removable catheter and burr attachment. (*1*) Brake defeat knob, (*2*) Air pressure close, (*3*) WireClip, (*4*) Rotablator wire, (*5*) Burr position control knob, (*6*) Fiberoptic tachometer, (*7*) Pressurized saline infusion port with lubricant that can be independently advanced and steered. CPC, catheter protector connection. The guidewire comes with a 0.017-mm (maximum) spring tip (0.43 mm inch diameter), facilitating negotiation of the wire through the vasculature. (Courtesy of Boston Scientific Corp., Natick, MA.)

Table 6-2

Recommended Guide Catheter Sizes for Use With the Coronary Rotablator

Rotablator Burr Size (mm)	Recommended Guide Catheter Internal Diameter (inch)	Guide Size (French [F])*
1.25	0.053	6–8
1.50	0.063	6–8
1.75	0.073	6–8
2.00	0.083	7–9
2.15	0.089	7–9
2.25	0.093	7–9
2.50	0.102	9–10

*For a given size of catheter, the inside diameter varies from manufacturer to manufacturer. French sizes assume thin-wall (high-volume flow) catheters with side holes.

Technique and Technical Tips

RA technique is aimed at plaque debulking to facilitate stent delivery while at the same time minimizing slow reflow/no reflow (resulting from large particulates) and avoiding significant arterial wall damage (e.g., perforations).

The initial clinical decision before beginning RA is to determine the optimal burr-to-vessel ratio. While larger burrs (i.e., >0.85 burr-to-artery ratio) will result in more aggressive debulking, their use may also be associated with a higher complication rate. In general, a good practice is to first use a small diameter burr (1.25–1.5 mm) to create a pilot channel, and then gradually work up to a maximum burr diameter that is no larger than 70% to 80% of the normal arterial luminal reference segment diameter. For the sole purpose of device delivery (e.g., balloons and/or stents), however, RA with smaller burrs is usually sufficient.

Crossing of the lesion can be performed either with the RotaWire or with a standard 0.014-inch guidewire that can subsequently be exchanged for a RotaWire using either a tracking catheter or an over-the-wire balloon system. Although the RotaWire size (0.009-inch) often makes crossing lesions challenging, in cases where exceptionally severe lesions preclude the passage of either a tracking catheter or over-the-wire balloon catheter, direct wiring with the RotaWire may in fact be necessary. The infusion port on the drive shaft is connected to a pressurized bag of saline and lubricant mixture (i.e., Rotaglide—egg yolk/olive oil/EDTA mixture). A combination of verapamil (10 mg/L), nitroglycerin (4 mg/L), and heparin (2000 U/L) can also be added to the saline flush in order to minimize vessel spasm during RA. After loading onto the RotaWire, the burr's speed is tested (i.e., platforming) prior to introduction into the guide catheter. The burr speed during platforming should range from 160,000 to 180,000 rpm, depending on the burr size (Table 6-3). Following successful platforming, the burr is advanced through the guide catheter and is positioned immediately proximal to the lesion. Advancement of the burr through the guide catheter around the aortic arch often requires the operator tasked with securing the back end of the RotaWire to provide additional back tension to both facilitate burr advancement and limit acquired tension. Although many operators will transiently activate the system inside the guide to further alleviate acquired tension within the system, activating the system in the vessel proximal to the lesion accomplishes the same goal of preventing the burr from "leaping forward" during the initial RA pass. Direct intracoronary administration of vasodilators prior to system activation can be performed at this time to combat coronary spasm potentially instigated by RA.

After the burr is positioned and transiently activated proximal to the lesion, the system is activated and the burr is advanced gently and slowly in a "pecking motion" (i.e., gentle forward and backward motions of the advancer so that the burr effectively "pecks" at the

Table 6-3

Recommended Rotablator Advancer Turbine Speed			
Burr size (mm)	**Burr size (French)**	**Design rotational speed range* (rpm)**	**Optimum rotational speed range (rpm; no tissue contact)**
1.25	3.75	150,000–190,000	180,000
1.50	4.50	150,000–190,000	180,000
1.75	5.25	150,000–190,000	180,000
2.00	6.00	150,000–190,000	180,000
2.15	6.45	140,000–180,000	160,000
2.25	6.75	140,000–180,000	160,000
2.50	7.50	140,000–180,000	160,000

Rotablator Catheter Sheath Outer Diameter		
Size (mm)	**Size (French [F])**	**Size (inch)**
1.35	4.0	0.058

*Preset speed outside of the body at the higher rotational speed—for example, for a 1.25-mm Rotablator advancer, set speed outside body at 190,000 rpm.

lesion) using the advancer integrated into the drive shaft. Burr decelerations signal obstruction to burr motion and should be minimized (i.e., less than 5000 rpm decelerations), as these deceleration speeds are associated with increased complications. In addition, burr activation runs should not exceed 30 seconds per pass, as prolonged RA sessions may be associated with increased ischemia and precipitation of slow reflow or no reflow. At the end of the initial RA pass, the burr is positioned in its starting position proximal to the lesion before the system is deactivated. The system should *not* be deactivated while the burr is contained within the lesion. Intracoronary nitroglycerin and/or nitroprusside may be administered at this time to help counteract any potential slow reflow in the distal vessel created by embolization of microparticles. Several burr passes are performed before the burr is removed and decisions are made to pursue more debulking with larger burr sizes.

Of note, in particularly severely narrowed lesions with heavy calcium, the RotaWire may retract proximally during burr advancement. By ensuring coaxial guide catheter alignment and applying gentle forward pressure on the guide catheter, distal wire position can be maintained. Finally, if excessive decelerations (i.e., >5000 rpm decrease) repeatedly occur during RA, it is recommended to downsize to a smaller burr. Figures 6-3 and 6-4 are case examples demonstrating the use of RA in various clinical settings.

Finally, a temporary pacing lead is recommended by the manufacturer during the treatment of right coronary or dominant circumflex arteries to resolve electrical aberrations that can occur during RA. In addition, instructing the patient to cough during episodes of RA-induced conduction block or arrhythmia often overcomes the hypotension associated with such electrical disturbances. In some catheterization laboratories, patients are actually instructed to practice coughing prior to RA burr activation in order to prepare them should electrical abnormalities arise during performance of RA.

No Reflow or Slow Reflow After Rotablator Ablation

No reflow or slow reflow is the occurrence of no blood flow (no reflow) or blood flow reduced by one angiographic thrombolysis in myocardial infarction (TIMI) study flow grade (slow reflow) in the treated artery despite the fact that the treated segment is patent. No reflow or slow

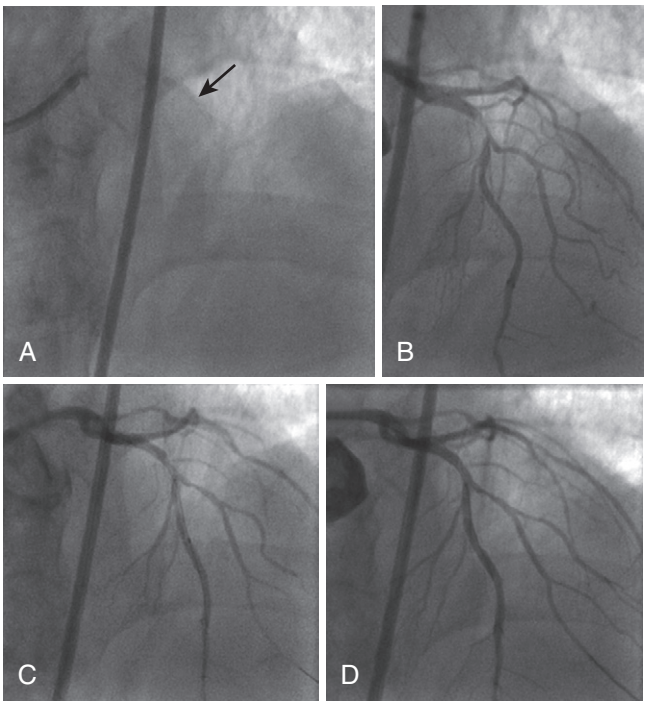

Figure 6-3 Case example using rotational atherectomy in the treatment of fibrocalcific disease. **A,** Baseline fluoroscopy demonstrating severe calcification (*arrow*) in the mid LAD. **B,** Baseline angiography demonstrating a severe, calcific plaque in the mid LAD. **C,** Post-RA angiography using a 1.5-mm burr. **D,** Post-PTCA angiography. *LAD,* left anterior descending; *PTCA,* percutaneous transluminal coronary angioplasty; *RA,* rotational atherectomy.

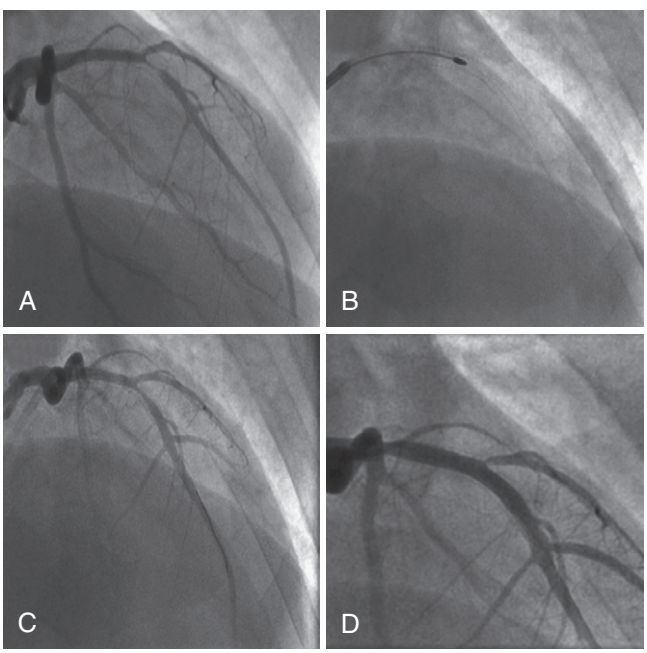

Figure 6-4 Case example using rotational atherectomy in the treatment of ISR. **A,** Baseline angiography demonstrating severe ISR (*arrow*) in the mid LAD stent. **B,** RA performed with a 1.5 mm burr. **C,** Post-RA angiography. **D,** Final angiography following PTCA with both a cutting balloon and noncompliant balloon. *ISR,* in-stent restenosis; *LAD,* left anterior descending; *PTCA,* percutaneous transluminal coronary angioplasty; *RA,* rotational atherectomy.

reflow is believed to occur because of the transient increase in blood viscosity due to the presence of microparticles or vasospasm at the level of the distal microvasculature. No reflow or slow reflow has been observed in 6% to 7% of patients undergoing PTCA (see Fig. 6-2). No reflow and slow reflow can be minimized by the following actions:

1. Advancing the burr slowly
2. Using a stepped burr approach (smaller, then larger) in long or calcified lesions
3. Using a "pecking" motion at the plaque to avoid blocking the arterial lumen
4. Maintaining maximum blood flow by repeated flushing with saline (bolus of 10–30 mL)
5. Using guide catheters with side holes
6. Maintaining the left ventricular filling pressures (and mean arterial pressure) by increasing the patient's volume status appropriately

No slow or slow reflow generally resolves within a short period of time (< 15 min) with or without the use of nitroglycerin. Intracoronary verapamil (200 mcg) or nitroprusside (50–100 mcg) has been reported to improve no slow or slow reflow.

When performed in a controlled setting by an experienced operator, RA offers a safe and effective means of debulking plaque and preparing lesions for stent implantation. Additional technical tips on performing safe and successful RA are listed in Table 6-4.

Clinical Outcomes

Although prospective and retrospective studies have demonstrated the safety and efficacy of rotational atherectomy in treating complex coronary lesions with regard to immediate procedural success and postprocedure MLD when compared to either balloon angioplasty or balloon angioplasty followed by stenting, the long-term data supporting the use of RA to reduce restenosis or TVR for treatment of both de novo coronary lesions (including chronic total occlusions) and in-stent restenosis remain less conclusive (Table 6-5).

Mechanical Thrombectomy

The prevalence of visible thrombus in acute coronary syndrome (ACS) is dependent on multiple factors, including clinical state (75%–90% prevalence in patients with unstable angina or non-ST-segment elevation myocardial infarction [NSTEMI]; close to 100% prevalence in patients with ST-segment elevation myocardial infarction [STEMI]), type and duration of anticoagulant and antiplatelet

Table 6-4

Technical Notes and Tips on Performing Rotational Atherectomy

- A nitrogen compressed-gas cylinder with pressure regulator capable of delivering a minimum 140 L/min at 90–100 psi is required.
- The compressed-gas cylinder valve must be open to supply compressed gas to the console. The regulator should be adjusted so that the pressure does not exceed 100 psi.
- Angulated lesions and branch ostial lesions have a higher incidence of dissection and/or perforation. Downsize initial burrs and stepwise increase burr size to achieve the final result.
- RA can be performed on chronic total occlusions only if the guidewire is confirmed to be in true lumen distally.
- Perforations are uncommon. Covered stents should be available in all cardiac catheterization laboratories performing RA.

Table 6-5

Clinical Data on the Rise of Rotational Atherectomy

Study	Comparison	Lesion Type	Restenosis	TLR	*P*-value
Reifart N, *et al.* (ERBAC)	RA vs. ELA or PTCA	De novo	42% (RA); 46% (ELA); 31% (PTCA)	NA	0.013
Mauri L, *et al.* (DART)	RA vs. PTCA	De novo	52% (RA); 48% (PTCA)	22% (RA); 18% (PTCA)	NS
Hoffman R, *et al.*	RA vs. RA + BMS vs. PTCA + BMS	De novo	—	31.6% (RA); 12.2% (RA + BMS); 24.5% (PTCA + BMS)	0.028
Buchbinder M, *et al.* (SPORT)	RA + BMS vs. PTCA + BMS	De novo	—	18.1% (RA + BMS); 15.3% (PTCA + BMS)	NS
Braden G, *et al.* (EDRES)	RA + BMS vs. PTCA + BMS	De novo	27% (RA + BMS); 34% (PTCA + BMS)	—	0.05
Vom Dahl J, *et al.* (ARTIST)	RA vs. PTCA	In-stent restenosis	64.8% (RA); 51.2% (PTCA)	47.8% (RA); 36.2% (PTCA)	0.04/0.06
Sharma SK, *et al.* (ROSTER)	RA vs. PTCA	In-stent restenosis	—	32% (RA); 45% (PTCA)	0.042
Tsuchikane E, *et al.*	RA + BMS vs. PTCA + BMS	CTO	29% (RA + BMS); 52% (PTCA + BMS)		0.006

BMS, bare-metal stent; *CTO,* chronic total occlusion; *ELA,* excimer laser atherectomy; *NA,* not applicable; *NS,* not significant; *PTCA,* percutaneous transluminal coronary angioplasty; *RA,* rotational atherectomy; *TLR,* target lesion revascularization.

therapy, and anatomic features (e.g., tortuous vessel segment, recent instrumentation, bifurcation, etc.). In addition, the presence of thrombosis is associated with increased rates of death, MI, and need for urgent revascularization.

The most serious complication of intracoronary thrombus is distal embolization resulting in microvascular obstruction often manifesting as slow reflow or no reflow. Despite patent epicardial coronary arteries, microvascular obstruction may contribute to persistent chest pain, ST-segment abnormalities, and compromised TIMI flow. Distal thromboembolization may be induced by forceful coronary injections, passage of intracoronary devices, and the initial balloon angioplasty and/or stenting. In addition, intracoronary thrombus may contribute to underestimation of vessel and stent sizing, increasing the subsequent risk of stent malapposition, in-stent restenosis, or stent thrombosis.

Indications

Mechanical thrombectomy is indicated when thrombus is present in a coronary artery of sufficient diameter to safely accommodate a thrombectomy device. Accurate detection and recognition of intracoronary thrombus, however, is fundamental to the performance of mechanical thrombectomy. Fiberoptic angioscopy is the "gold standard" for detection of intracoronary thrombus, as it is the only modality that can reliably distinguish between red, fibrin-rich and gray/white, platelet-rich thrombus. However, most catheterization laboratories do not have angioscopy. Intracoronary thrombus is thus identified with increasing sensitivity using standard coronary angiography, intravascular ultrasound (IVUS), or optical coherence tomography (OCT).

Angiographically, intracoronary thrombus is recognized as a filling defect surrounded on three sides by contrast visible in multiple projections in the absence of calcification, with or without persistent contrast staining (Fig. 6-5). Other angiographic features of thrombus include reduced contrast density and/or haziness. The overall sensitivity and specificity of detecting thrombus by angiography when compared to angioscopy is reported as 26% and 92%, respectively.

By angiography alone, however, intracoronary thrombus may be difficult to distinguish from irregular filling defects caused by protruding plaques or recently ruptured plaques. In these clinical situations, IVUS may better define angiographically ambiguous lesions and further guide appropriate therapy.

By IVUS and OCT (with higher resolution), coronary thrombus is recognized as a protruding mass of low echogenicity and a globular or layered appearance that may or may not be visibly attached to the vessel wall. Fresh thrombus may in fact be echolucent on IVUS and indistinguishable from fibrofatty plaque or a plaque with a necrotic lipid core. In contrast, organized thrombus is more echogenic and may cast an acoustic shadow similar to that seen in fibrous plaque if the thrombus is rich in collagen.

Mechanical Thrombectomy Systems

Mechanical thrombectomy devices that are currently available are classified into two primary mechanisms: (1) aspiration, and (2) physical disruption with extraction.

Aspiration Thrombectomy

Aspiration thrombectomy devices are dual lumen tubes (Fig. 6-6) that are passed across the target lesion over a standard 0.014-inch guidewire. The smaller lumen houses the guidewire using a rapid exchange monorail system while the larger, aspiration lumen connects the distal aperture(s) to a proximal port that is attached to a large (30–50 mL) lockable syringe.

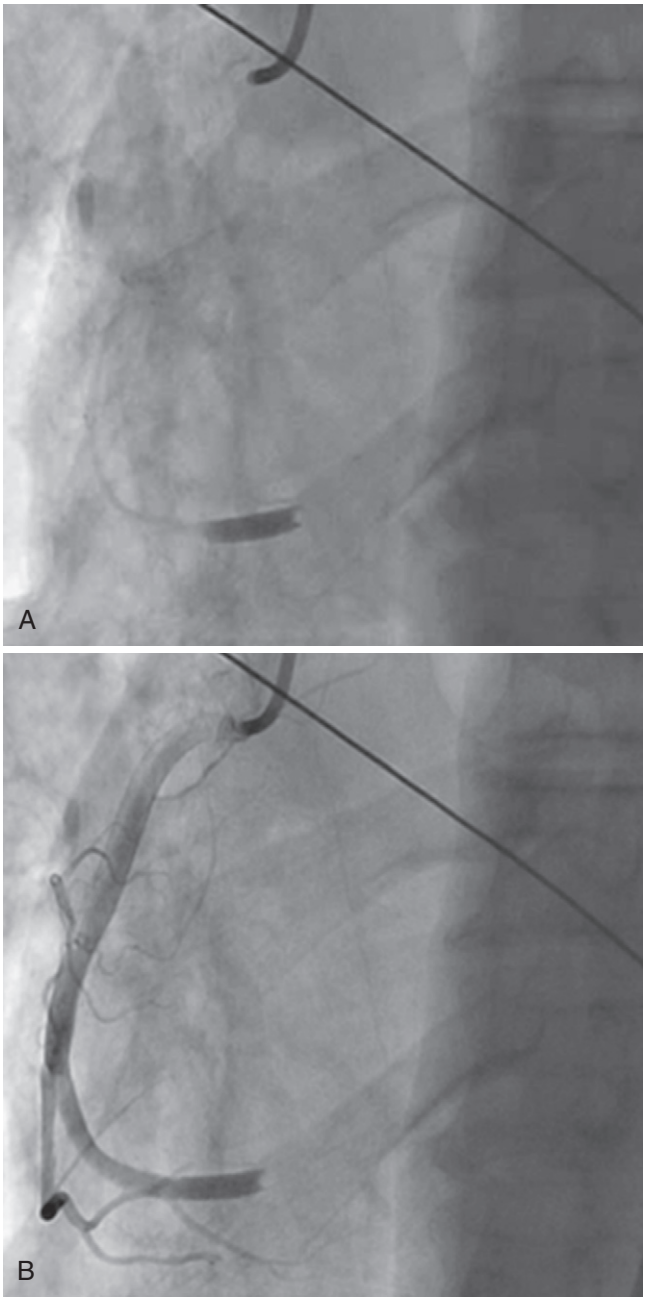

Figure 6-5 Angiographic appearance of intracoronary thrombus. **A,** Contrast staining noted in distal RCA suggestive of intracoronary thrombus. **B,** Complete occlusion of flow distal to the intracoronary thrombus. *RCA,* right coronary artery.

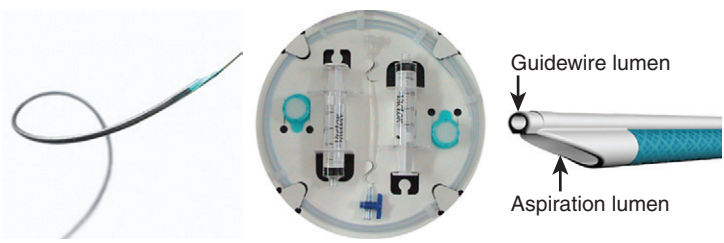

Figure 6-6 Medtronic Export XT Aspiration Catheter. (Courtesy of Medtronic, Inc., Minneapolis, MN.)

The most commonly used aspiration thrombectomy catheters used today are the Pronto V3 Extraction Catheter (Vascular Solutions, Inc., Minneapolis, MN), the Export XT Aspiration Catheter (Medtronic, Inc., Minneapolis, MN), and the Extract Catheter (Volcano Therapeutics, Rancho Mirage, CA), all of which are available in 6 F and 7 F sizes.

Technique and Technical Tips. Mechanical aspiration (i.e., suction using the lockable syringe attached to the proximal catheter port) should be performed while crossing the target thrombus in an antegrade fashion and continued during withdrawal of the catheter into the guide catheter and subsequently out of the body. In addition, several passes can be made across the thrombus before removal of the system from the body, as long as blood (and thrombus) is actively collecting into the lockable syringe. Continuous aspiration in this fashion helps to avoid withdrawing thrombus from the distal vessel and then prematurely releasing it proximally. Following removal of the aspiration catheter from the guide catheter, sufficient "back-bleeding" should be performed to ensure that the guide catheter and Y connector are clear of thrombus.

Aspiration thrombectomy catheters are appealing because of their simplicity and ease of use. Virtually no preparation of the catheter is necessary (short of flushing the aspiration lumen with saline), and thus there is no delay in achieving rapid reperfusion during primary PCI. The technique, however, is limited by catheter deliverability (especially in tortuous, small, or calcified vessels), trackability, and pushability. In addition, the maximum thrombus extraction rate is limited to the minimum diameter of the extraction lumen. Although extraction of blood and thrombus may be up to three times more effective using the larger 7 F thrombectomy catheters, these benefits are traded for the increased risk of difficult delivery (i.e., larger profile, stiffer catheter), restriction of use in only larger epicardial vessels, and increased risk of vessel injury (e.g., dissection, perforation, etc.). Figure 6-7 is a case example demonstrating the utility of aspiration thrombectomy.

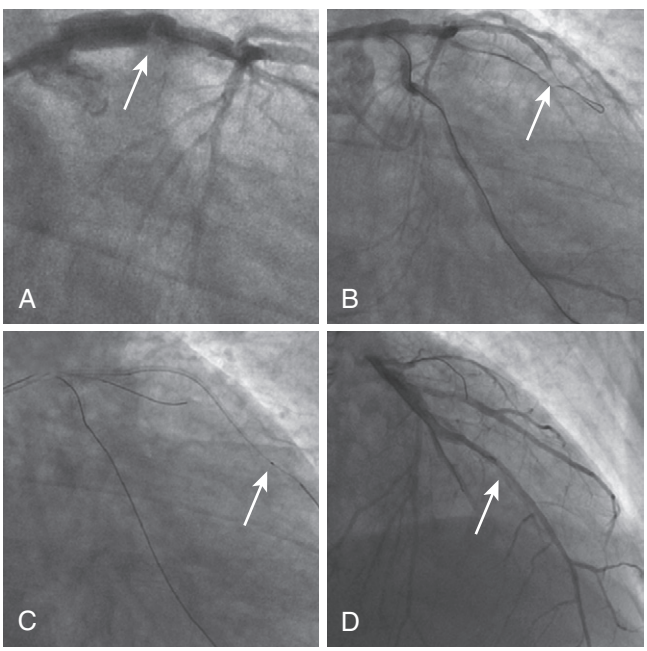

Figure 6-7 Case example using mechanical thrombectomy. **A,** Heavy thrombus burden in the left main coronary artery (*arrow*). **B,** Embolization of thrombus to the mid LAD occluding distal flow (*arrow*). **C,** Aspiration thrombectomy (*arrow*). **D,** Restoration of flow to the distal LAD (*arrow*). *LAD,* left anterior descending.

Clinical Data. Early trials failed to demonstrate that the adjunctive use of aspiration thrombectomy improved clinical outcomes. However, recently, the TAPAS (Thrombus Aspiration During Percutaneous Coronary Intervention in Acute Myocardial Infarction Study) trial showed benefit of thrombus aspiration in patients presenting with STEMI. TAPAS was a large (n = 1071 patients), randomized, controlled trial comparing manual thrombus aspiration to conventional PCI in STEMI patients. Adjunctive use of manual thrombus aspiration resulted in more frequent complete ST-segment resolution, lower incidence of suboptimal myocardial blush scores (e.g., 0 or 1), and lower rates of both death and major adverse cardiac events at 30 days. At the 1-year follow-up, STEMI patients treated with adjunctive aspiration thrombectomy demonstrated significantly lower incidences of both cardiac death and nonfatal MI. Based in large part on the results of the TAPAS trial, initial aspiration thrombectomy is now commonly performed during primary PCI in patients presenting with STEMI.

Rheolytic Thrombectomy

The AngioJet Rheolytic Thrombectomy System (MEDRAD, Inc., Warrendale, PA) aspirates thrombus by creating high-pressure water jets directed backward into the aspiration catheter, thereby producing a strong suction (approximately 600 mm Hg) at the space near the catheter tip (i.e., Venturi effect). Thrombotic material is drawn into the catheter shaft where the powerful water jets macerate and extract it. Cross-Stream technology enhances thrombus removal by allowing a small amount of saline to wash into the coronary artery prior to maceration and extraction (Fig. 6-8). The system can be used to aspirate and remove intracoronary thrombus in the setting of acute MI, stent thrombosis, saphenous vein graft thrombosis, and thrombosed peripheral vessels or grafts (Fig. 6-9).

The AngioJet system is comprised of three components: driver, pump set, and replaceable catheters. The driver is a pump system that generates approximately 10,000 psi of water pressure and monitors the aspiration and system flow during the procedure to maximize patient safety. The pump set drives saline into the aspiration catheter and helps to maintain a balance between the fluid both leaving and entering the catheter so as to maintain a constant pressure within the artery. The AngioJet catheter is a 135- to 140-cm long, 4 F to 6 F catheter that tapers from the distal 5 cm to the tip. The AngioJet Spiroflex, SpiroflexVG, and XMI catheters are indicated for use in both native coronary arteries and saphenous vein grafts.

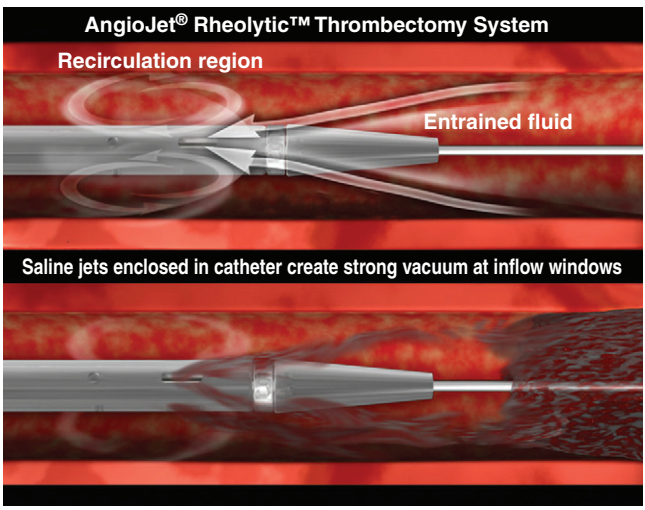

Figure 6-8 AngioJet Rheolytic Thrombectomy System Cross-Stream technology. (From MEDRAD, Inc., Warrendale, PA.)

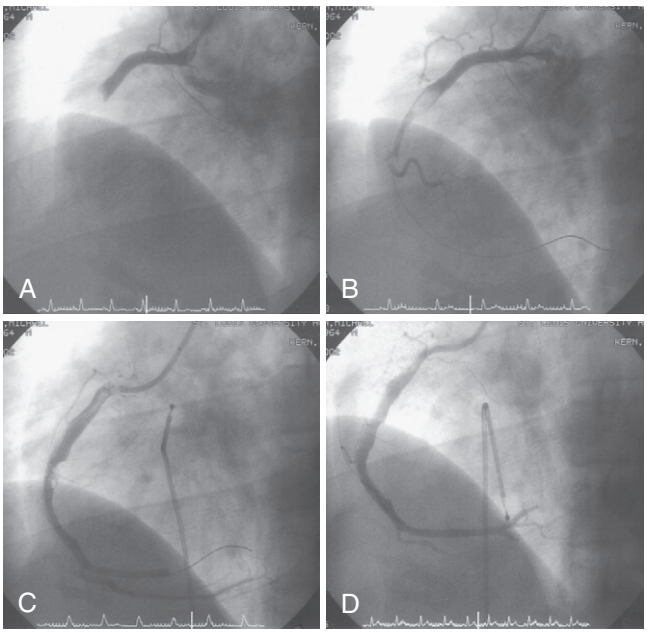

Figure 6-9 Example of AngioJet thrombectomy in a 37-year-old man 8 hours after the onset of chest pain for acute inferior wall myocardial infarction. **A,** Right coronary artery with thrombus in proximal portion. **B,** Angioplasty guidewire traversing lesion with large amount of clot in the proximal portion of the artery. **C,** Right coronary artery after 4 F AngioJet. A temporary pacemaker was also inserted. **D,** The thrombus was almost completely extracted from the vessel. The final angiogram demonstrates residual distal embolic occlusions but good patency, with TIMI grade 3 flow. *TIMI,* thrombolysis in myocardial infarction.

Technique and Technical Tips. The AngioJet catheter is first prepped and primed outside of the body while submerged in saline. The prepared catheter is positioned proximal to the target thrombus, the system is activated, and the catheter is slowly advanced through the thrombotic region at a rate of approximately 0.5 mm/sec and then pulled back slowly to the proximal starting position at the same rate. Multiple passes are typically performed until no further improvement by angiography is noted, although total device use should not exceed 10 minutes as prolonged sessions of rheolytic thrombectomy may precipitate the development of hemolytic anemia.

Significant bradyarrhythmias can occur during the performance of rheolytic thrombectomy and are thought to be mediated by hemolysis-induced adenosine release that occurs during the aspiration process. For this reason, placement of a temporary pacing wire is recommended prior to performing rheolytic thrombectomy, especially when thrombectomy is performed in either the right coronary artery or a dominant left circumflex coronary artery.

Although rheolytic thrombectomy effectively removes intracoronary thrombus, performing the procedure is often limited by the time required for setting up and priming the device and placement of a temporary pacing wire (if required). Either of these processes may potentially lead to significant delays in establishing rapid vessel reperfusion, which may subsequently negatively impact long-term prognosis.

Clinical Data. Clinical trials investigating the safety and efficacy of adjunctive rheolytic thrombectomy during primary PCI for STEMI have been largely favorable, though not definitive. One single-center study of 100 patients with STEMI randomized to primary PCI with or without pretreatment with rheolytic thrombectomy using the AngioJet system demonstrated that pretreatment with the AngioJet system resulted in

improved ST-segment resolution, smaller infarct size, and no increase in adverse events. These findings, however, were not confirmed in the larger AIMI (AngioJet Rheolytic Thrombectomy in Patients Undergoing Primary Angioplasty for Acute Myocardial Infarction) trial. The ongoing JETSTENT (AngioJet Thrombectomy and Stenting for the Treatment of Acute Myocardial Infarction) trial has been designed to address the potential limitations of the AIMI trial. Although current evidence does not support the routine use of the AngioJet system in primary PCI, it can be argued that, with regard to the efficacy of adjunctive use of rheolytic thrombectomy in primary PCI, the door is not yet shut.

Cutting Balloons

The Flextome Cutting Balloon (Boston Scientific Corporation, Natick, MA) is a special balloon catheter that was designed to reduce trauma to the vessel wall and on plaque by making small incisions into the plaque. Doing so theoretically may limit the splitting and tearing of the plaque and vessel wall as commonly occurs during standard balloon angioplasty. The Flextome Cutting Balloon has three or four 0.1- to 0.4-mm thick stainless steel blades (i.e., atherotomes) that are fixed to the surface of the balloon (Fig. 6-10). The blades are safety embedded within the folds of the undeployed balloon to allow for safe delivery to the lesion site. Upon balloon inflation, the blades are purported to make microscopic incisions in the plaque and do not cut through the plaque completely. The force of inflation is concentrated on the incising element, thereby allowing for predictable cutting of the coronary plaque.

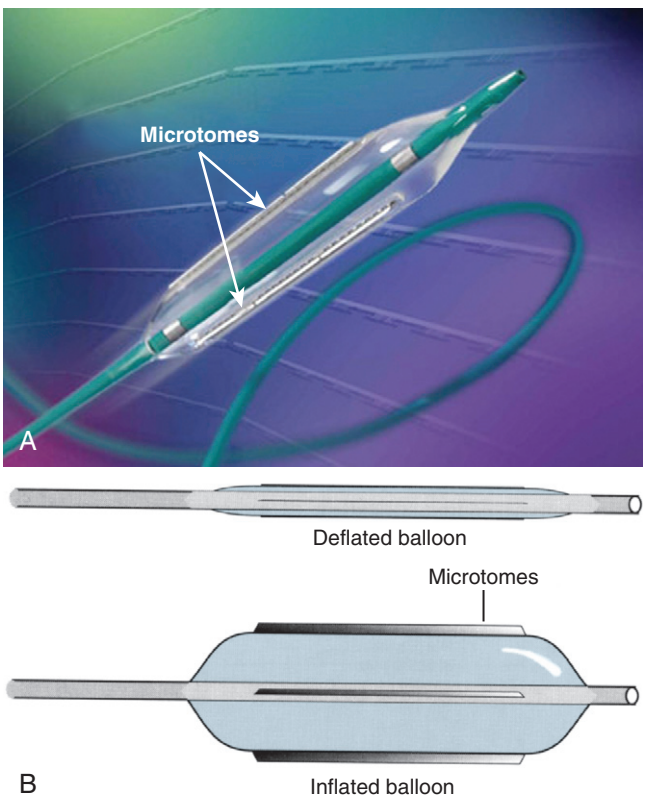

Figure 6-10 **A,** Flextome Cutting Balloon in its inflated state. Microtomes (*arrows*) can be seen extending outward from the balloon. (Courtesy of Boston Scientific Corp., Natick, MA.) **B,** Flextome Cutting Balloon (*above*) in the deflated state and (*below*) in the inflated state. The microtomes can be seen extending outward from the balloon.

Indications and Contraindications

The cutting balloon is indicated primarily in three clinical situations:

- Bifurcation lesions
- In-stent restenosis
- Ostial lesions

Lesions best suited for cutting balloon atherectomy (CBA) are those that are relatively short (< 20 mm in length), concentric lesions in areas of less tortuosity, and those without significant thrombus. Lesions in small vessels (< 2 mm in diameter), total occlusions, heavily calcified lesions, or long lesions are not appropriate for CBA.

Equipment

The coronary Flextome Cutting Balloon ranges in sizes from 2.0 to 4.0 mm in diameter and 6 to 15 mm in length. Appropriate sizing of the cutting balloon is crucial, where a balloon-to-artery ratio of 1:1 is desirable; oversizing may increase the risk of coronary dissection or perforation. Smaller ratios (i.e., balloon diameter < artery diameter) can also be used in more severe lesions although this may result in a hazy angiographic appearance postinflation. In the treatment of in-stent restenosis, the ratio can slightly exceed 1:1, as long as the borders of the device are kept entirely within the stented segment.

Technique and Technical Tips

Delivery of the cutting balloon to the lesion is often more difficult than delivery of conventional balloons because the cutting elements on the cutting balloon make for a stiffer device with a less favorable profile. In situations where the device cannot be delivered, the following maneuvers may be helpful:

- Use a 1.5- to 2.0-mm conventional balloon to predilate the lesion.
- Use the buddy wire technique in tortuous segments or into a stent.
- Use a Wiggle wire (Abbott Vascular, Abbott Park, IL) to aid with wire bias.
- Inflate the device when it is partially in the lesion and then advance the device as it deflates.

Once delivered to the target lesion, careful attention to the method of device deployment and retrieval will help to limit complications. Slow and gradual inflation (1 atm/sec) to nominal pressure (6 atm) allows the atherotomes to correctly unfold. Upon reaching nominal inflation, maintaining inflation for 60 to 90 seconds allows the device to score the lesion and flatten the incisions. In addition, performing multiple slow inflations may improve angiographic results. Similarly, during balloon deflation, a slow, graded deflation down to low pressure is recommended before "pulling" negative pressure on the device. Without slow deflation, the device may "wing," and resistance may be met when attempting to retrieve the device into the guide catheter.

Clinical Data

Initial clinical data on the immediate and long-term results of CBA when compared to standard angioplasty demonstrated high procedural success rates, few complications, and significantly reduced restenosis rates. Subsequent data, however, were less encouraging. The Cutting Balloon Global Randomized Trial compared CBA to standard balloon angioplasty in 1238 patients with significant de novo coronary stenoses. The primary end point of binary angiographic stenosis at 6 months was equivalent between groups, although the CBA group experienced more coronary perforations. Given these relatively unfavorable clinical results, coupled with the advent of more deliverable coronary stents with

superior radial strength and alternative methods available for plaque modification (i.e., rotational atherectomy), CBA is not commonly performed in the contemporary practice of interventional cardiology.

Embolic Protection Devices

Approximately one half of saphenous vein grafts (SVGs) either occlude or develop severe occlusive disease within 10 years of coronary artery bypass graft surgery. In the vast majority of such cases, PCI of either the graft or the native coronary artery is pursued because of the inherent risks associated with repeat surgery. SVG interventions, however, are laden with an array of technical challenges, most notably of which is an increased risk of the no-reflow phenomenon due to distal embolization of atherosclerotic debris. Although administration of vasodilators (i.e., nitroglycerin and/or nitroprusside) assists in restoring distal flow in these situations, there is little to no evidence to suggest that restoration of flow by this mechanism actually improves long-term clinical outcomes. It therefore stands to reason that either preventing or minimizing distal embolization can improve both procedural and clinical outcomes in patients undergoing SVG interventions.

Indications

Embolic protection devices (EPDs) are designed to minimize distal embolization of atherothrombotic and atherosclerotic disease during PCI. These devices should be used in clinical scenarios where the risk of distal embolization is high (i.e., PCI of an SVG). As will be discussed later in this chapter, clinical data currently do not support the use of EPDs in primary PCI for acute MI.

Embolic Protection Systems

A number of embolic protection systems have been developed throughout the years, each employing one of two primary mechanisms to capturing embolic material: balloon occlusion (either proximal to distal to the lesion) to trap particles which are subsequently aspirated, or deployment of a filter device distal to the lesion to trap antegrade traveling particulate matter. Table 6-6 outlines the major advantages and disadvantages of each system type (i.e., balloon occlusion vs. filter).

Balloon Occlusion

The best known EPD utilizing proximal balloon occlusion is the Proxis Embolic Protection System (St. Jude Medical, Inc., St. Paul, MN). The device is housed in a 3.6 F infusion catheter that is advanced through a 7 F guide catheter over a standard guidewire and is positioned proximal to the lesion. The balloon is inflated, which occludes antegrade flow, creating a stagnant column of blood that is aspirated after the intervention before coronary blood flow is restored upon balloon deflation (Fig. 6-11). The Proxis system is designed for use in vessels 3.0 to 5.0 mm in diameter. Use in larger diameter vessels is not recommended, as the occlusion balloon may not allow for complete vessel occlusion. Similarly, use of the device in smaller diameter vessels is not recommended because of the risk of vessel trauma during inflation of the occlusion balloon.

The main benefit of the Proxis system is its ability to protect against distal embolization even before the lesion is crossed with a guidewire. Although it can be used in any SVG where there is an adequate "landing zone" proximal to the lesion, its use is especially beneficial in settings where the absence of an adequate "distal landing zone" precludes the

Table 6-6

Advantages and Disadvantages of Embolic Protection Device Systems

	Filter	Balloon Occlusion
Perfusion	Permits antegrade blood flow	Prevents antegrade blood flow during use precipitating ischemia if no collateral flow is present
Emboli	Traps emboli > filter pore size (e.g., 100 µm)	All emboli and debris remain stagnant, allowing for aspiration prior to restoration of antegrade blood flow
Vasoactive substances & cytokines	Freely flows through filter	Limited ability to reach the distal bed due to lack of antegrade blood flow
Technical considerations in crossing lesions	Bulky; risk of distal embolization prior to device deployment	Lower profile; ability to be deployed prior to crossing the lesion, minimizing distal embolization
Retrieval considerations	Full of debris; may be difficult to collapse and fully retrieve filter; may become ensnared in proximal stent	Slow balloon deflation may prolong ischemic time
Embolization during device placement	Possible	Possible (unlikely with proximal balloon occlusion devices, however)
Visualization of distal vessel	Adequate	Compromised during balloon inflation

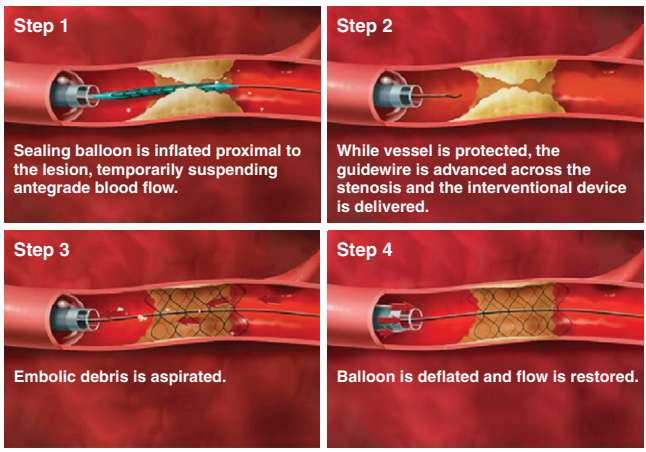

Figure 6-11 Proxis Embolic Protection System. (Courtesy of St. Jude Medical, Inc., St. Paul, MN.)

use of a distal filter device. The primary downside in using the Proxis system is that antegrade flow down the vessel is temporarily occluded, predisposing to myocardial ischemia and limiting the ability to achieve adequate contrast opacification of the distal vessel.

In contrast to the Proxis system, which utilizes proximal balloon occlusion to disrupt antegrade blood flow, the GuardWire Temporary Occlusion and Aspiration System (Medtronic, Inc., Minneapolis, MN) balloon occludes the vessel several centimeters distal to the lesion. The debris that is released during PCI is suspended in a stagnant column of blood that is subsequently aspirated prior to deflation of the balloon occluder. Similar to the filter-based EPDs, a sufficient distal "landing zone" must be present to deploy the device. Like the Proxis system, however, the GuardWire system is limited both by the need to disrupt antegrade flow, thereby predisposing to myocardial ischemia, and minimizing contrast opacification of the distal vascular bed.

Clinical Data. The PROXIMAL (Proximal Protection During Saphenous Vein Graft Intervention Using the Proxis Embolic Protection System) trial compared efficacy of the Proxis system to distal EPDs in preventing clinical events during SVG interventions. The primary end point was a composite of death, MI, emergent coronary artery bypass graft (CABG), and TVR (i.e., Major Adverse Cardiac Event) at 30 days. The study demonstrated that for MACE, the Proxis system was statistically equivalent to distal EPDs (7.1% vs. 11.7%; $P = 0.10$ for superiority; $P = 0.001$ for noninferiority).

The SAFER (Saphenous Vein Graft Angioplasty Free of Emboli Randomized) trial compared the GuardWire system to conventional SVG PCI without the use of distal embolic protection. The primary end point studied was a composite of death, MI, emergency CABG, or TVR (i.e., MACE) at 30 days. Use of the GuardWire system resulted in a significant reduction in the primary end point (9.6% vs. 16.5%; $P = 0.004$), equating to a 42% relative risk reduction in MACE.

Distal Embolic Protection

The Filterwire EZ Embolic Protection System (Boston Scientific Corporation, Natick, MA) is comprised of a uniform, 110-micron-pore basket filter fixed to a guidewire that, when released, expands up to 5.5 mm (Fig. 6-12). Prior to deployment, the entire Filterwire EZ system is advanced across the lesion, positioned in the distal vessel, and subsequently deployed. At the conclusion of the procedure, the filter is collapsed into a proprietary retrieval catheter, trapping the particulate matter, and is removed from the body. The primary advantage of the

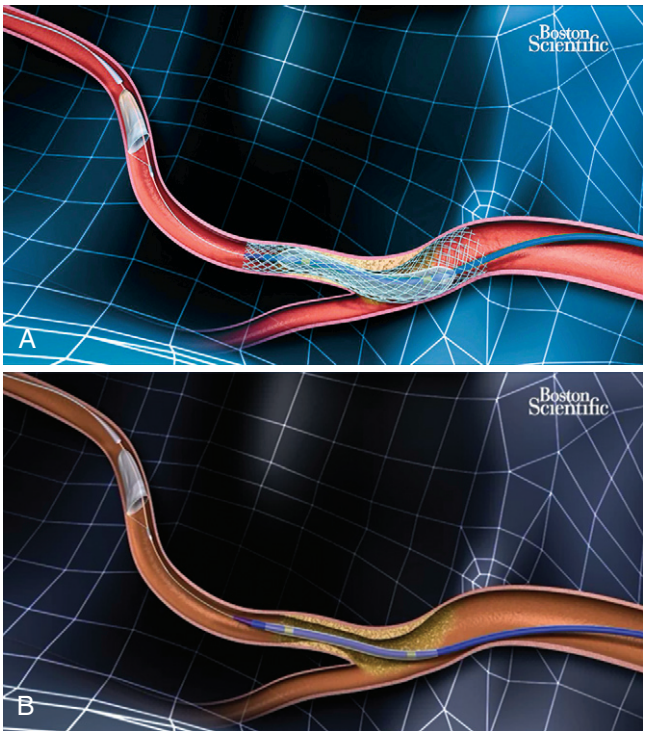

Figure 6-12 Boston Scientific Filterwire EZ Embolic Protection System. **A,** The filter is deployed distal to the lesion. **B,** Embolic material is captured during intervention. (Courtesy of Boston Scientific Corp., Natick, MA.)

Filterwire EZ system over the balloon occlusion-based systems is that it allows for antegrade blood flow throughout the procedure while still capturing larger embolic particles. Although the Filterwire EZ system may theoretically not capture small particulate matter because of limitations in filter pore size, studies comparing it to balloon occlusion systems have demonstrated similar debris size distribution and equivalent clinical outcomes. The primary limitation of the Filterwire EZ system is the need for an adequate distal "landing zone" to safely deploy the device (25–30 mm from the distal edge of the lesion).

The SpiderFX Embolic Protection Device (ev3, Inc., Plymouth, MN) is another distal protection device that can be employed during SVG interventions (Fig. 6-13). The device comes in a variety of filter sizes (ranging from 3.0 to 7.0 mm), is heparin coated, and offers the advantage of delivery over any standard 0.014-inch interventional guidewire (unlike the Filterwire EZ, which is integrated onto the guidewire itself). The filter is delivered via a 3.2 F catheter employing a rapid exchange (SpideRX) system and, following intervention, is retrieved using a separate 4.2 F or 4.9 F SpideRX retrieval catheter.

Clinical Data. The FIRE (Filterwire EX Randomized Evaluation) trial compared the Filterwire EX EPD to the GuardWire system during SVG PCI. The primary end point was a composite of death, MI, and TVR. At 30 days, the primary end point was reached in 9.9% of patients treated with the Filterwire EX EPD versus in 11.6% of patients treated with the GuardWire system ($P = 0.53$ for superiority; $P = 0.0008$ for noninferiority). At the 6-month follow-up, however, MACE rates had increased (driven largely by both recurrent MI and TVR) to 19.3% in the Filterwire EX EPD group and 21.9% in the GuardWire system group, indicating the complex disease pattern often present in patients undergoing SVG PCI.

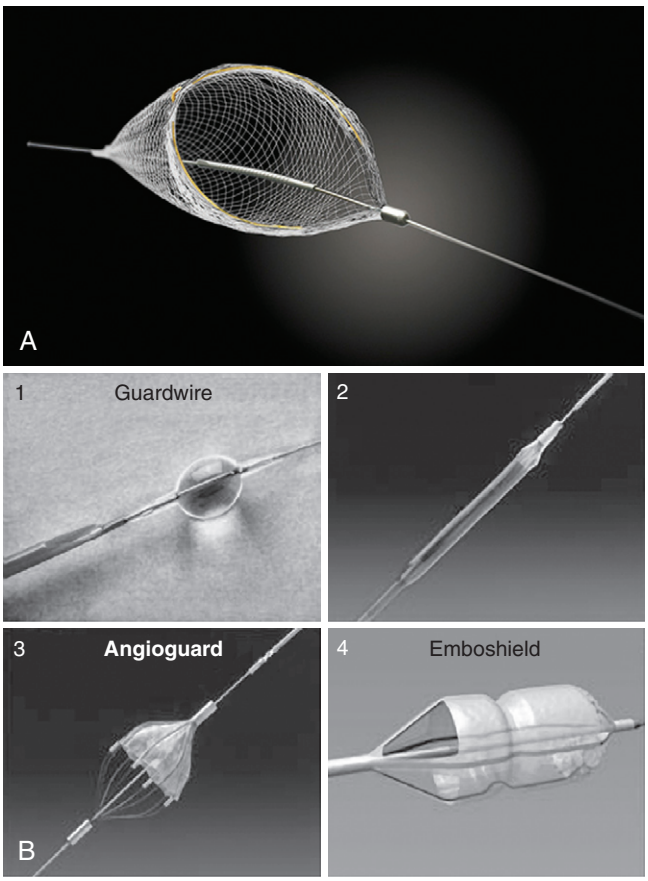

Figure 6-13 **A,** The SpiderFX Embolic Protection Device. (Courtesy of ev3, Inc., Plymouth, MN.) **B,** Other Distal protection devices. (*1*) The guard wire, PercuSurge balloon occlusion, and export catheter. (*2*) AngioGuard in the undeployed state. (*3*) AngioGuard in the deployed state acting as an umbrella-type filter. (*4*) An Emboshield filter device.

The SPIDER (Saphenous Vein Graft Protection in a Distal Embolic Protection Randomized) trial (not published) compared the SpiderFX EPD to a control group treated with either the Filterwire EZ EPD or GuardWire system during SVG PCI. The primary end point was a composite of death, MI, TVR, or urgent CABG (i.e., MACE). At 30 days, the primary end point was reached in 9.1% of patients treated with the SpiderFX EPD versus 8.4% in the control group ($P = 0.59$ for superiority; $P = 0.012$ for noninferiority).

Summary

As the complexity of coronary disease (i.e., heavily calcified lesions, bifurcation lesions, saphenous vein grafts, etc.) increases, the traditional "predilation and stenting" approach used in less complex lesions often cannot be realistically employed. In these situations, alternative interventional devices as an adjunct to traditional stenting often results in improved clinical and angiographic outcomes. Familiarity with these devices their indications, limitations, and overall efficacy is a necessity for effective and safe PCI in contemporary interventional cardiology practice.

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7

Restenosis and Drug-Eluting Stents

AHMAD EDRIS · NAUMAN SIDDIQI · MORTON J. KERN

Restenosis

Restenosis is defined as vessel narrowing of a previous angioplasty site. After balloon expansion, this narrowing occurs as a result of two mechanisms, negative remodeling (vessel constriction after stretching) and reaccumulation of material within the lumen (or stent). Reaccumulation of cellular material (also known as *endothelial proliferation*) is initiated by vessel injury with a release of thrombogenic, vasoactive, and mitogenic factors. Endothelial and deeper injury leads to platelet aggregation, thrombus formation, inflammation, and activation of smooth muscle cells and macrophages. The production and release of growth factors and cytokines promotes further synthesis of such factors and release from the cells involved. These factors result in the migration of new smooth muscle cells from their location within the arterial media to the endovascular lumen. These cells become a synthetic type of cell that produces extracellular matrix, leading to cellular proliferation and mechanical obstruction of the vessel lumen.

The second component of restenosis, recoil and negative remodeling of the arterial wall is inhibited by stents. Compared to balloon angioplasty, stents have reduced restenosis from 40% to 50% after percutaneous transluminal coronary angioplasty (PTCA) to 20% after bare-metal stenting. Drug-eluting stents (DESs) have brought restenosis rates to <10% in most patient subgroups. Restenosis still occurs inside stents (called *in-stent restenosis* [ISR]) mostly, if not exclusively, as a result of endothelial cell proliferation. Rarely does vascular recoil make a contribution, but it must be considered in treating the ISR lesion. Restenosis is not device-specific but rather a function of the anatomic substrate and the type of injury produced (Fig. 7-1).

Definitions of Restenosis

There are two types of restenosis recognized in patients, angiographic and clinical, which are not mutually exclusive.

Angiographic Restenosis

Angiographically measured luminal renarrowing after PCI has been the "gold standard" for restenosis. Angiographic restenosis is a continuous phenomenon, with no obvious threshold separating "restenosers" from "nonrestenosers." Studies have shown that the percentage of stenosis or minimal lumen diameter has a near Gaussian (normal) distribution on follow-up angiograms after balloon angioplasty. Thus, restenosis is best measured as a continuous variable. Nevertheless, because of practicality, the most commonly used definition of restenosis employs a dichotomous value (e.g., 50% diameter narrowing).

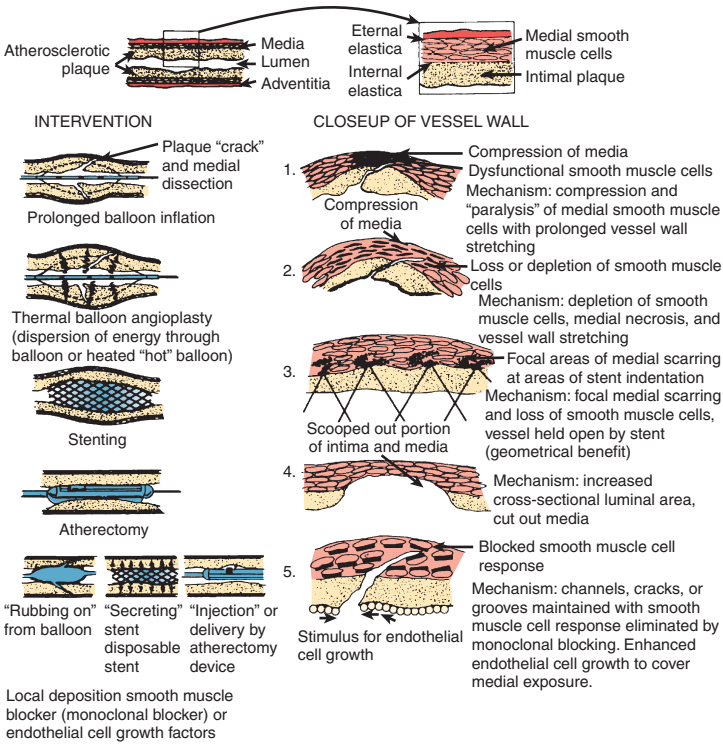

Figure 7-1 Interventional devices and presumed mechanisms of action of arterial plaque in vessel wall lead to restenosis. The indication of immediate outcome and restenosis rates depend on both the device and the arterial substrate encountered. (From Waller BF, Pinkerton CA, Orr CM. Restenosis 1 to 24 months after clinically successful coronary balloon angioplasty: A necropsy study of 20 patients. *J Am Coll Cardiol* 1991;17:58–70.)

Several different angiographic definitions of restenosis have been published with overlapping differences in some patients. Most studies define angiographic restenosis as either a greater than 50% loss of initial gain after intervention or an absolute lesion stenosis of greater that or equal to 50% at follow-up angiogram. The late loss of the acute luminal enlargement, or net gain in millimeters at the lesion site 6 months after treatment by quantitative angiography, should be around 0.7 mm for balloon angioplasty.

The *late loss index* is the loss at the lesion site divided by the amount of acute gain (Fig. 7-2). The loss index is accepted as the most sensitive measure of the effectiveness of the technique and should range from 0.4 to 0.6 mm for balloon angioplasty. The lower the loss index is, the more effective the antirestenosis treatment will be.

Restenosis is both a lumen-related and a vessel wall–related phenomenon. It appears that 40% to 60% of the acute luminal gain is lost during follow-up in all patients treated, independent of the devices. A similar degree of intimal thickening (restenosis by wall measurements) may or may not cause a significant luminal narrowing (restenosis by lumen measurement). As expected, the vessel size itself exerts a significant positive influence on minimal lumen diameter at follow-up and an equally negative effect on late loss. A larger artery will have a larger lumen at follow-up and vice versa for a smaller artery. Using percentage stenosis rather than absolute lumen diameter will neutralize this effect by correcting automatically for artery size.

Intravascular ultrasound (IVUS) imaging is superior to angiography for anatomic and morphologic restenosis definitions. Recent IVUS studies have shown that an important component of restenosis is vessel recoil, a feature prevented by stenting. Normal vessel modeling

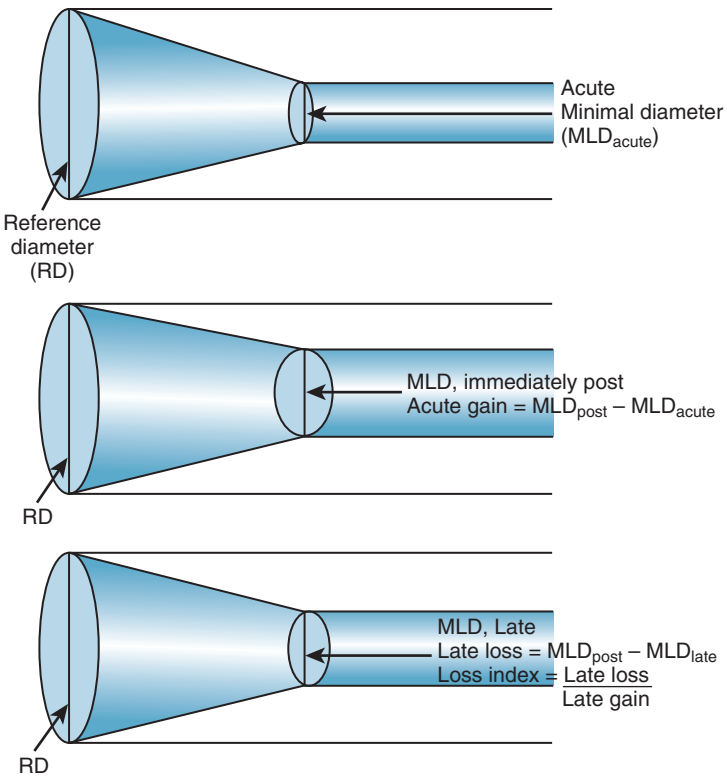

Figure 7-2 Calculations of acute gain, late loss, and loss index.

maintains the coronary lumen. Late negative remodeling of the injured vessel is also prevented by stenting (Figs. 7-3 and 7-4).

Clinical Restenosis

Clinical restenosis is defined as recurrent angina or anginal-equivalent symptoms after PCI. Other causes of symptoms might be mistaken for clinical restenosis, such as disease progression in the nondilated arterial segment, which occurs in 10% to 15% of cases late after PCI or new disease elsewhere. Incomplete revascularization also causes symptoms in about 10% of patients. Recurrence of typical angina after an asymptomatic period following angioplasty is a very specific clinical indicator for restenosis. On the other hand, atypical chest pain is a poor predictor. Restenosis is documented in 15% of asymptomatic cases.

Early (<1 month) exercise tests after balloon angioplasty (PTCA) were often persistently positive and failed to predict future restenosis and recurrent events. An exercise test at 6 months in patients who have

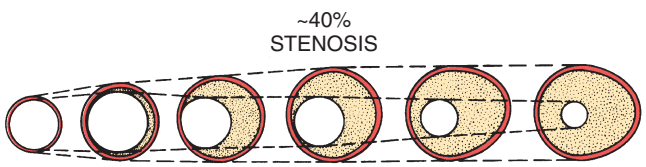

Figure 7-3 The Glagov phenomenon. According to serial intravascular ultrasound, normal segments showed proximal enlargement of the vessel as plaque volume increases. Vascular dilatation is compensated for by substantial plaque formation inside the vessel wall leaving the vessel's angiographic appearance unchanged and normal looking. (From Glagov S, Wisenberg E, Zarins CK, *et al.* Compensatory enlargement of human atherosclerotic coronary arteries. *N Engl J Med* 1987;316:1371–1375.

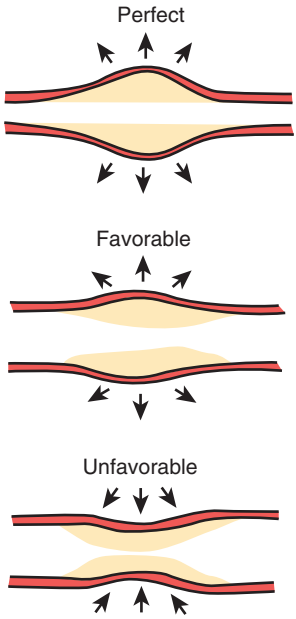

Figure 7-4 Adequacy of arterial remodeling with respect to changes in vessel size. (From Schwartz RS. Pathophysiology of restenosis: interaction of thrombosis, hyperplasia, and/or remodeling. *Am J Cardiol* 1998;81:16E.)

not yet presented with clinical recurrence shows a modest positive predictive value. Exercise testing early after PCI is not recommended. For symptoms appearing late after PCI in which restenosis is suspected, angiography is recommended. If the angiographic restenosis severity is intermediate (40%–70%), then in-lab functional testing with fractional flow reserve can be helpful in making a decision regarding whether repeat stenting is required.

Risk Factors for Restenosis

It is not possible to predict reliably whether restenosis will occur in a given patient. A multivariate analysis found the following conditions are predictors of restenosis: severe angina, left anterior descending artery lesions, diabetes, a higher degree of residual restenosis, hypertension, absence of an intimal tear, eccentric lesion morphology, and older age.

It is difficult to obtain follow-up angiograms in all patients undergoing coronary angioplasty. Less than complete angiographic follow-up with preferential recatheterization of symptomatic patients creates bias in that symptomatic patients artificially increase the restenosis rate in that population. At the same time, asymptomatic restenosis cases will go unrecognized clinically. This approach may underestimate the actual angiographic restenosis rate. Target vessel revascularization (TVR) rate is another surrogate for angiographic restenosis rates.

Time Course

Stents prevent very early (<24 hr) restenosis due to elimination of acute elastic recoil. The incidence of restenosis increases, peaking around 6 months. Late restenosis occurs uncommonly after 12 months. Restenosis after angioplasty using non-balloon, non-stent devices alone was highly variable with a reported incidence of restenosis between 15% and 55% (see Suggested Readings).

Different mechanisms produce restenosis in a time-dependent manner. Early restenosis is due to thrombus, whereas late restenosis is related more to remodeling (Fig. 7-5).

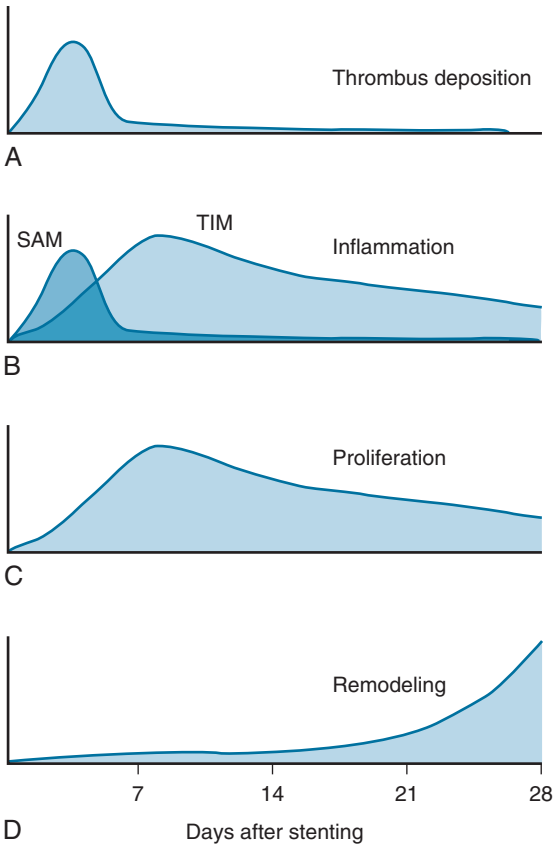

Figure 7-5 The four phases of vascular repair after stent-induced arterial injury in terms of time after stenting. **A,** Platelet-rich thrombus accumulates at areas of deep strut injury and peaks at 3 to 4 days after stent deployment, accounting for most early lumen loss. **B,** Coincident with thrombus deposition, inflammatory cells are recruited to the injury site, both at and between stent struts. At 3 to 7 days after stenting, the surface-adherent monocytes (SAMs) migrate into the neointima as tissue-infiltrating monocytes (TIMs) and remain in place. **C,** Proliferation of smooth muscle cells and monocyte macrophages within the neointima peaks at 7 days after implantation and continues above baseline levels for weeks thereafter. **D,** Collagen deposition in the adventitia and throughout the tunica media and neointima leads to arterial shrinkage or remodeling, causing compression of the artery on stent struts from without. (Modified from Garasic J, Edelman E, Rogers C. Stent design and the biologic response. In Beyar R, Keren G, Leon M, Serruys PW, eds. *Frontiers in interventional cardiology*. London: Martin Dunitz, 1997: 95–100.)

Patient Subsets at Higher Risk of Restenosis

Diabetes Mellitus

Poor outcomes can be seen in diabetic patients undergoing percutaneous coronary intervention (PCI). In one study, angiographic follow-up at 6 months in 418 diabetic and 2672 non-diabetic patients undergoing PCI showed that restenosis occurred in 550 of 2672 (20.6%) non-diabetic and 130 of 418 (31.1%) diabetic patients (P = 0.01). Vessel caliber, stented length of vessel, and lower BMI were reported predictors of in-stent restenosis in patients with diabetes. Another study evaluated 1288 patients (263 diabetic patients [21%]) and showed that repeat revascularization of the stented lesion was performed more frequently during the first year in patients with diabetes (16% vs. 10.9%, P = 0.01). Also, cardiac death and myocardial infarction (MI) were more frequent

among patients with diabetes (5-year rates, 25.4% vs. 17.9%, $P = 0.008$) and remained significant after adjustments were made for differences in baseline characteristics.

Chronic Renal Failure

It has been reported that patients with chronic renal failure who undergo PCI have a high restenosis rate (>30%). A study compared 40 lesions in 34 patients with end-stage renal disease (ESRD) with 80 lesions from patients without renal impairment who underwent coronary stenting. Despite comparable initial angiographic results over the 9-month follow-up period, repeat TVR was twice as frequent in the ESRD group compared with the control group (35% vs. 16%, $P < 0.05$). Another study evaluated the effect of moderate renal insufficiency in patients undergoing primary angioplasty for acute MI and found that significant restenosis was seen more frequently in patients with renal insufficiency compared to those with normal renal function (20.6% vs. 11.8%, $P = 0.024$).

Transplantation

Cardiac allograft vasculopathy (CAV) is a rapidly progressive form of atherosclerosis and is one of the main limitations to long-term survival after orthotopic heart transplantation. PCI has been used as a palliative treatment option for CAV but is associated with worse clinical outcomes and greater rate of restenosis compared with PCI of native coronary arteries. Several studies have shown that when compared with BMS, PCI with DESs was safe and reduced the rate of angiographic restenosis in patients with CAV. However, treatment of patients with CAV with DESs does not seem to alter the natural deleterious history of this disease process.

Acute Myocardial Infarction

Several randomized trials have demonstrated that PCI is superior to thrombolysis in reducing mortality, the recurrence of MI, and TVR. However, restenosis occurs in 40% to 50% of patients after initial successful angioplasty and in 20% to 30% of patients after stenting. The choice of DESs or bare-metal stents (BMSs) for STEMI PCI is based on vessel size and ability to maintain dual antiplatelet therapy over the following year.

Chronic Total Occlusion

Total occlusion has a higher restenosis rate than subtotal stenosis. The recurrence of total occlusion lesions seldom results in MI because of reformation of prior collateral protection.

A recent study, the ACROSS/TOSCA-4 trial, examined angiographic and clinical outcomes with DESs in coronary total occlusion (CTO) revascularization. Patients with CTO ($n = 200$) (78.8% >6 weeks CTO age) were enrolled for treatment with DESs. The primary end point was 6-month angiographic binary restenosis within the treated segment. A total of 199 patients (99.5%) were treated with DESs, and procedural success was 98.0%. The 6-month binary restenosis rates were 9.5% in-stent, 12.4% in-segment, and 22.6% in-"working length" representing the entire treatment segment. Rates of 1-year target lesion revascularization (TLR), MI, and target vessel failure were 9.8%, 1.0%, and 10.9%, respectively.

Saphenous Vein Graft Lesions

Saphenous vein graft (SVG) lesions are associated with a higher restenosis rate, particularly in the proximal anastomotic (58%) and body (52%) portions of the graft. Distal anastomotic narrowing responds to angioplasty well, especially in patients with recurrent coronary artery

bypass graft surgery. The time course of restenosis in vein grafts is different than in native coronary vessels, with continued significant attrition beyond 6 months.

The long-term patency rate of the SVG has improved with advances in medical therapies but still remains suboptimal. A review of several studies evaluating SVG durability consistently shows poor graft patency and a high rate of total occlusion. One study evaluated 27,211 patients and showed a 5-year SVG patency rate (defined as less than 70% stenosis) of less than 40%.

Internal Mammary Artery Graft Lesions

The internal mammary graft anastomotic site responds very favorably to angioplasty, with a 10% to 15% or less restenosis rate. One study comparing the SVG and internal mammary artery graft showed 10-year patency rate of 57% and 90%, respectively, with patency defined as not totally occluded.

Non-Balloon Device Restenosis

Rotational Atherectomy

Rotational atherectomy has distinct mechanical advantages for calcified lesions in the native coronary circulation. The 6-month restenosis rate after percutaneous transluminal coronary rotational angioplasty (PTCRA) approximates the rates observed after standard balloon–only angioplasty. In some circumstances, the PTCRA restenosis rate exceeded the expected PTCA rate. The predisposition to restenosis after PTCRA has limited the use of stand-alone PTCRA to rare cases where stents cannot be used afterward.

In-Stent Restenosis

In-stent restenosis (ISR) is primarily due to neointimal hyperplasia produced by vessel injury of the balloon and/or stent struts. The injured segments promote activation of platelets, mural thrombus, and inflammatory cells. Vascular injury, mural thrombus, and a metallic foreign body activate circulating neutrophils and tissue macrophages. These elements release cytokines and growth factors, activating smooth muscle as well as stimulating upregulation and expression of genes promoting cell division, such as *c-myc,* leading to further cell proliferation. Metalloproteinases are produced, leading to increased matrix material and remodeling of the extracellular support matrix, initiating smooth muscle cell migration. Uncontrolled proliferation of vascular smooth muscles into the vessel intima and the deposition of extracellular matrix lead to significant in-stent luminal narrowing 3 to 6 months after PCI.

There are two major categories of in-stent restenosis—focal and diffuse (Fig. 7-6)—and within each category several subtypes of responses relative to the proliferation within and/or adjacent to the stent are noted. Figure 7-7 suggests a scheme for the treatment of ISR. Note that brachytherapy is now rarely used.

Stent fracture is associated with in-stent restenosis in Drug-Eluting Stents.

Lee MS *et al.* reviewed angiograms on 530 of 2728 patients who underwent drug-eluting stenting from 2003 to 2005. The incidence of DES fracture–related adverse events was rare and identified in 10 patients. None of these fractures was detectable at the time of stent placement. The median time from implant to fracture detection was 226 days (range, 7–620 days). Adverse stent fracture events occurred in seven patients (six patients had binary restenosis and one patient had stent thrombosis), all necessitating repeat intervention. Factors predisposing to stent fracture included excessive tortuosity in the proximal segment, and overlapping stents. In this small patient registry, all stents were sirolimus DESs.

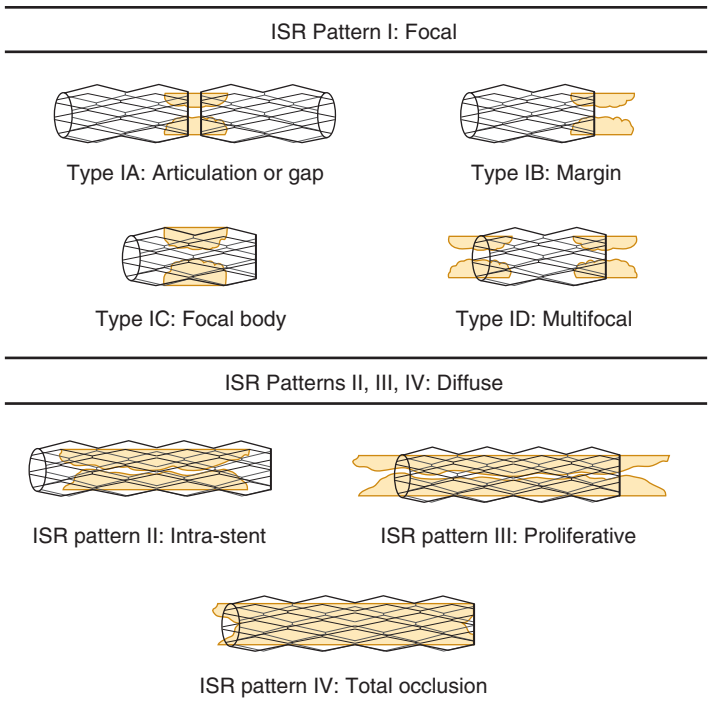

Figure 7-6 Classification system proposed for in-stent restenosis (ISR). (From Mehran R, Dangas G, Abizaid AS, *et al.* Angiographic patterns of in-stent restenosis classification and implications for long-term outcome. *Circulation* 1999;100:1872–1878.)

Management of Restenosis

IVUS, Balloon Angioplasty, and Restenting

The ISR lesion may be due to underexpansion of the stent for the size of the vessel on the initial implantation or exuberant neointimal hyperplasia or a combination of these mechanisms. The treatment of ISR should begin with IVUS assessment of vessel/stent relationship. Then an appropriately sized balloon can be used to expand the stent and compress the hyperplastic tissue. A repeat IVUS is often helpful to gauge success of this maneuver. Recently, use of optical coherence tomography in patients undergoing balloon angioplasty of ISR shows tissue disruption, leading the operator to select another stent to seal this material. Although appealing to the operator, there are few data to support this routine approach at this time.

The success and complication rates are lower than for the initial procedure because the restenosis lesion is primarily fibroproliferative rather than an atherosclerotic plaque. Stenting of restenotic lesions, although easily performed, may not resolve the problem long term since outcomes after multiple overlapping stents may predisposed to higher subacute thrombosis rates.

Surveillance angiography is not recommended because of the potential for false positive restenosis, that is, narrowing without significant clinical importance. Intermediately severe ISR lesions (40%–70%) should be associated with evidence of ischemia. It is appropriate to use stress testing or fractional flow reserve measurement (FFR) before treatment.

Use of intravenous ultrasound is *critical* to decide whether to reexpand an underdeployed stent relative to the vessel size or attack the endothelial proliferation and consider an additional stent.

Use of a cutting balloon should be considered because blades provide excellent balloon stability inside stent during inflations.

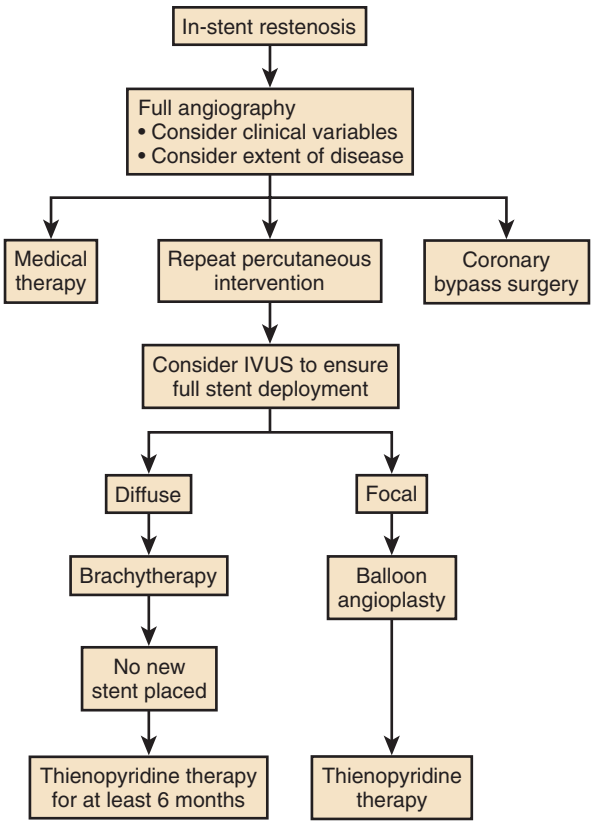

Figure 7-7 Algorithm for treatment of in-stent restenosis. (Modified from Topol EJ. *Textbook of interventional cardiology*, 4th ed. Philadelphia: Saunders, 2003: 468.)

Brachytherapy

Vascular brachytherapy, using beta and gamma emitters for treating PCI-related restenosis, and especially in-stent restenosis, had demonstrated safety and marginal efficacy. Brachytherapy is not currently used for routine treatment of in-stent restenosis because of logistical complexity and complications such as late thrombosis and edge effects after radiation therapy. A full discussion of this topic can be found elsewhere.

The adverse effects of brachytherapy included the following:

- Edge effects
- Late thrombotic occlusion
- Stent vessel separation
- Long-term effects

Of all the adverse effects, late thrombosis occurring more than 30 days after radiation therapy was one of the most feared major complications of vascular brachytherapy. Late thrombosis in early clinical trials was reported in up to 14% of patients. Late thrombosis also occurs with other vascular brachytherapy and relates to the healing arrest and lack of stent re-endothelialization. An effective strategy to prevent late rethrombosis is limiting restenting at the time of radiation treatment. It is essential to administer at least 12 months of antiplatelet therapy, preferably clopidogrel in addition to aspirin, for all radiation cases, both beta and gamma emitters. Definitions of artery and stent segments address by brachytherapy are shown on Figure 7-8.

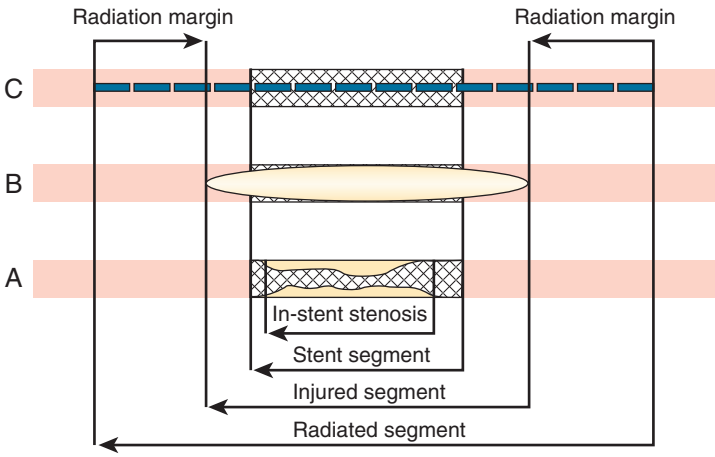

Figure 7-8 Definition of vessel segments. **A,** Preprocedural in-stent stenosis in stent segments. **B,** Angioplasty determines the injured segments. **C,** After angioplasty, the radiation source is placed in the vessel. (From Cheneau E, Wolfram R, Leborgne L, *et al.* Understanding and preventing the edge effect. *J Interv Cardiol* 2000;16:1–7.)

Drug-Eluting Stents

Compared to BMSs, DESs reduce the rate of TLR and in-stent restenosis. The components of a DES system are (1) the specific metal stent design, (2) the use and type of polymer for drug absorption, and (3) the type of antiproliferative agent and its elution kinetics.

Current DESs available in the United States include drug compounds that contain antiproliferative agents such as paclitaxel, sirolimus, everolimus, or zotarolimus (Fig. 7-9).

Stent Design

Drug delivery is dependent on strut spacing, the number of struts, and the homogeneity of strut placement over the target surface. Stents were initially designed to physically scaffold arterial dissection flaps, not for drug delivery. Significant changes were made to allow for drug coating and elution. The geometry of the stent must allow a sufficient area

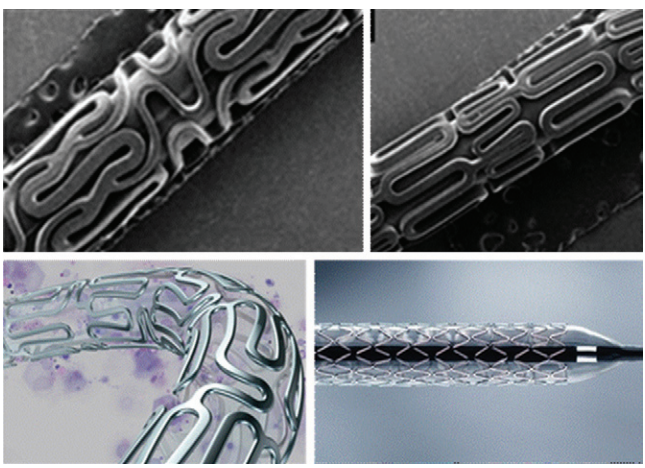

Figure 7-9 Cell designs of drug-eluting stents: Cypher (*top left*), Taxus (*top right*), Xience (*bottom left*), Endeavor stent (*bottom right*).

for delivery of the agent. The drug-carrying units of the stent cells must allow a sufficient area for diffusion to deliver optimal tissue drug levels. Biodegradable stents with temporary scaffolding and drug delivery during the healing process are currently being tested.

Coating

Passive stent coatings to modify the surface characteristics of stainless steel or cobalt chromium alloy have included ceramics, noble metals, polishing, thermal plating, and biochemical mimicry with phosphorylcholine or fibrin. Polymeric materials act as drug repositories and allow for controlled drug release over time. Pharmacologic agents can be maintained in the polymer reservoir when covered by a film on or within a polymeric matrix. Drug release occurs through three mechanisms—diffusion, chemical reaction, or solvent activation. Nondegradable polymers enable drug release by particle dissolution, whereas biodegradable polymers permit drug diffusion in concert with matrix degradation. For the current generation of DESs, drug release from the polymer occurs by passive diffusion.

Drugs for Coated Stents (Fig. 7-10)

Drugs used for stent coatings to reduce neointimal proliferation should have a large therapeutic window and a low inflammatory potential, inhibit multiple mechanisms of the complex restenotic biology, and reduce smooth muscle cell proliferation without unacceptable toxicity to the medial and adventitial cell layers. Unlike radiation, local drug elution should not inhibit stent re-endothelialization. Drugs for coated stents should have favorable local pharmacokinetics and distribution properties. Hydrophilic drugs, such as heparin, permeate into tissue but are rapidly cleared. Hydrophobic agents, such as paclitaxel or sirolimus, are insoluble in the aqueous phase and bind to hydrophobic sites on the arterial wall. Both hydrophilic and hydrophobic drugs have large spatial concentration gradients across the arterial wall, with hydrophobic drugs distributing better and more homogeneously than hydrophilic agents.

Sirolimus is rapamycin, a naturally occurring macrocyclic lactone discovered in the soil of Easter Island (Rapa Nui) in the 1960s. Rapamycin is a product of fermentation of *Streptomyces hygroscopicus*

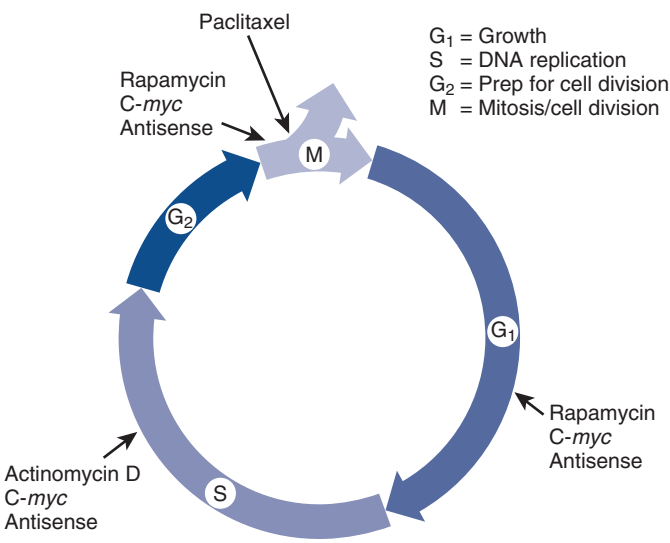

Figure 7-10 Sites of action in the cell phase for selected pharmacologic stent coating to inhibit restenosis.

and was used as an antifungal antibiotic. Sirolimus blocks the cell cycle of proliferating cells binding to the high-affinity cytosolic receptor protein FK506, leading to the inhibition of mammalian target of rapamycin (mTOR), which prevents downregulation of tumor suppressive cell P27. The gene p27 inhibits cell-dependent kinase activity and blocks G1- to S-phase cell cycle progression. Sirolimus is lipophilic and easily crosses the cell membrane. The inhibition of mTOR suppresses T-cell proliferation and is a powerful antiproliferative and antimigratory agent acting on smooth muscle cells. Systemic sirolimus reduces neointimal proliferation after balloon injury in porcine coronary arteries. Local sirolimus administration inhibits neointimal proliferation.

Paclitaxel is a powerful antineoplastic drug found in the Pacific yew tree (*Taxus brevifolia*) and is used in the treatment of malignant ovarian and breast cancer. Paclitaxel stabilizes polymerized microtubules and enhances microtubular assembly, forming unorganized and decentralized microtubules in the cytoplasm. Cell replication is inhibited predominately in the G0/G1 and G2/M phase of the cell cycle. Paclitaxel is highly lipophilic, promoting rapid uptake through hydrophobic cell membranes and minimizing systemic loss. Paclitaxel is suitable for polymer-based delivery. It has long-lasting antiproliferative effects after a single administration and can be directly applied to metal as a durable simple coating.

Everolimus is a novel semisynthetic highly lipophilic macrolide with immunosuppressant and antiproliferative properties. The chemical name is 40-O-(2-hydroxyethyl)-rapamycin and it is created by modifying rapamycin. Similar to rapamycin, inhibiting mTOR is the likely mechanism for suppression of cell proliferation. At the cellular level, it blocks growth factor–driven transduction signals in the T-cell response to alloantigen and proliferation of both hematopoietic and non-hematopoietic cells. Following stimulation of the IL-2 receptor on the activated cell, it inhibits p70 S6 kinase, thereby arresting the cell cycle in the late G1 phase. Systemic everolimus suppresses in-stent neointimal growth in the rabbit iliac artery following stenting.

Zotarolimus is also a novel semisynthetic derivative of rapamycin, which was designed to have a shorter in vivo half-life. It is a highly lipophilic immunosuppressive and antiproliferative agent. As with rapamycin and everolimus, zotarolimus inhibits mTOR, blocks growth factor–driven cell proliferation, which ultimately results in cell cycle arrest in the G1 phase.

Drug-Eluting Stent Systems

The Cypher (Cordis Corp., Bridgewater, NJ) sirolimus-eluting coronary stent system is comprised of two components: a BX Velocity coronary stent system (Cordis Corp., Bridgewater, NJ) and the sirolimus drug product. It was approved for clinical use by the U.S. Food and Drug Administration (FDA) in April 2003. It comes premounted on either an over-the-wire (OTW) or rapid exchange (RX) delivery system. The Cypher stent is comprised of 316 L stainless steel with six to seven circumferential cells. The inactive ingredients are parylene C and two non-erodible polymers: polyethylene-co-vinyl acetate (PEVA) and poly n-butyl methacrylate (PBMA). The base coat is made of a combination of the two polymers and sirolimus (67%/33%). This is then applied to the stent, which has been pretreated with parylene C. A solution of PBMA polymer is applied as a topcoat to the stent. Lastly, the drug/polymer combination solution is applied to the entire surface. The drug delivery kinetics allows for 80% of the sirolimus to be released over 30 days. The stent is available in 2.25 mm to 3.5 mm diameter sizes and 8 mm to 33 mm in length. It currently has the FDA-approved indications for improving coronary luminal diameter in patients with symptomatic ischemic heart disease due to discrete de novo lesions of 30 mm in native coronary arteries with a reference vessel diameter of 2.25 mm to 3.50 mm.

This stent is contraindicated in patients with known hypersensitivity to sirolimus, polymethacrylate, or polyolefin copolymers. It is also contraindicated in patients who are unable to take recommended antiplatelet and anticoagulant therapy.

The benefit of the Cypher stent in reducing in-stent restenosis was documented in the large, pivotal, randomized controlled trial SIRIUS and the smaller randomized supportive trial RAVEL.

The SIRIUS trial compared the Cypher stent with the control BX Velocity bare-metal stent in de novo coronary artery lesions in 1058 patients. These were considered somewhat complex patients because many were diabetics and had, on average, long lesions (14.4 mm) and small vessels (2.8 mm). Overall, 92% of patients had AHA/ACC type B1, B2, or C lesions. It examined target vessel failure at 9 months as the primary end point, which was defined as cardiac death, MI, or TVR. The Cypher stent was found to significantly lower the primary end point to 8.6% from 21% in the BMS group. This was largely driven by reduction in TLR in the Cypher arm (4% vs. 17%). Overall improvements were seen in rates of in-stent restenosis (3% vs. 35%) and late lumen loss (0.17 mm vs. 1.0 mm), which were assessed by angiography and IVUS. The lower rates of TLR persisted at 2 years (5.8% vs. 21.3%). Follow-up data reveal no significant difference in late stent thrombosis compared with BMS at 4 to 5 years (0.8% vs. 0.6%).

The RAVEL trial compared the Cypher stent with the control BX Velocity bare-metal stent in de novo coronary artery lesions in 238 patients. There was a significant reduction in the primary end point, which was late lumen loss assessed by angiography (–0.01 mm vs. + 0.80 mm in BMS) at 6 months. There was also a significant reduction in neointimal hyperplasia (2.5 mm^3 vs. 37 mm^3 in BMS) and the frequency of restenosis of more than 50% of the lumen diameter (0 vs. 27%). TLR at 1 year was 5.8% in the sirolimus group and 28.8% in the control group. Neointimal hyperplasia was also markedly inhibited in the sirolimus group by IVUS substudy.

The Taxus (Boston Scientific Corp., Natick, MA) paclitaxel-eluting coronary stent system is comprised of a balloon-expandable Liberté stent coated with an 8.8% slow-release formulation of paclitaxel. It is available in either the Taxus Express or Taxus Liberté versions. The Taxus Express was first approved for clinical use by the FDA in March 2004, and the Liberté was approved in October 2008. Liberté is newer, has thinner struts, and has more flexible cell geometry. Express and Liberté have similar polymers, drug delivery, and release kinetics but different stent geometry and different strut size. Both are available premounted on either an RX or OTW delivery system.

The stent itself is made of 316 L stainless steel. The Taxus system uses the inactive compound Translute, a tri-block copolymer that is made of SIBS [poly(styrene-b-isobutylene-b-styrene)]. The polymer is mixed with paclitaxel and then applied to the entire surface of the metal stent without primer or top coat. The stent is currently available in 2.25 mm to 4.0 mm diameter sizes and 8.0 mm to 32 mm (Express) or 38 mm (Liberté) in length. It currently has FDA-approved indications for improving the luminal diameter for de novo native coronary artery lesions of 2.25 mm to 4.00 mm in diameter in lesions of 28 mm in length (Express) or 34 mm (Liberté). Taxus Express has the additional indication in bare-metal stent restenotic lesions of 2.5 to 3.75 mm in diameter and 28 mm in length. It is contraindicated in patients with known hypersensitivity to paclitaxel or Translute. It is also contraindicated in patients who are unable to take recommended antiplatelet and anticoagulant therapy.

The benefit of the Taxus stent systems in reducing in-stent restenosis was evaluated in the TAXUS trials.

The TAXUS II randomized controlled trial randomly assigned 536 patients to the Taxus stent or a BMS in patients with a single primary lesion in native coronary arteries. Primary end points were percentage of in-stent net volume obstruction at 6 months as measured by IVUS.

Taxus use was associated with significantly lower rates of in-stent restenosis (3.5% vs. 19.1%) and lower rates of TLR (3.9% vs. 13.3%) at 6 months. The incidence of major adverse cardiac events at 12 months was significantly reduced at 10.9% versus 22%. There was no difference in the slow- versus moderate-release formulations in the Taxus stent. Cordis currently markets only a slow-release formulation.

The TAXUS IV trial was a large randomized trial that assigned 1314 patients with a single previously untreated coronary artery stenosis to the Taxus stent or a BMS. The primary end point was the rate of ischemia-driven TVR at 9 months. Taxus use was associated with significant reductions in angiographic restenosis (8% vs. 27%), TLR (3% vs. 11%), and late lumen loss (0.39 mm vs. 0.92 mm) at 9 months. These significant benefits persisted to 1 year, with additional reductions in major adverse cardiac events (10.8% vs. 20%). The incidence of stent thrombosis at 4 years was not significantly different as compared to BMS (1.6% vs. 1.1%).

Xience V (Abbott Vascular, Santa Clara, CA) everolimus-eluting stent system is comprised of the inactive non-erodible polymer PBMA, which adheres to the stent and drug coating. It was first approved for clinical use by the FDA in July 2008. It also contains PVDF-HFP (vinylidene fluoride and hexafluoropropylene monomers) as the drug matrix layer containing everolimus. The drug matrix copolymer is mixed with everolimus (83%/17%) and applied to the entire PBMA coated stent surface without a topcoat. The stent itself is L-605 cobalt chromium alloy. The system is available premounted on either RX or OTW delivery systems. The stent is available in 2.5 mm to 4.0 mm diameter sizes and 8 mm to 28 mm in length. It is indicated in patients with symptomatic heart disease for improving coronary luminal diameter in de novo coronary artery lesions of 28 mm in length and with reference diameters of 2.5 mm to 4.2 mm.

This stent is contraindicated in patients who cannot receive recommended antiplatelet and anticoagulant therapy; in lesions where proper placement and complete balloon angioplasty is not possible; and in patients with hypersensitivity to everolimus, cobalt, chromium, nickel, tungsten, acrylic, or fluoropolymers.

The Xience stent system was studied in SPIRIT clinical trials. SPIRIT III was a randomized clinical trial involving 1002 lower risk patients which demonstrated the non-inferiority of Xience compared to Taxus Express. The primary end point was in-segment late loss at 240 days and the co-primary end point was ischemic-driven TVF (composite of cardiac death, MI, clinically driven TVR) at 270 days. Xience was found to be significantly superior to Taxus with reference to in-segment late loss (0.14 mm vs. 0.28 mm). Xience was also found to be non-inferior in TVF at 9 months (7.6% vs. 9.7%). Two-year follow-up data reveal that stent thrombosis occurred in 1% of patients in the Xience arm at 2 years, with 0.3% occurring very late (>1–2 years). Of note, Boston Scientific also markets the Xience stent under its trade name Promus.

Endeavor (Medtronic Vascular, Santa Rosa, CA) zotarolimus-eluting stent system is comprised of a thin strut, low profile, cobalt chromium alloy Driver (Medtronic Vascular, Santa Rosa, CA) stent, phosphorylcholine polymer, and zotarolimus. It was first approved for clinical use by the FDA in July 2008. The polymer used is a hydrophilic biomimetic polymer that is similar to erythrocyte membranes. The stent contains a dose of 10 μg of zotarolimus per 1 mm of stent length. This allows for 98% of the drug to be eluted within 2 weeks and treatment level doses for approximately 28 days after implantation. The stent is available in 2.5 mm to 3.5 mm diameter sizes and 8 mm to 30 mm in length. It is indicated in patients with ischemic heart disease to improve coronary luminal diameter in de novo coronary artery lesions of 27 mm in length and with reference vessel diameter of 2.5 mm to 3.5 mm.

This stent is contraindicated in patients with known hypersensitivity to zotarolimus, cobalt-based alloy (cobalt, chromium, nickel, tungsten), or phosphorylcholine polymer. As with all coronary stents, it is

contraindicated in patients who are unable to receive recommended antiplatelet or anticoagulant therapy, as well as in those that have a lesion that prevents complete balloon angioplasty or proper stent placement.

The Endeavor stent system was studied in the large ENDEAVOR II clinical trial, which compared the stent to the Driver BMS in 1197 patients with single coronary artery stenosis. The primary end point was TVF (composite of TVR, MI, cardiac death) at 9 months. Endeavor was found to significantly reduce TVF (7.9% vs. 15.1%). There was no difference in stent thrombosis between the two arms.

The ENDEAVOR III randomized trial compared the Endeavor stent versus Taxus in 436 patients. The follow-up data at 3 years revealed no significant difference in TVF or major adverse cardiac events between the two arms.

The Future—Bioabsorbable Stents

Bioabsorbable stents are currently being evaluated. Just as the need to deliver antiproliferative drugs is temporary, so is the need to scaffold the vessel with a metal stent. The goal with bioabsorbable DESs is to limit the shortcomings of metal DESs, which include the requirement of prolonged dual antiplatelet therapy, possible permanent side branch occlusion, difficulty of subsequent surgical revascularization, elimination of reactive vasomotion, and the risks of late stent thrombosis. An absorbable stent would need to be in place long enough to protect against vessel recoil and subacute closure, which typically leads to restenosis.

One particular stent system, the bioabsorbable everolimus-eluting stent system by Abbott Vascular (BVS) has been studied in the ABSORB open-label study to assess its safety and efficacy. The stent is made from a bioabsorbable polylactic acid that is coated with a more rapidly absorbed polylactic acid that contains everolimus and controls its release. Elution kinetics allowed for 80% of the everolimus to be eluted within 28 days. A total of 30 patients with de novo single coronary artery lesions were enrolled. The composite end point was cardiac death, MI, and ischemia-driven TLR, measured at 6 and 12 months. The study reported only one MI at 12 months, with no stent thromboses or TLR. At 6 months, there was angiographic late loss of 0.44 mm, mainly due to a mild reduction in stent area as measured by IVUS (–11.8%). This degree of late lumen loss is similar to data reported from Taxus DES trials. Recently, 2-year follow-up data were reported. A multiimaging approach was taken, which revealed that by echogenicity, virtual histology, and optical coherence tomography, the stent was incorporated into the vessel wall and absorbed. No stent thrombosis occurred despite the discontinuation of thienopyridine drugs. In-stent late loss was 0.48 mm, which did not differ significantly from 6 months. Vasomotion was also noted to occur at stented segments in response to administration of vasoactive agents. There is no FDA-approved bioabsorbable DES available currently, but it may prove to be an option for the treatment of coronary artery disease in the near future.

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8

Bifurcation Stenosis Percutaneous Coronary Interventions

MORTON J. KERN · ARNOLD H. SETO · PRANAV M. PATEL · WILLIAM M. SUH

Treating bifurcation lesions involves weighing the risk of side-branch closure and the need for additional stent, sometimes requiring complex techniques. The approach to bifurcation lesions is based on the angiographic configuration of the lesion(s) in the main branch and the side branch. Significant disease (>50% stenosis) in the ostium of the side branch increases the likelihood of side-branch closure as well as the restenosis rate after percutaneous coronary intervention (PCI). Several classification schemes have been developed; these are summarized in Figure 8-1. Side branches at low risk (not likely to be compromised) include prestenosis branches, poststenosis branches, and those branches that do not straddle a stenosis. PCI across an uninvolved side branch carries a less than 1% risk of occlusion. The requirement for side-branch protection for the three side-branch locations above (prestenosis, poststenosis, not straddling a stenosis) is minimal, as the technical difficulty of approaching the target branch is also low.

Bifurcation lesions that are at high risk for side-branch closure are side branches that straddle the stenosis of the main vessel and side branches with ostial stenosis. The technical difficulty of treating these stenoses increases with the severity of side-branch narrowing. The risk of side-branch closure with an ostial narrowing approaches 15%.

When there is an equal distribution of coronary plaque across a bifurcation stenosis, simultaneous balloon angioplasty of both branches should be considered to maintain vessel patency, followed by one-stent or two-stent PCI. In some cases, operators can choose to debulk the involved side branch with rotational atherectomy or cutting balloon angioplasty to decrease the likelihood of side-branch closure with main-branch PCI.

Medina							
Duke (modified)	D	C	F	G	A	B	E
Sanborn	I	–	–	III	IV	II	IV
Lefevre	1	2	–	4	3	4a	4b
Safian	IA	IB	IIA	IIIA	IIB	IIIB	IV
Movahed	L	S	2	1m	1s	V	T
Staico-Feres	3	2A	2B	2C	1A	1B	1C

Figure 8-1 Seven classification systems for bifurcation lesion descriptions.

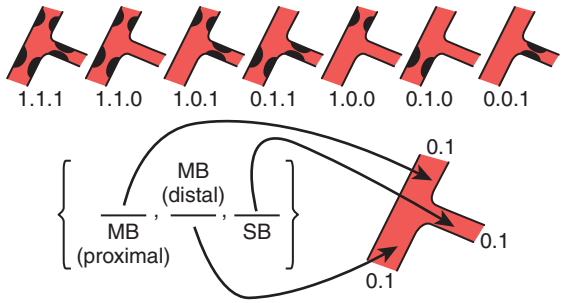


Figure 8-2 The Medina Classification System.

Classification of Bifurcation Lesions

The treatment of bifurcations depends on the distribution of disease, ostial involvement, and size of branch from the parent vessel. The most commonly used classification system is the Medina (Fig. 8-2), which assigns a 0 or 1 to the presence or absence of disease in the proximal segment, distal segment, and branch vessel. The major objection to this scheme is that it does not account for angulation, which significantly contributes to procedure success rates. Another schema is depicted in Figure 8-3.

Choosing Between One-Stent (Provisional) and Two-Stent Techniques

Even in the drug-eluting stent (DES) era, several large studies including meta-analyses have shown that one-stent techniques are as good, if not better, compared to two-stent techniques for late outcomes. Trials using DES for bifurcation stenting have shown higher incidences of subacute

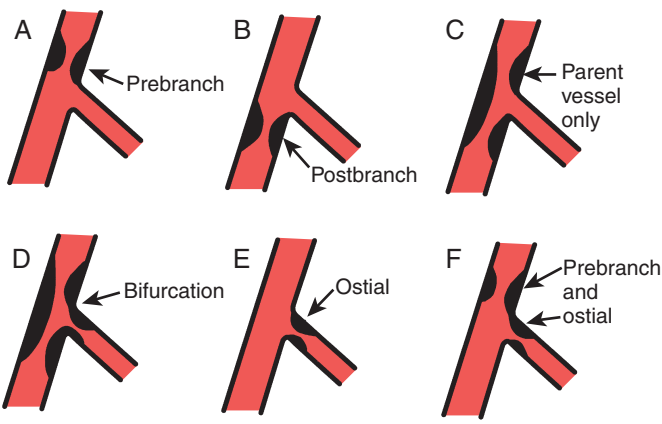


Figure 8-3 Schematic representation of lesion and side-branch involvement. **A, B,** and **C** represent parent vessel involvement with no disease located in the side-branch vessel. **D, E,** and **F** represent parent and side-branch involvement with more than 50% ostial stenosis in the side branch. (Adapted from Freed M, Grines C. *Manual of interventional cardiology*. Birmingham, MI: Physicians' Press, 1992.)

thrombosis with two stent techniques. It is unclear what the risk-benefit ratio is of having more metal, drug, and polymer at the bifurcation site.

There are no specific guidelines established in choosing a one-stent versus a two-stent technique for a bifurcation lesion. The decision is highly dependent on its anatomic configuration and operator preference and expertise. The operator must make a judgment based on the importance of the side branch (i.e., amount of myocardium at risk), the risk of side-branch closure, and the risk of two-stent PCI. In addition to disease burden in the ostium of the side branch, angulation of the side branch is another important factor since steep angulation makes access to the side branch more difficult after main-branch PCI and is associated with higher procedural complications.

The general consensus is that for bifurcation lesions without high risk features, the default approach of one-stent PCI with provisional angioplasty + stent is appropriate. Hemodynamic assessment of the jailed side branch can also be considered because angiographic severity may not always correlate with physiologic significance, especially for ostial lesions. For bifurcation lesions with high-risk features as described above, two-stent techniques may be safer due to protection and treatment of the side-branch vessel.

General Approach to Bifurcation Lesions

Guide Catheter Selection

A 7F or 8F guiding catheter should be selected if the operator anticipates using two stents. A 6F guiding catheter can accommodate only two monorail balloon catheters, whereas an 8F guiding catheter can accommodate two stent systems as well as other large-diameter PCI devices such as the Rotablator or the Flextome Cutting Balloon. The maximum Rotablator burr that can be used with a 6F guiding catheter is 1.5 mm. It may be prudent to "upsize" guiding catheters when approaching any bifurcation lesion so that all options remain available if trouble occurs during the procedure.

Guidewire Technique

To protect the side branch, two guidewires are placed, one in the side branch and one in the main vessel. The order of inflation is relatively unimportant. Wire markers or using two different wire types is helpful to reduce confusion during balloon inflations and wire repositioning. When using a two-guidewire system, the guidewires may become entangled after multiple wire manipulations. Efforts should be made to avoid guidewire entanglement, which will prevent advancement of the balloon and may result in failure to recross the stenosis.

Balloon Catheter Selection and Inflation Strategies

Standard balloon catheters can be used, but different balloon sizes may be required for each branch (Table 8-1). Sequential balloon inflations or simultaneous "kissing" balloon inflations can be performed with elimination of plaque shifting being the advantage of the latter. It is important to make sure that the main vessel can accommodate both balloon diameters when performing kissing balloon inflations (proximal vessel should be at least two thirds of the combined balloon diameters). After stent placement in the main branch and the side branch, simultaneous kissing balloon inflations are critical to restore the circular and fully expanded stent to each lumen. Failure to perform final kissing balloon inflation will likely lead to restenosis.

Table 8-1

Approach to Bifurcation Stenosis

Approach	Advantages	Disadvantages
Guide Catheter Selection		
Two-guide catheters Large variety of catheters	Separated devices	Two artery punctures Two-catheter manipulation Long procedure time
One-guide catheter	One arterial puncture Fewer catheter manipulations, low risk of ostial trauma Reduced procedure time	
Balloons and Guidewires		
Two wires, one balloon catheter	Maintains access, upsizing, Permits exchanges Less obstruction to protected side-branch coronary flow than deflated balloon-on-a-wire Less expensive Good vessel opacification	
Two balloon-on-a-wire catheters	Immediate dilatation capability during acute closure	Expensive Must use guidewires for exchanges
One over-the-wire balloon, one on-a-wire catheter	Allows immediate dilatation of side branch Reduces procedure time	Expensive balloon Limited fixed-wire exchanges
Bifurcation Balloon Inflation Strategies		
1. Sequential balloon	Uses same balloon for both vessels	More catheter manipulations
2. Simultaneous balloons	Minimizes atheroma shifting to opposite branch Allows dilatation without oversizing the balloon relative to small post-bifurcation vessel diameter	More balloons and inflation devices

Sequential Branch Inflations

Dilate the main vessel first, the side branch second, and finish dilation in the main branch. A sequential main-side-main branch inflation strategy provides a safe and straightforward approach. However, shifting of atherosclerotic plaque during sequential inflations may result in suboptimal main vessel dilation, requiring repeated dilatations. An unprotected major vessel dissection will require reinstrumentation and jeopardize further attempts to open the side branch. Serial inflations, first in one branch then in the other, as opposed to simultaneous balloon inflations in both branches, may limit the need for extra maneuvers.

Bifurcation Stenting

If the decision is to stent both branches, several techniques can be used depending on the size of the proximal segment and the angle of the side-branch origin. Operator expertise and preference also are factors when choosing a two-stent technique. Although there are more than eight different bifurcation stent techniques (Fig. 8-4), this section will address the most commonly used methods.

Simultaneous kissing stents or "V" stenting can be used when the proximal main vessel is sufficiently large enough to accommodate

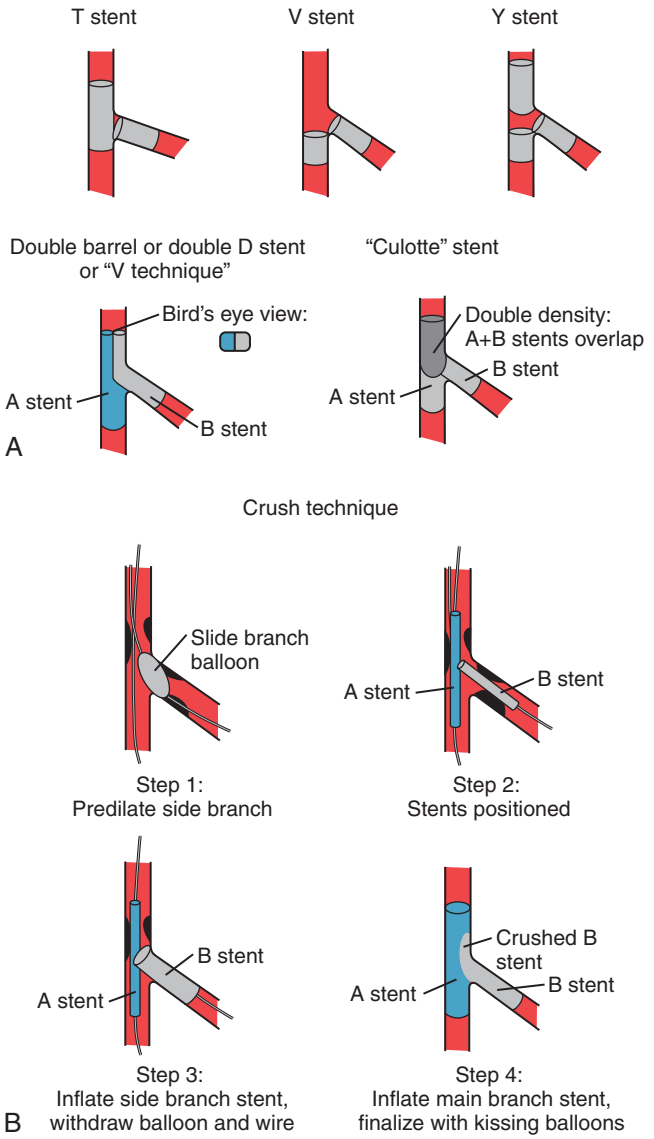


Figure 8-4 **A,** Types of bifurcation stent techniques. **B,** Crush bifurcation stent technique. (Adapted from Lunsford C. Advanced stenting strategies for complex coronary artery bifurcation lesions. *Cath Lab Digest*, June 2006.)

two stents; its size should be approximately two thirds of the aggregate diameter of the two stents. Both vessels are wired and sequential or kissing balloon predilations are performed. Two stent systems are advanced together and positioned in each vessel with the proximal portions of each stent parallel to one another. Both stents are deployed simultaneously, initially to a low pressure (6–8 atm). Both stent delivery balloons are deflated, and each balloon is then inflated sequentially to a high pressure (14–16 atm). Final kissing balloon inflations are again performed at low pressure to complete the procedure. The major advantages of the kissing stent technique is its simplicity and continuous access to both vessels (i.e., unlike the other two stent techniques, no rewiring is required). The major drawbacks with this technique are edge dissection and the theoretical risk of stent thrombosis from stent strut exposure at the "new" carina.

"T" stenting is used when the angle of origin approaches 90 degrees and the side branch is smaller than the main vessel. Both vessels are

wired and sequential or kissing balloon predilations are performed. The side-branch wire is removed, and the main branch is stented. The side-branch wire is then repositioned; the operator must ensure that it has gone through and not under a stent strut. A balloon is advanced to the ostium of the side branch, and the stent cell is dilated. Next, a second stent is advanced past the ostium of the side branch. A stent pullback technique can be helpful to ensure proper positioning (Fig. 8-4A). A balloon is advanced into the main branch and inflated to low pressure. The side-branch stent is then pulled back to the side-branch ostium with the main-branch balloon in place, preventing excessive side-branch stent malapposition. The side branch is then deployed. Final kissing balloon inflations are performed to complete the procedure. This technique has become the most common with the adoption of provisional side-branch PCI being the default approach. The main disadvantage of this technique is the loss of direct side-branch access after main-branch stenting. Additionally, if the side-branch stent is not positioned properly, there may be inadequate stent coverage of the side-branch ostium.

When the angle of origin is less than 70 degrees, crush and culotte techniques can be considered. Both techniques provide excellent coverage, but they can be challenging even for experienced interventionalists. For the crush technique (Fig. 8-4B), both vessels are wired and predilated. Two stents are then advanced and positioned into each vessel of the bifurcation with the proximal end of the side-branch stent in the main vessel and being covered by the main-branch stent. The side-branch stent is deployed first. The balloon is deflated, and both balloon and guidewire are removed. The main-branch stent is then deployed, crushing the proximal segment of the side-branch stent to the main-branch vessel wall. The side branch then needs to be rewired and balloon dilated, which is the challenging part of this technique since there are now three stent layers at the side-branch ostium. Final kissing balloon inflation is then performed to complete the procedure. Figure 8-5 shows an example of treatment of a distal right coronary artery (RCA) bifurcation with the crush technique.

A recent randomized trial comparing crush versus culotte techniques utilizing sirolimus-eluting stents demonstrated that culotte stenting was associated with a significant reduction in in-stent restenosis. For this reason, culotte stenting (Figure 8-6A) may become the preferred bifurcation technique. With this technique, each branch is predilated, and the operator stents the less angulated or most diseased vessel first. Next, the other branch is rewired and balloon dilated through the stent struts. A second stent is advanced into the second branch with the proximal end of the stent within the proximal part of the first stent. The second stent is deployed after the guidewire of the first vessel is removed. The first vessel guidewire is then rewired through stent struts, and final kissing balloon inflation is performed to complete the procedure. The major drawback to this technique is the operational expertise required to perform the multiple rewiring of vessels. Figures 8-5 and 8-6 show examples of crush and culotte stenting.

Physiologic Guidance for Bifurcation or Jailed Side-Branch Stenting

The treatment of bifurcation lesions is complex and includes multiple decision points during the procedure that have significant practical implications. Angiography, unfortunately, remains a poor tool to guide decision making in lesions involving the ostia of a vessel or the ostium of a "jailed" side branch. Intravascular ultrasound (IVUS) plays a significant role in helping the operator in the treatment of bifurcation disease, but fractional flow reserve (FFR) provides real-time ability to determine ischemic significance of these lesions. More importantly, an FFR guided strategy can be performed easily in bifurcation lesions and provide good clinical results.

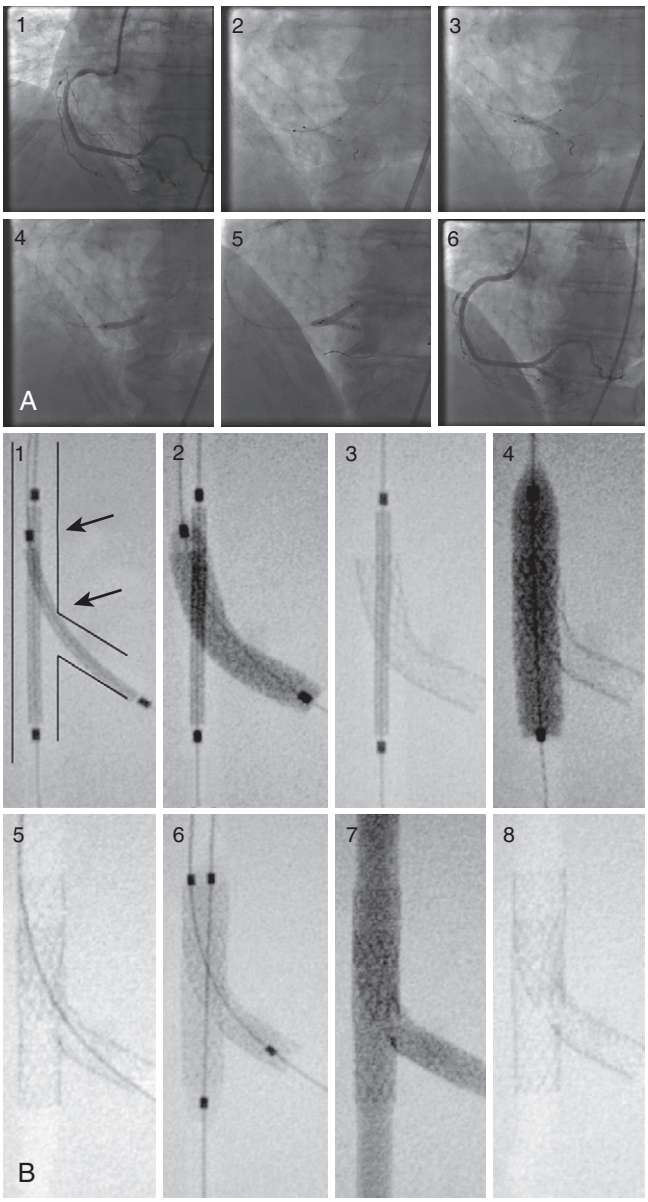
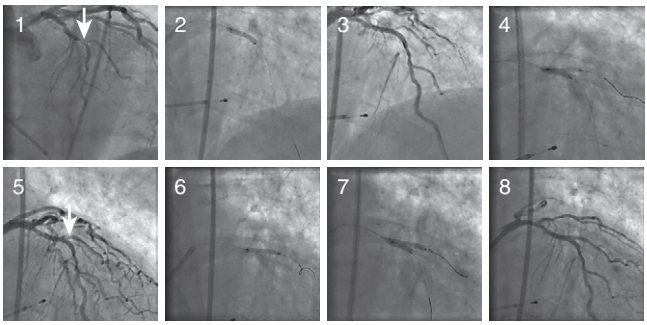


Figure 8-5 **A,** Crush stenting for RCA/PDA bifurcation. (*1*) Angiography demonstrated severe bifurcation stenosis of the ostial PDA and the AV segment of the distal RCA. (*2*) After balloon pre-dilatation, two stents were simultaneously positioned at the bifurcation. The proximal segment of the PDA stent was covered by the RCA stent. (*3*) The PDA stent was deployed first. (*4*) The PDA wire was removed and the RCA stent was then deployed, crushing the proximal portion of the PDA stent onto the caudal aspect of the RCA arterial wall. (*5*) The PDA was then re-wired and final kissing balloon dilatations were performed. (*6*) The mid and ostial RCA lesions were also treated and final angiography showed an excellent angiographic result with no residual stenosis and TIMI III flow. (Courtesy of Igor F. Palacios, MD and William M. Suh, MD, Massachusetts General Hospital, Boston, MA.). **B,** In vitro model of crush technique illustrating the changes in the stents during the procedure. (*1*) Two stents placed across the bifurcation model, (*2*) Side branch stent inflated, (*3*) Image after removal of side branch stent balloon, (*4*) Main branch stent inflated, (*5*) Image showing guidewire crossing into the stented side branch in preparation for kissing balloon inflations, (*6*) Two balloons position in main and side branches, (*7*) Two balloons inflated in kissing technique, (*8*) Final result. *AV,* arteriovenous; *PDA,* posterior descending artery; *RCA,* right coronary artery.



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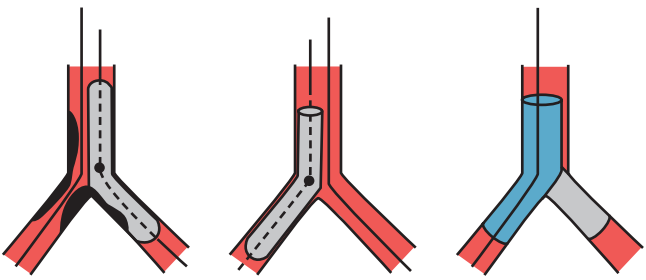
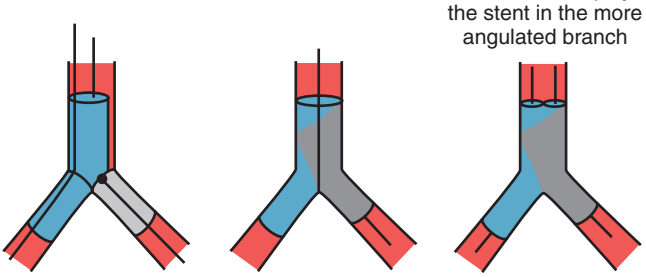


Step 1: Both branches are wired and dilated

Step 2: Remove wire from the straighter branch and deploy the stent in the more angulated branch



Step 3: Advance wire in the branch via stent struts and dilate

Step 4: Position the second stent toward the unstented second branch and expand the stent leaving proximal overlap

Step 5: Recross the first stent with the wire and perform final kissing balloon inflation

B

Figure 8-6 **A,** Bifurcation PCI with culotte technique for acute anterior infarction. (*1*) There is critical stenosis in the mid LAD (*arrow*) also involving the diagonal artery. (*2*) Main vessel stenting was performed. (*3*) The diagonal artery ostium is jailed and has an 80% ostial narrowing. (*4*) Kissing balloon PTCA was performed. (*5*) After PTCA, angiography revealed proximal diagonal artery dissection (*arrow*). (*6*) The diagonal artery was stented to cover the dissection. For culotte stenting, the proximal portion of the diagonal stent overlaps with the proximal portion of the LAD stent. The LAD wire is removed prior to stent deployment. (*7*) The LAD is rewired and final kissing balloon inflations are performed. (*8*) Angiography demonstrates an excellent angiographic result with no residual stenosis and TIMI III flow. (Courtesy of Ignacio Inglessis, MD and William M. Suh, MD, Massachusetts General Hospital, Boston, MA.). **B,** Diagram of technique of culotte stenting. (From Sharma et al., 2004). *LAD,* left anterior descending; *PCI,* percutaneous coronary intervention; *PTCA,* percutaneous transluminal coronary angioplasty; *TIMI,* thrombolysis in myocardial infarction.

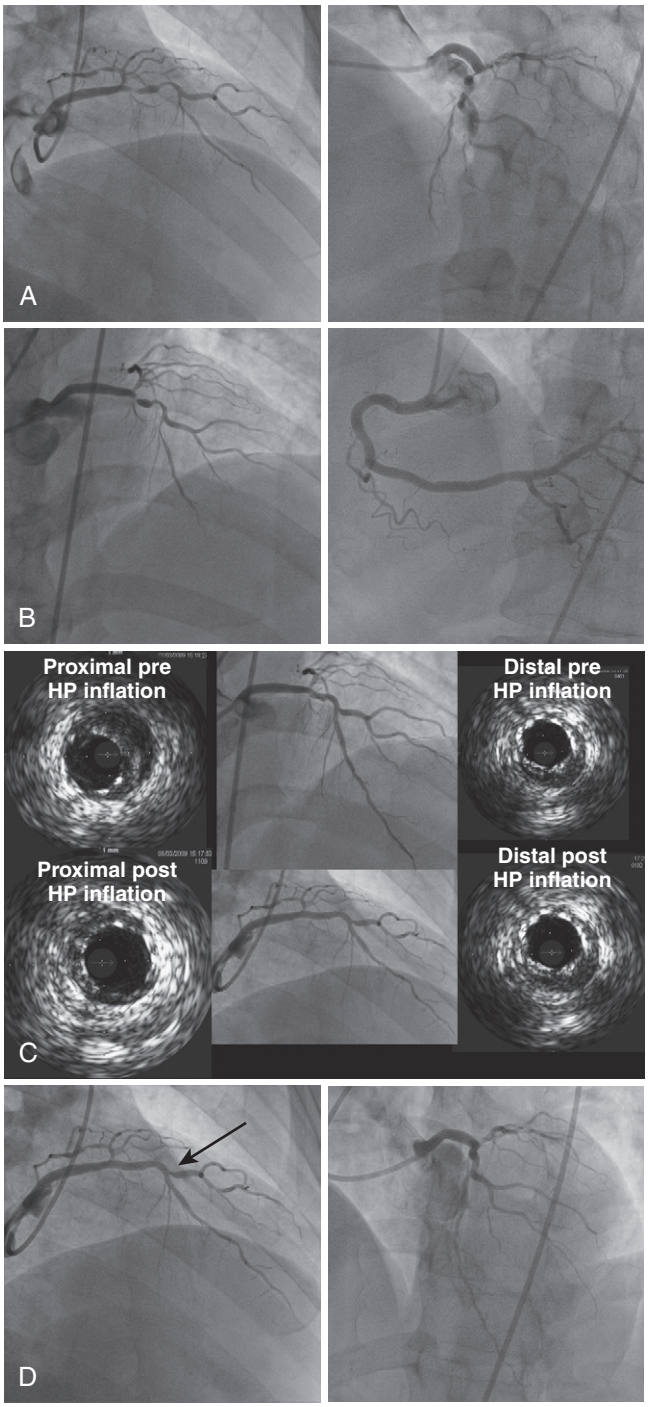


Figure 8-7 **A,** Cine frames in 58-year-old patient with chest pain, abnormal ECG, and severe LAD lesion with large diagonal branch that has no ostial disease. Left panel is RAO cranial and right side is LAD cranial angulations. **B,** Left side is AP cranial angulation. Right side is RCA, which shows no significant narrowings. **C,** IVUS and angiograms of proximal and distal stent segments before and after high-pressure (HP) balloon inflation. Note new narrowing of side branch across newly stented segment. **D,** Final angiograms show similar final result with FFR (arrow) of 0.86 (non-ischemic value), permitting operator to stop the procedure without further intervention. *AP,* anteroposterior; *ECG,* electrocardiogram; *FFR,* fractional flow reserve; *IVUS,* intravascular ultrasound; *LAD,* left anterior descending; *RAO,* right anterior oblique; *RCA,* right coronary artery.

Table 8-2

Key Points for Bifurcation PCI

- Think KISS (Keep It Simple Stupid) when approaching bifurcation lesions. Default approach is one-stent technique ± provisional angioplasty/stent to side branch. Use two-stent technique if side branch is significant and has high-risk features for closure.
- Wire both main branch and side branch if side-branch loss is important.
- Consider treating side branch first (i.e., balloon dilatation, rotational atherectomy, or cutting balloon).
- Dilate and stent main branch; reassess side branch (can use FFR to determine hemodynamic significance).
- Provisional PTCA + stent side branch. If stenting side branch, stent with pullback technique.
- Choice of two-stent technique depends on size of proximal vessel, an assessment of the importance and risk of side-branch closure, and operator expertise and preference.
- Use two wires if side branch loss is important.
- Dilate smaller branch first or use Rotablator or cutting balloon.
- Dilate and stent main branch; reassess side branch.
- Redilate side branch.
- Stent side branch through main stent only when absolutely necessary; use FFR to assess physiologic significance of side branch.
- If a two-stent technique is used, final kissing balloon inflation is necessary to optimize outcomes.

FFR, fractional flow reserve; *PTCA,* percutaneous transluminal coronary angioplasty.

FFR provides operators with an ability to determine the physiologic significance of any coronary stenosis and, especially for bifurcations, is an easily incorporated method to gather more objective information. FFR is a factor in making a correct and supported decision before embarking on a more, and possibly unnecessary, complex intervention. Performing FFR of ostial side-branch lesions that appear to be <70% from angiography can prove that most of these lesions are not physiologically significant. Assessing angiographic abnormalities in side branches that are "jailed" by main vessel stents has been proven to be a useful strategy to determine the physiologic significance of these abnormalities. By using FFR, the "jailed" side branches with an FFR >0.75 have a very low clinical event rate without further balloon or stent therapy to the side branch. Figure 8-7 shows an example of FFR in patient with side-branch jailing.

Table 8-2 summarizes key points for bifurcation PCI.

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9

Difficult Subsets for Percutaneous Coronary Interventions: Calcific Vessels, Coronary Bypass Conduits, Elderly Patients, and Cardiac Transplantation

NAUMAN SIDDIQI · WILLIAM H. SUH · BARRY F. URETSKY · AHMAD EDRIS · MOHAMMAD MARASHDEH · TODD K. ZYNDA · MORTON J. KERN

Specific anatomic subsets require preparation and a game plan to deal with the potential problems resulting in a suboptimal result or failed procedure. A complication, even during the most straightforward procedure, should always be anticipated. The key to overcoming difficult percutaneous coronary intervention (PCI) is planning and anticipation of problems. No operator should begin a procedure without having mentally performed all the necessary steps and having visualized the optimal result.

As the first step, the operator should assess the need for "support" for guide catheter seating. Reviewing the diagnostic images will provide an estimate of the degree of difficulty in both seating and stabilizing the guide catheter. Guide catheter diameter selection is also important as certain cases, for example, bifurcation stenting, require a larger guide, typically 7 F or 8 F. Appreciation of the tortuosity, calcification, and angulation of the target lesion origin will also contribute to the shape and diameter of the guide catheter.

Second, a working knowledge of multiple guidewires and their capabilities in different circumstances is an important prerequisite in performing a smooth procedure. It is not unusual to use multiple PCI guidewires in a trial-and-error fashion before achieving the final result. However, a clear guidewire plan should be developed before starting the procedure. Difficulties in guidewire, balloon, and stent advancement may dictate the use of a second or "buddy" wire of some stiffness, or the use of a deep-seated guide position, to accomplish the task.

Finally, concern about the patient's tolerance for ischemia and hemodynamic stability must be included in planning. The operator may opt for an additional arterial and/or venous access for possible intra-aortic balloon pumping or left ventricular assist support (e.g., Impella catheter) or temporary pacemaker placement.

This chapter will review common approaches to several difficult PCI situations. Because many cases of difficult PCI also involve situations of high or extreme risk, further discussion of these patients is provided in more detail in the following chapters. Chronic total occlusion PCI, ostial, and unprotected left main stenting are addressed in subsequent chapters.

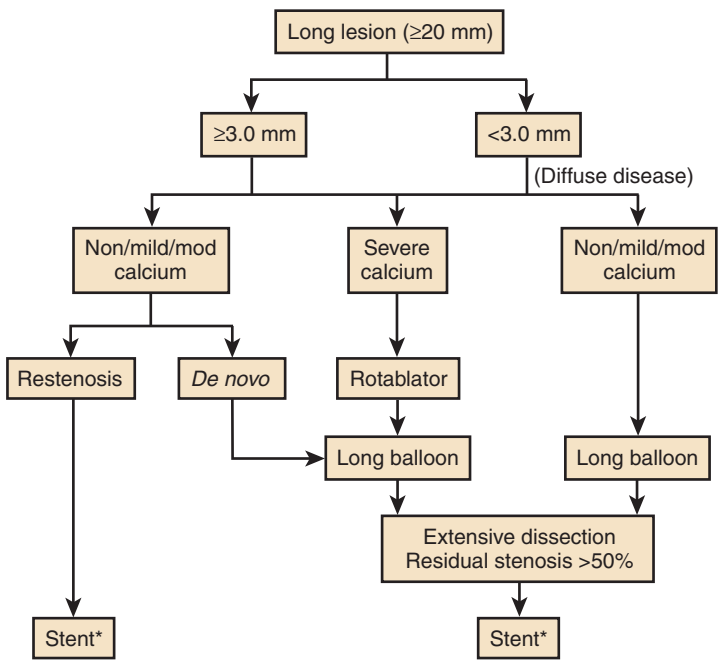
Severely Calcified Stenoses

Balloon angioplasty of heavily calcified stenoses stretches the noncalcified vessel wall, promoting dissection (or [rarely] rupture) originating at the border region of the calcified and elastic regions of the stenosis. Severe calcification is associated with reduced primary success rates and increased complications. Because PCI of calcified lesions often requires high-pressure inflations (>15 atm), noncompliant balloon catheters are preferred. However, heavily calcified lesions may puncture polyethylene terephthalate balloon material. Removal of a ruptured and entrapped balloon can be difficult. In calcific lesions, direct stenting without balloon dilation is not recommended since it may result in incomplete stent deployment and a potentially ruptured and entrapped balloon catheter.

Rotational atherectomy (Rotablator, see Chapter 6) may be used primarily in this type of lesion, particularly in view of the increased complications and dissection rates from balloon angioplasty. The value of the Flextome Cutting Balloon (Boston Scientific Corporation, Natick, MA) or the AngioSculpt Balloon (Vascular Solutions, Minneapolis, MN) is less certain in this setting.

Long and Diffuse Lesions

PCI of long, diffuse lesions with or without calcification can be managed by long balloon catheters, rotational atherectomy, and stents. After rotablation, balloon lengths of 30 mm and 40 mm followed by similar lengths of stent can cover long diseased segments, reducing the risk of dissection. A graduated dilation approach can be used by introducing progressively larger inflation balloons. If the lesion is heavily calcified, Rotablator should be used first. An algorithm for approaching long lesions is shown in Figure 9-1. Key points for calcified lesions are shown in Table 9-1.



*One long stent preferred

Figure 9-1 Potential approach to the treatment of long lesions and diffuse disease. (From Topol EJ. *Textbook of cardiovascular medicine.* Philadelphia: Saunders, 2000: 376.)

Table 9-1

Key Points for Highly Calcified Lesions
• Use Rotablator first; be conservative with burr sizing. • Predilate before stenting. • Use firm backup support. • Use high pressure to implant stent. • Consider intravascular ultrasound to ensure full stent expansion.

Coronary Artery Bypass Conduits

Some 15% to 20% of all patients entering the catheterization laboratory have undergone previous coronary artery bypass graft surgery and may require further revascularization. For these patients, the objective of PCI is to provide symptom relief through reestablishing perfusion to ischemic zones instead of a second or third bypass operation. Repeat coronary artery bypass graft operations have increased operative mortality rates (2%–8%), postoperative myocardial infarction (MI) rates (2%–8%), and postoperative bleeding rates (1.3%–11%).

PCI for saphenous vein graft (SVG) stenosis has a success rate of more than 85%, and rates for complications of less than 10%, urgent bypass surgery 4%, MI 3%, and mortality 1% to 3%. The risks and benefits of SVG PCI must be weighed against those of repeat coronary artery bypass graft surgery.

Compared to native arteries, PCI for SVG stenosis has an increased risk of complications and lower long-term success rates, particularly if the vein graft has a degenerated appearance (usually an irregular surface or ulcerations on angiography), or if the graft is older than 3 years.

Several technical aspects of SVG PCI also contribute to lower success rates. Because the aorto-ostial anastomosis may be upward, flush, or downgoing without aortic cusp support, guide catheter support can be compromised. Also, the saphenous veins may be too large for coronary stents (i.e., >4.5 mm diameter). No adjunctive pharmacotherapy has ever been demonstrated to reduce ischemia during SVG PCI.

An especially critical consideration is the protection from distal embolization during SVG angioplasty (also see Chapter 6, Non-balloon PCI devices). Distal protection devices that limit the effects of embolization have resulted in a 50% reduction in periprocedural complications. The limitations of the currently available distal protection devices are discussed in Chapter 6. Despite a satisfactory angiographic appearance, PCI associated with myocardial no-reflow may produce myocardial ischemia or infarction, a problem in 5% to 10% of procedures. For SVG PCI, direct stenting and minimal poststent manipulation may be preferable. Figure 9-2 shows an example of SVG PCI.

The major factor associated with successful SVG PCI is graft age. Grafts more than 3 years old are associated with lower success rates than grafts less than 1 year old. SVGs less than 1 year old are often narrowed more by thrombus than by plaque. Grafts more than 3 years old degenerate because of atherosclerotic material and are more prone to emboli than grafts under 1 year.

Stenting is the preferred approach for SVG lesions because of excellent early success rates and lower rates of restenosis, subacute closure, embolization, MI, and death. Restenosis rates after SVG stenting are approximately 25% to 30% at 1 year. The value of drug-eluting stents (DESs) compared to bare-metal stents (BMSs) is still not fully determined. A scheme for approaching SVG PCI is shown in Figure 9-3. Specific angiographic locations are associated with different outcomes.

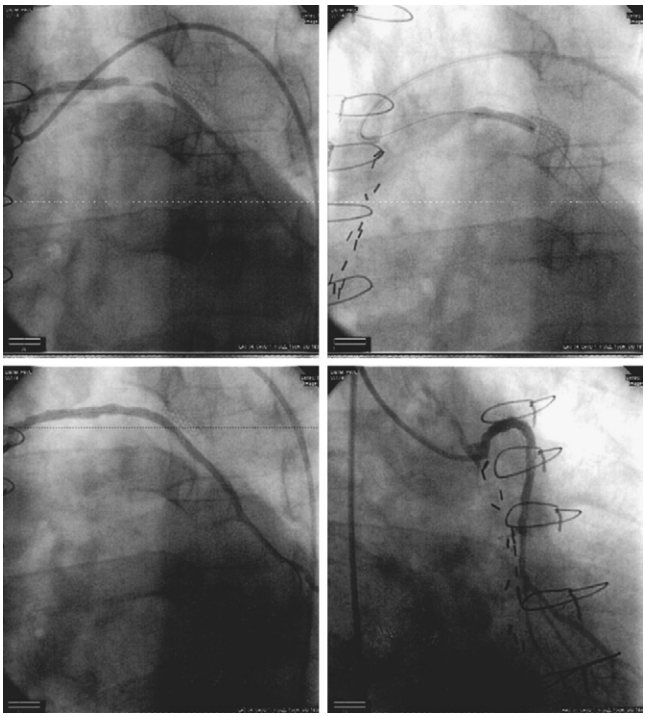


Figure 9-2 PCI of SVG lesion in mid-body (*top left*). Balloon/stent in lesion (*top right*). Post PCI RAO view (*bottom left*) and LAO (*bottom right*). *LAO,* left anterior oblique; *PCI,* percutaneous coronary intervention; *RAO,* right anterior oblique; *SVG,* saphenous vein graft.

- Aorto-ostial lesions have lower success and higher restenosis rates than mid-body stenoses. (Fig. 9-4)
- Mid-body locations have lower complications and lower restenosis rates relative to aorto-ostial locations. (Fig. 9-5)
- Distal SVG–native vessel anastomosis sites have results similar to native vessels. The morphology of the stenosis carries the same implications in SVGs as for those in native vessels, with an increased propensity for thrombogenic complications.

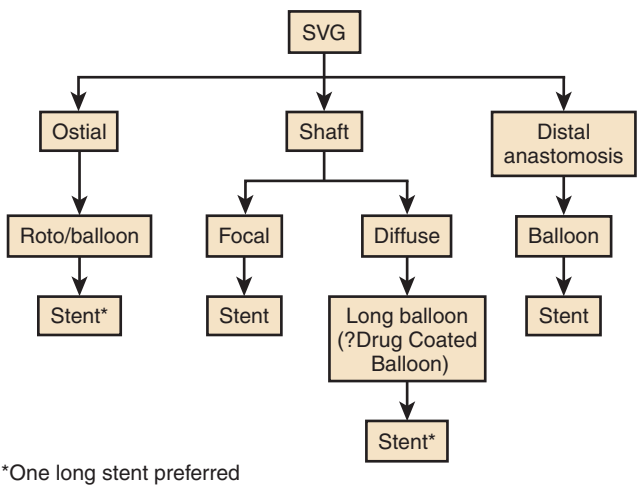


Figure 9-3 Scheme for approach SVG PCI. *PCI,* percutaneous coronary intervention; *SVG,* saphenous vein graft.

SVG (1984) ostial lesion
90% → 10% (3.5 mm balloon + 0.018 in. flowire)

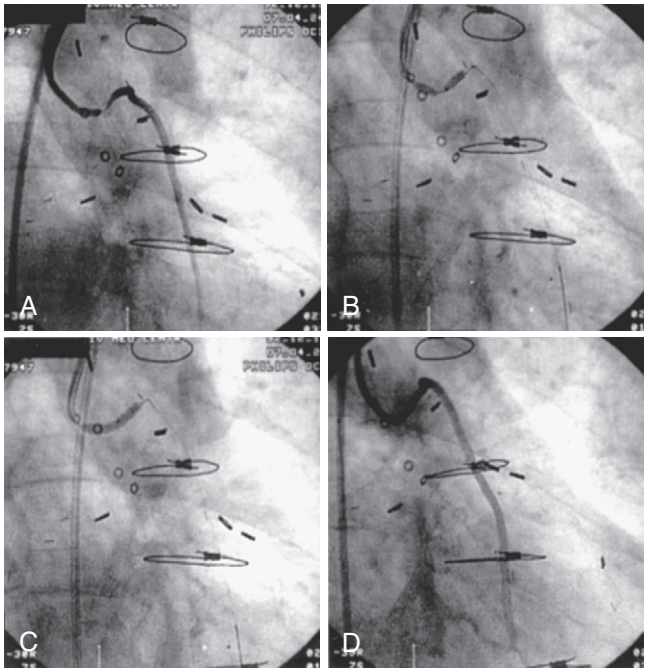


Figure 9-4 Aorto-ostial percutaneous coronary intervention (PCI). **A,** ostial SVG lesion; **B,** placement of ostial balloon partly in aorta, **C,** placement of stent to cover ostium; **D,** final result.

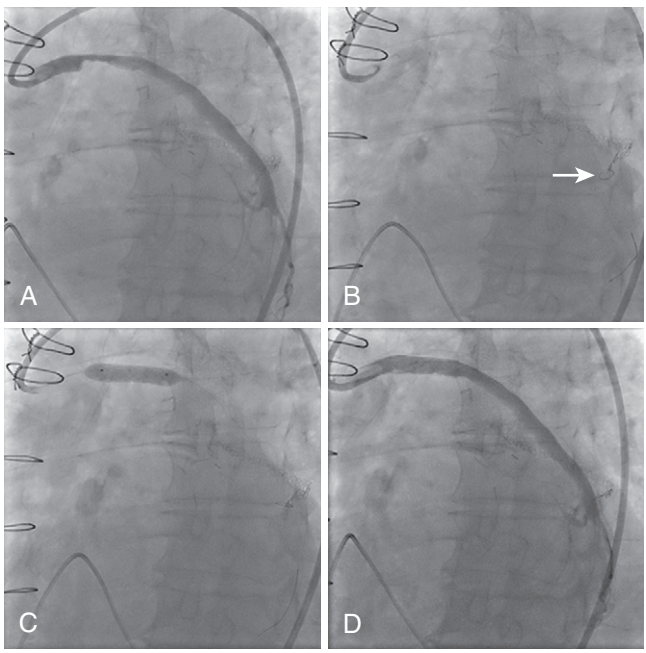


Figure 9-5 Mid-body locations for SVG PCI. **A,** Initial angiogram; **B,** wire position; **C,** Stent inflation; **D,** final result. *PCI,* percutaneous coronary intervention; *SVG,* saphenous vein graft.

Total Chronic Occlusion of Saphenous Vein Grafts

PCI in an occluded SVG represents a highly complex, high-risk procedure and requires a specialized approach. Bypass surgery should be strongly considered before selecting PCI for total coronary occlusion of SVG. The recanalization of chronically (>3 months) occluded SVGs should not be considered unless there is an antegrade channel. For recent (<3 months) SVG occlusions presumed to be thrombotic, thrombectomy catheters or thrombus aspiration systems (AngioJet) have been used successfully. Key points for SVG PCI are shown in Table 9-2. Chronic total occlusion PCI of SVG is addressed in detail in Chapter 10.

Internal Mammary Artery PCI

Internal mammary artery (IMA) PCI presents another difficult technical challenge. IMA stenosis commonly is located at the ostial or distal anastomotic site. Technical challenges include IMA guide intubation and stent delivery of stents to the anastomosis. Because of the extra length of vessel to access anastomotic lesions, a shorter guide, that is, 90 cm rather than the usual 100 cm, may be helpful. A left radial approach may improve guide catheter intubation and stability in individual cases. Vasospasm of the IMA during passage of the device can be managed with generous doses of intra-arterial nitroglycerin. Careful catheter manipulation is important to prevent ostial dissection.

PCI in the Elderly

PCI in elderly patients has been associated with superior clinical outcomes compared to thrombolysis in the acute MI setting. A significant benefit with routine stent implantation has been shown in patients greater than 75 years of age, including reduced rates of stent thrombosis (1 month) and subacute thrombosis (1 year) as the risk of PCI is increased in elderly as compared with younger patients. This is due at least in part to elderly patients having more frequent significant comorbidities (e.g., stroke, hypertension, peripheral arterial disease, congestive heart failure, hyperlipidemia, and chronic kidney disease) and more extensive coronary artery disease, smaller coronary vessels, heavy arterial calcification, diffuse disease, tortuosity, and impaired endothelial dysfunction.

Mortality for PCI in the elderly is higher and heavily influenced by comorbidities, acuity of presentation, presence or absence of shock, congestive heart failure, or MI. Shock is the strongest predictor of an adverse outcome in octogenarians, with in-hospital mortality as high as 43%. Mortality at 1 year post-PCI in patients 75 years or older in a large study was noted to be 11.1%, and complications (bleeding, stroke, and vascular complications) were also significantly increased. Each

Table 9-2

Key Points for Saphenous Vein Graft Percutaneous Coronary Intervention
• Consider all material in graft as embolic debris.
• Consider intra-graft pretreatment installation of an arteriolar vasodilator such as adenosine, verapamil, nitroprusside, or nicardipine to prevent no-reflow phenomenon.
• Use embolic protection device.
• Consider thrombectomy for high probability thrombus.
• Use minimal touch techniques to limit balloon inflations.

elderly patient must be evaluated and treated individually; however, a nomogram based on 7472 octogenarians may help predict outcomes in this population. Age, systolic function ejection, acuity of MI, chronic obstructive pulmonary disease, and pulmonary vascular disease are potential additive predictors of death, while the only protective factor was prior history of PCI.

Strategies for managing complications should be carefully discussed beforehand with patient, family, and operator because some emergency procedures may not be feasible (e.g., intra-aortic balloon pumping, left ventricular assist devices) or may carry a particularly high risk (e.g., left main stenting). Myocardial perfusion and hemodynamics should be optimized before beginning the procedure. Adequate hydration and limiting the amount of contrast medium are also important. Anticoagulation regimens should be individualized. After the procedure, extra precautions need to be taken during sheath removal and hemostasis to reduce risk of vascular complications.

PCI in Cardiac Transplant Recipients

Coronary artery disease commonly occurs in cardiac transplant patients and, when present, is typically a diffuse process described as cardiac allograft vasculopathy (CAV). CAV is the leading cause of mortality after the first year following transplantation and is a significant cause of morbidity and mortality in cardiac transplant recipients. CAV is characterized by endothelial dysfunction, vascular remodeling, and intimal hyperplasia with concentric intimal thickening. PCI using balloon angioplasty, BMS, and DES have been used in this patient group; the acute results appear similar to nontransplant patients. PCI has not yet shown a significant mortality benefit over medical management in the treatment of CAV; however, PCI is a commonly utilized palliative treatment for physiologically significant coronary stenoses.

Compared with BMSs, DESs have been associated with a lower incidence of in-stent restenosis (ISR) and target lesion revascularization. Despite the reduction of ISR with DES implantation, long-term mortality remains similar after PCI regardless of the type of stent used; this is likely due to the extensive and diffuse nature of CAV.

Suggested Readings

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10

Percutaneous Coronary Interventions of Chronic Total Occlusions

BARRY F. URETSKY · MOHAMMAD MARASHDEH

Percutaneous coronary intervention (PCI) of a chronic total occlusion (CTO), defined as a total occlusion (with TIMI grade 0 flow) of > 3 months duration, is one of the most technically challenging coronary subsets. Some lesions have minimal antegrade flow. These lesions, often called CTOs or functional CTOs, are not truly totally occluded and, by virtue of the small antegrade channel, have an increased probability of being recanalized antegradely. CTO composition is a function of age, with the older CTO typically being harder and more fibro-calcific. The rationale behind PCI of a CTO is to decrease ischemia and cardiac morbidity, improve left ventricular function and wall motion, avoid coronary artery bypass graft (CABG) surgery, improve quality of life, and possibly prolong survival.

PCI success rates for true CTOs are reported to be in the 50% to 80% range (compared to >80%–90% for occlusions <3 month-old CTO). Newer series with techniques described in this chapter describe success rates approaching 90% or higher. CTO PCI mortality rate is reported to be 0% to 2% and emergency coronary artery bypass surgery <1% to 2%. Abrupt vessel closure following CTO PCI may occur in up to 5% to 10% of patients but is often clinically silent, depending on the collateral supply.

PCI Strategy

Prior to intervention, a formal strategy ("game plan") should be devised (Fig. 10-1). By developing a game plan, overextending an already difficult procedure and increasing the risk of complications may be minimized. This plan must start with a decision as to whether the CTO is producing symptoms and/or ischemia, and if so, whether revascularization is actually required (as opposed to medical therapy). If revascularization is chosen, it must be decided whether the patient would be better served with CABG or PCI, as CTOs typically occur in patients with multivessel disease. If PCI is chosen, the next decision is whether the complexity is within the operator's technical expertise or should be referred to a CTO super-specialist.

The preprocedure plan must include the proposed limits of the attempt if success is not achieved, including the upper limits for contrast media, radiation exposure, and time on the cath table. The extent of the procedure may be influenced by the CTO characteristics, such as whether the lesion has favorable or unfavorable characteristics. Further, the plan should include a decision regarding the possibility of bringing the patient back for a second attempt and whether such an attempt would utilize a similar or a revised strategy, for example, a retrograde approach.

Favorable characteristics for the antegrade approach are shown in Figure 10-2 and listed in Table 10-1. Any combination of unfavorable characteristics significantly decreases the chance of success.

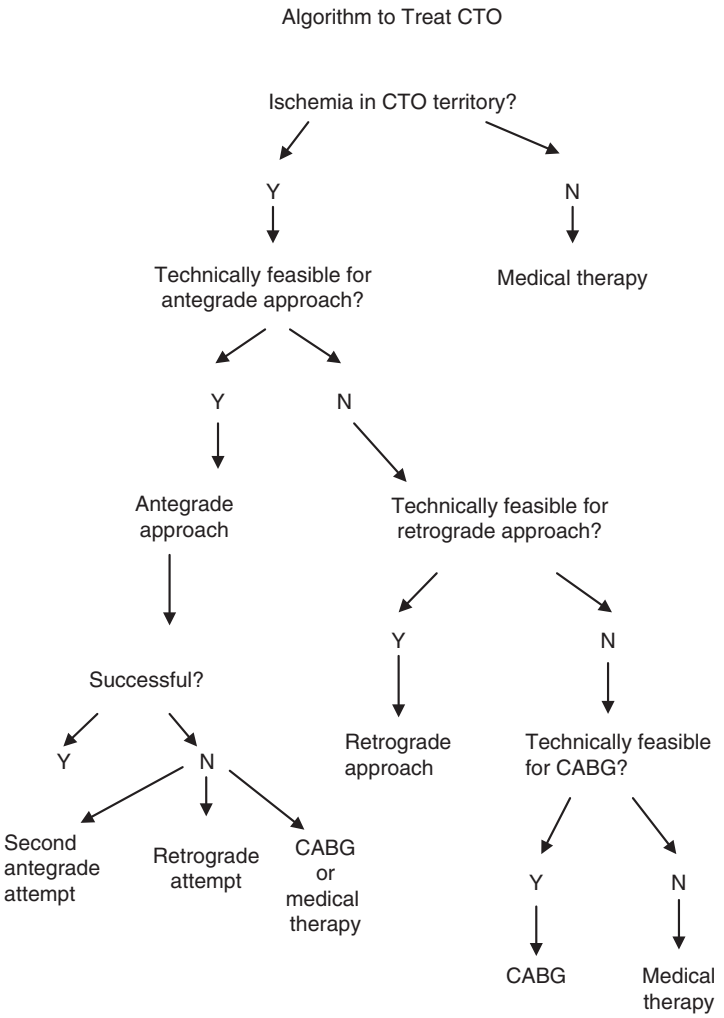


Figure 10-1 The algorithm considers treatment of the CTO only. It should be used as part of decision-making within the wider context of deciding on appropriate therapy considering the patient's clinical syndrome, extent of coronary artery disease, left ventricular function, co-mordities, surgical risk, and other relevant factors to determine the best treatment strategy. If PCI is considered, the above algorithm is applicable.

Stenting a CTO with a drug-eluting stent has been shown to improve acute and long-term results compared to balloon angioplasty and bare metal stenting. In CTOs that cannot be crossed antegradely, the technique of retrograde recanalization has been shown to be effective in some cases and will be discussed briefly.

Technical Considerations for CTO PCI

Angiography

Excellent vessel opacification and knowledge of the occluded segment length and course are important factors for PCI success. Visualization of retrograde collateral filling of the target vessel is often essential. Bilateral coronary angiography is an invaluable aid in many CTO cases (Fig. 10-3). Using the antegrade approach, opacification through the target vessel

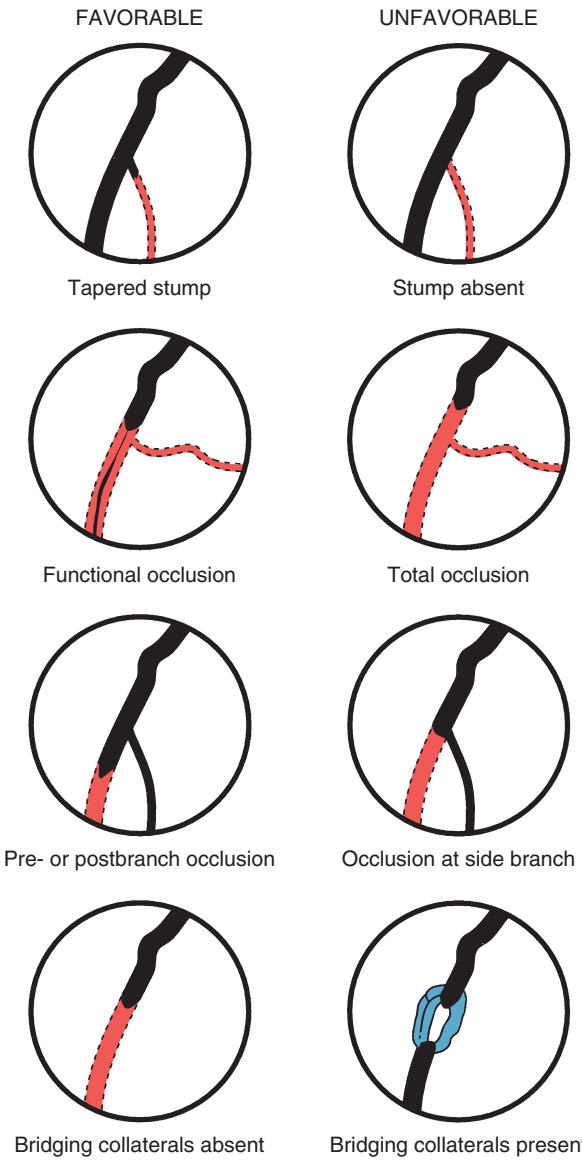


Figure 10-2 Morphology of total coronary occlusion: favorable and unfavorable morphology for procedural success. (Modified from Safian RD, Freed M, Grines C, eds. *The manual of interventional cardiology,* 3rd ed. Birmingham, MI: Physicians' Press, 2001, p. 295.)

Table 10-1

Favorable and Unfavorable Characteristics for Antegrade Success for Chronic Total Occlusions

Favorable
1. Tapered occlusion, especially with a "bird's beak" configuration
2. Short length (<10 mm) occlusion
3. Absence of bridging collaterals
4. Absence of calcification
Unfavorable
1. Flush occlusions, particularly at side branches
2. Long occlusions
3. Presence of bridging collaterals
4. Heavy calcification

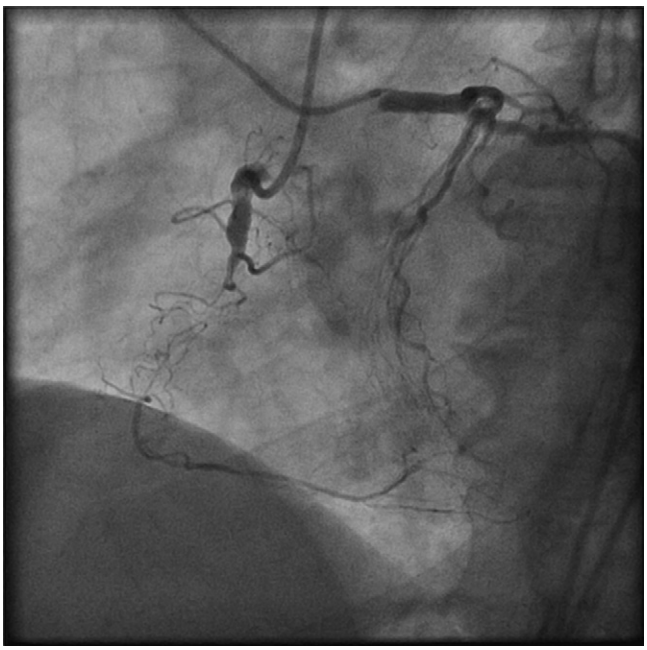


Figure 10-3 Bilateral angiography shows the length and presumed course of the chronic total occlusion (CTO) in the right coronary artery.

may be insufficient to visualize the CTO and the course of the potentially recanalized channel. The contralateral vessel injection may allow for visualization of the vessel segment distal to the CTO. Administration of intravenous nitroglycerin may further improve visualization.

Antegrade Approach

Guide and Support Catheters

A guide catheter with good backup is extremely important. The diameter of the guide remains an operator choice. In general, the greater the backup required and the amount of hardware to be introduced into the vessel, the larger should be the catheter diameter. Although standalone guidewire passage across a CTO may be effective, support for wire passage is usually required. Support for guidewire passage can be obtained with end-hole microcatheter, e.g., Corsair (Fig. 10-5B) or small-diameter (1.25–1.5 mm) over-the-wire (OTW) balloon catheter and will increase the chance for wire passage through the total obstruction. Wire passage through a CTO into the true lumen increases the success rate to nearly that of a non-CTO, that is, >90%–95%. Although passage of the wire distally through the true lumen is another major key for success, subintimal wire passage can still be effective.

CTO Guidewires

Wire choice is another key element to treatment success. There is a very large portfolio of available wires. In general, guidewires may be classified as hydrophilic and non-hydrophilic; Table 10-2 lists a few examples of each. Each wire has its own unique combination of flexibility, trackability, torque transmission (or steerability), lubricity (or hydrophilicity), shaft support, wire tip load or strength, wire tip prolapsibility, radiovisibility, ability to shape and retain tip configuration, tip taper and thickness, and tactile feedback. The operator should become familiar with the properties of each wire that might be applied to a lesion so that a wire plan can be developed.

Table 10-2

Examples of Equipment for Recanalization of Chronic Total Occlusion Using the Antegrade Approach

Category	Example	Rationale for Use
Guiding catheter	Left: Amplatz, XB (Cordis), EBU (Medtronic), Voda (BSC) Right: Amplatz	Increased backup support
Guidewires	Hydrophilic wires: Fielder, Fielder XT (Asahi), Pilot 50 (Abbott)	Passage through microchannel
	Increased tip load: Miracle Bros 3-12 (Asahi), Confianza Pro (Asahi)	Passage through "hard" proximal cap
OTW balloon	1.25–1.5 balloon diameter (multiple companies)	Increase wire force to proximal cap Predilation after crossing CTO
Microcatheter	Corsair (Asahi), FineCross (Terumo, Tokyo, Japan)	Provide increased wire force to proximal cap
Tornus		Enlarge lumen when balloon cannot pass lesion
Guide extender	GuideLiner (Vascular Solutions)	Increase backup support in tortuous, calcific, or difficult to CROSS lesions and vessels
Rotational atherectomy	Rotablator (Boston Scientific Corp.)	Enlarge lumen in undilatable lesion

There is no consensus regarding the first choice guidewire; some operators prefer a hydrophilic wire first in all cases, others prefer an individualized approach, and still others a stiff-tipped wire. The hydrophilic wire decreases frictional resistance, improving movement through the vessel. However, this type of wire may have a greater propensity to travel into the subintimal space or, if lodged, distally perforate a small branch. One commonly used strategy is the "wire strength step-up" starting with a wire with minimal tip strength, usually hydrophilic (e.g., Fielder, Pilot 50, or Fielder XT) and working up to moderate stiffness (e.g., Miracle Bros 3.0, 4.5, or 6 g) and if unsuccessful to a very stiff tip (e.g., Miracle Bros 12, Confianza Pro). Other operators individualize choice of the first wire depending on the angiographic characteristics of the CTO and the coronary anatomy.

A CTO may have a microchannel or soft elements that will allow a hydrophilic wire to slide through. On the other hand, and more frequently, the proximal CTO cap will be hard and require penetration with a relatively stiff wire. A combination of both stiff-tipped and hydrophilic wires may be needed to negotiate a long CTO.

Wire Movement Techniques

Three main wire movement techniques have been described: sliding, drilling, and penetrating. Sliding takes advantage of microchannels and soft areas in the lesion using a hydrophilic wire. Drilling is a form of controlled spinning whereby the wire tip is rotated to find the path of least resistance. The operator's tactile sense *may* be helpful in this approach, but careful observation that the wire tip is freely moving is essential. Penetration uses shorter, more precise wire tip movements to penetrate the intraluminal plaque. No technique has obvious advantage over the others in preventing the wire in taking a subintimal course. In many CTO cases, a combination of movements and wires is used.

An important aspect of wire use is shaping the wire tip. It should be shaped to maneuver the expected vessel course and, at the same time, minimize the number and severity of wire bends to maximize transmitted force. A typical bend might be a 45-degree angle at the last 0.5 to

1 mm of the wire and a gentler secondary bend of 15 degrees 2 to 3 mm behind the distal bend. Each lesion requires individual evaluation in this respect.

When crossing CTOs, one should be sure that the guidewire is in the true lumen vessel rather than in the subintimal space. One technique to ensure proper position is to advance a small tracking or OTW balloon catheter, remove the wire, and inject contrast distally to verify the lumen. Injection should be weighed against the possibility of increasing the size of a dissection if the catheter is subintimal. Should the wire track subintimally, there are methods to recanalize the vessel, which will be discussed in subsequent sections.

Treatment After Wire Passage

Usually a balloon catheter can cross a CTO after wire passage. Balloon dilatation can then prepare the vessel for stenting. Occasionally a balloon cannot cross or, even rarer, the balloon crosses but the lesion is undilatable. When a balloon catheter cannot cross a lesion, a particularly useful device is the Tornus (Asahi Intec, Tokyo, JP; Fig. 10-5A), which acts somewhat like a screw to enlarge the channel. If that maneuver is ineffective, or if the amount of calcification is large, consideration of rotational atherectomy should be given if a Rotablator wire can pass through the total occlusion. The operator is sometimes faced with the decision of removing a non-Rotablator wire for a Rotablator wire; this may be necessary but the operator should appreciate that the life line, that is, the previously passed guidewire, has been lost during this interval.

Selected Devices and Techniques to Recanalize the CTO

PCI for CTO treatment is in rapid evolution. It is likely that new CTO techniques will increase the success rate to levels approaching that of non-CTO lesions. A full description is beyond the scope of this section, but a few of the more common devices and techniques are described. The reader is referred to the selected readings listed at the end of this chapter for more comprehensive descriptions of the technical aspects of PCI for CTO.

Double (or Triple Wire) Parallel Wire Technique

It is common that a guidewire passes subintimally during an attempted CTO crossing. One approach is to maintain the wire in place and use a second wire with an OTW balloon catheter to attempt to traverse the true lumen using the first wire as a marker of the subintimal space (Fig. 10-4*A*). A variant of this technique, known as the see-saw technique, utilizes an OTW catheter for wires, manipulating one wire and then the other, alternating their position between dissection plane and true lumen until one wire is able to cross the CTO intraluminally.

Anchoring Technique

In some lesions where the proximal cap is hard, advancing the guidewire pushes the guide catheter out of the vessel (even with an excellent backup guide). A technique known as anchoring may be applied (Fig. 10-4*B*). A small angioplasty balloon is passed to a side branch proximal to the CTO and the balloon inflated. This maneuver will anchor the guide catheter in the coronary ostium. The force along the guidewire will be transmitted more effectively to the CTO and thus increases the chance of puncturing the cap or creating a subintimal wire dissection.

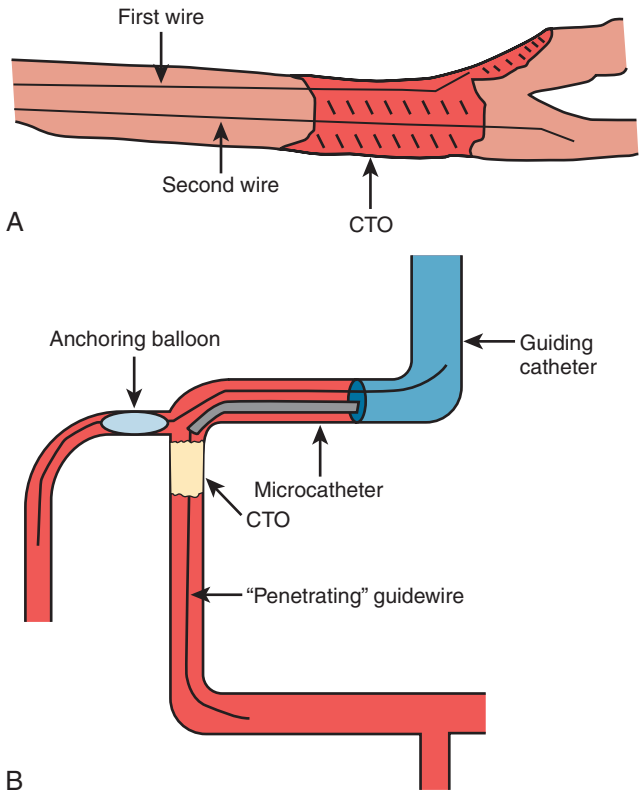


Figure 10-4 **A,** Example of double wire technique. The first wire was passed subintimal. It was left in place and a second wire was placed through the chronic total occlusion (CTO) in the true lumen. **B,** The anchoring technique is shown. With attempted passage of the stiff wire through the CTO using a microcatheter for increased support, the guide catheter prolapsed out of the vessel. A small balloon catheter was passed into a side branch proximal to the CTO, and the balloon was inflated. This prevented guide catheter retraction and allowed for more effective force transmission to the CTO cap.

The balloon may also be inflated proximal to the CTO, which will allow increased force transmission by the wire.

Open Sesame Technique

By placing a wire in a side branch proximally to a CTO, the configuration of the vessel at the CTO point may be modified, allowing a guidewire to penetrate the hard proximal cap.

Microchannel Technique

A stiff-tipped wire over an OTW balloon catheter or microcatheter is used to penetrate the proximal cap, as perpendicularly as possible. Nitroglycerin is instilled, followed by full-strength contrast to evaluate the existence of any microchannels. A hydrophilic wire can then probe the CTO for the presence of microchannels. This technique is recommended when the CTO is in a straight vessel segment, the proximal cap appears concave, and there are no adjacent side branches proximal to the CTO.

Mother-Child or Guide-in-Guide Approach

The mother-child technique utilizes one small-diameter guide catheter within a larger guide with passage of the smaller guide into the coronary near the occlusion. There is also a commercially available guide

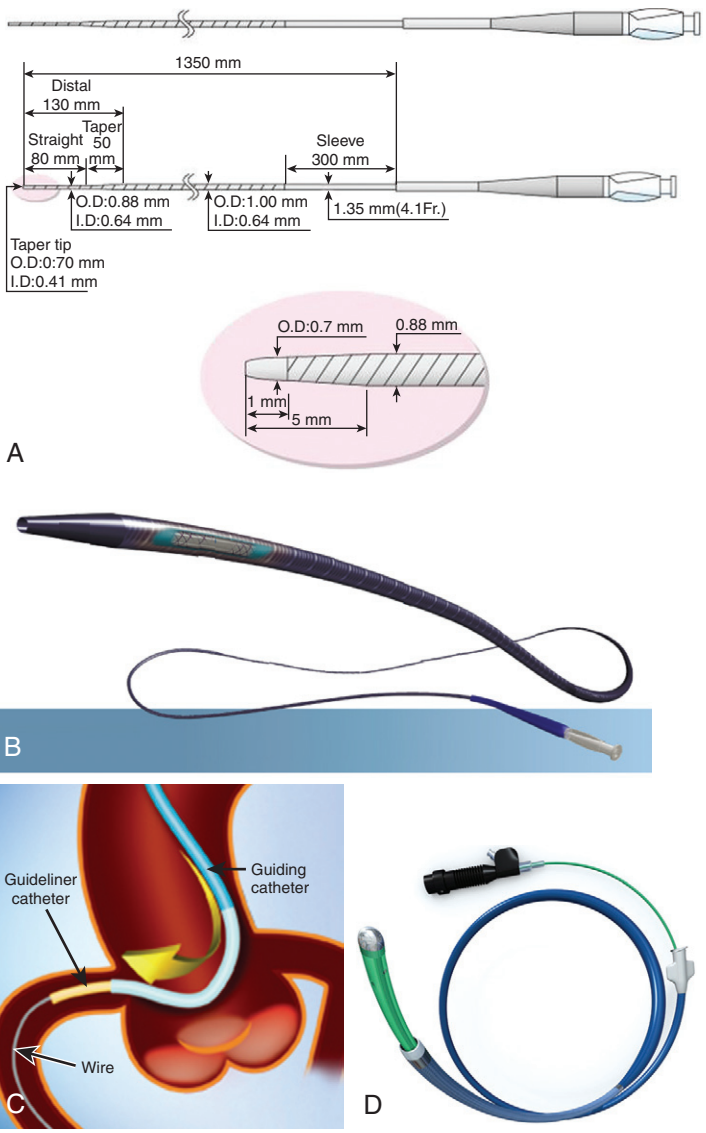


Figure 10-5 Unique catheters for chronic total occlusion (CTO) percutaneous coronary intervention (PCI). **A**, Tornus (Asahi Intec, Tokyo, JP). **B,** Corsair microcatheter (Asahi). **C,** GuideLiner catheter (Vascular Solutions, Minneapolis, MN). **D,** Crosser (FlowCardia, Sunnyvale, CA).

extender, the GuideLiner (Vascular Solutions), which may accomplish the same purpose (Fig. 10-5*C*). This technique allows for more efficient force transmission of the wire through the microcatheter or the OTW balloon catheter to the proximal CTO end, increasing the chance of puncturing the proximal cap.

Adjunctive Imaging

Intravascular ultrasound (IVUS) has been used to determine where the true lumen lies. When the CTO occurs at a side branch, the IVUS may be parked in the side branch, allowing the operator to visualize the origin of the CTO. If the wire enters the subintimal space, passage of the IVUS may provide visualization of the adjacent true lumen and allow for observing if the guidewire is, in fact, in the true lumen.

Coronary CTA has been used preprocedure to describe the vessel course and the severity of calcification. The use of these techniques is likely to undergo further refinement in the future.

Other Devices

The Crosser (FlowCardia, Sunnyvale, CA) is a mechanically driven catheter that uses vibrational energy to aid in crossing the CTO (Fig. 10-5*D*). The CrossBoss (Bridgepoint Medical, Plymouth, MN), a manually applied catheter with a slightly bulbous tip, has been utilized to cross a CTO intraluminally. It may also be used to traverse the subintimal space and, with the use of the Stingray balloon catheter and guidewire, allow guidewire lumen re-entry. Both the Crosser and CrossBoss have been utilized without a guidewire to cross the CTO.

Use of the Subintimal Space to Recanalize the CTO

The subintimal tracking and re-entry (STAR) and the related mini-STAR techniques have been used, primarily in the right coronary artery (> 80% of successful cases), for recanalization using the subintimal space. The hydrophilic wire is tracked subintimally, and the subintimal track is enlarged. In the STAR technique, the guidewire may track back into the lumen, frequently at a branch point, allowing for reconnection to the true lumen. As with the retrograde approach, this approach should be considered an advanced technique and be performed only by highly experienced interventionalists. The operator should appreciate that a 5% to 10% risk of perforation may occur with this technique.

A modification of the STAR technique, the mini-STAR, uses soft-tipped hydrophilic wires to cross the CTO subintimally and, by virtue of the wire type and tip bend, to re-enter the lumen distal to the CTO but more proximal than in the STAR technique.

There is a specialized OTW balloon catheter, the Stingray (BridgePoint Medical), which is used in the subintimal space to facilitate guidewire re-entry to the true lumen. The catheter is passed distal to the CTO after enlarging the subintimal space with a companion device, the CrossBoss, and the Stingray balloon inflated distally to the CTO. A specialized guidewire is passed to the balloon, exiting from one of two ports into the true lumen.

Common problems associated with the antegrade approach to CTO are listed in Table 10-3.

Table 10-3

Commonly Encountered Problems With the Antegrade Approach and Potential Solutions

Issue	Potential Solution
Cannot cross proximal cap	1. Use increased support guide catheter. 2. Pass microcatheter near proximal cap to increase wire force. 3. Use wire with increased tip strength or penetration power. 4. Use anchor technique. 5. Use open sesame technique. 6. Use mother-child deep intubation. 7. Consider other devices, e.g., Crosser, CrossBoss. 8. Consider retrograde approach.
Wire passes subintimally	1. Use parallel wire technique. 2. Use Stingray to re-enter lumen. 3. Use STAR technique.
Wire does not pass through entire CTO	1. Consider different wire. 2. Increase backup support (see above)

Approaches to PCI for Total Occlusion of Saphenous Vein Grafts (SVGs)

PCI of a chronically occluded SVG represents a highly complex, high-risk procedure. According to the 2011 AHA/ACC/SCAI PCI guidelines update, attempting recanalization of *chronically* occluded SVG is a class III indication. If evidence of ischemia exists in a myocardial territory supplied by a graft CTO, one should always consider PCI of the native coronary artery first. If this is not possible, then consideration of graft CTO PCI may be given with the understanding that it has a lower likelihood of success and a higher risk of adverse events. For recent (<3 months) SVG occlusions presumed to be thrombotic, thrombectomy catheters, thrombus aspiration systems, and distal protection devices have been used successfully.

Retrograde Recanalization Approach

Retrograde CTO recanalization is an advanced technique and should be performed only by highly experienced interventionists. Only the basic concepts will be discussed in this chapter.

The distal cap of the CTO, which may be softer than the proximal cap, can be approached retrogradely through a bypass graft, septal perforators, or epicardial collateral. Septal perforators are usually preferred, as they have a relatively straight course compared with typical tortuous epicardial collaterals. Further, perforation of septal collateral will usually not produce symptoms or tamponade with hemodynamic compromise and will usually close off spontaneously. When the bleeding from a perforated septal persists, it enters a cardiac chamber, usually the right ventricle, while an epicardial collateral perforation is more likely to produce serious adverse consequences, typically cardiac tamponade.

Various techniques in retrogradely recanalizing a CTO have been described, including (1) passage of a guidewire retrogradely across the CTO in the true lumen with balloon dilatation, followed by antegrade guidewire passage with antegrade PCI; and (2) retrograde wire passage from lumen to subintimal space, enlarging the subintimal space with balloon dilatation and connecting with the true lumen retrogradely (controlled antegrade and retrograde tracking [CART] technique). Enlarging the subintimal space from the antegrade approach to meet the retrograde wire is known as the reverse CART technique.

There is currently great interest in simplifying and standardizing techniques to allow them to be applied by a larger group of operators.

Complications

A common misconception is that one cannot make a CTO worse. This is not true. In fact, as with every PCI, complications occur, the most dreaded being a free flowing (Type III) coronary perforation. The risk of each maneuver in producing a perforation must be considered, and the medical team should be prepared to manage the consequences should it occur. The general management principles for coronary perforation of a CTO are similar to other coronary perforations and are discussed elsewhere in this text (Chapter 4). Distal embolization, collateral closure, and rarely guidewire entrapment may also complicate the procedure. Because of the technical complexity, large contrast and radiation doses may be used, increasing the risk of contrast-induced nephropathy and radiation dermatitis. The operator must be aware of these doses during the procedure in order to minimize the risk of these complications.

Choice of Anticoagulation

In general, heparin is preferable in view of the ability to reverse its anticoagulant effect with protamine should a bleeding complication or perforation develop.

Key Points for CTO PCI

- Develop a game plan prior to procedure, including limits of procedure for contrast, radiation, and time on cath lab table, and the technical approach, including guide catheter, wire, and stepwise strategy.
- Use bilateral coronary angiography in most cases to identify CTO characteristics, particularly length and presumed course.
- Consider stopping if myocardial staining of the myocardium or small contained perforation occurs.
- Stop if Type II or III perforation occurs, and treat perforation as described for management of complications. Employ anticoagulation reversal, balloon tamponade, and covered stent if necessary.
- If procedure is not successful, consider second attempt if other technical approaches may be used with a reasonable chance of success.

Suggested Readings

Godino C, Sharp ASP, Carlino M, *et al*. Crossing CTOs—the tips, tricks, and specialist kit that can mean the difference between success and failure. *Catheter Cardiovasc Interv* 2009;74:1019–1046.

Morino Y, Abe M, Morimoto T. Predicting successful guidewire crossing through chronic total occlusion of native coronary lesions within 30 minutes: the J-CTO (Multicenter CTO Registry in Japan) score as a difficulty grading and time assessment tool. *JACC Cardiovasc Interv* 2011;4:213–221.

Saito S. Different strategies of retrograde approach in coronary angioplasty for chronic total occlusion. *Catheter Cardiovasc Interv* 2008;71:8–19.

Stone GW, Kandzari DE, Mehran R, *et al*. Percutaneous recanalization of chronically occluded coronary arteries: a consensus document: Part I. *Circulation* 2005;112:2364–2372.

Stone GW, Kandzari DE, Mehran R, *et al*. Percutaneous recanalization of chronically occluded coronary arteries: a consensus document: Part II. *Circulation* 2005;112:2530–2537.

Sumutsuji S, Inoue K, Ochiai M, *et al*. Fundamental wire technique and current standard strategy of percutaneous intervention for chronic total occlusion with histopathological insights. *JACC Cardiovasc Interv* 2011;4:941–951.

11

Aorto-Ostial and Branch Ostial Lesions and Unprotected Left Main Percutaneous Coronary Interventions

MICHAEL S. LEE · AHMAD EDRIS · MORTON J. KERN

Narrowing of the aorto-ostium involving native coronary arteries or bypass grafts is associated with more complicated techniques and worse long-term outcomes. The tensile strength of the aortic wall and disease of the native or coronary artery bypass graft (CABG) conduit may fail using standard balloon/stent methods. Because of the location, guiding catheter support may not be secure. Balloon inflations in coronary ostial location have the potential for aortic dissection, especially during right coronary artery (RCA) percutaneous coronary intervention (PCI), or for dissection of the left main (LM) artery from dilation in the ostium of the circumflex (LCX) or left anterior descending (LAD) arteries. Ostial lesions may be best managed by rotablation or a scoring balloon, followed by balloon angioplasty and stenting.

Branch Coronary Ostial Stenoses

A coronary branch ostial stenosis is a narrowing at the origin of the branch takeoff from a main coronary vessel. LAD coronary ostial, diagonal, or LCX ostial lesions are common. One of the most difficult lesions is the ostial LAD artery. PCI of this lesion may injure the LM artery during device delivery or deployment. An LAD stenosis within 2 to 3 mm of the origin should be considered as an ostial lesion with similar technical risks, because most PCI devices cover vessel segments more than 10 mm in length.

Techniques for Ostial PCI

Guide Catheter Selection

For the RCA aorto-ostial lesion, standard right Judkins catheters often cannot provide satisfactory device support. Configurations such as modified Amplatz (left or right), multipurpose, Arani, or El Gamal catheters have been used successfully. Ostial lesions, especially of the RCA, may be occluded during seating of the guide catheter, as seen by damping of arterial pressure. Damping requires guide catheters with side holes to permit some perfusion during equipment maneuvers. While adequate for coronary perfusion after re-establishment of a patent lumen, side holes may limit coronary visualization (contrast escapes through side holes), especially when using large devices (e.g., Rotablator).

Careful engagement of the guide catheter should minimize aortic trauma and avoid an ostial dissection which would complicate an already difficult procedure. The use of Rotablator catheters requires nearly coaxial alignment of the guide catheter upon device entry in the ostium. Significant angulation between the guide catheter and the ostial takeoff will reduce procedure success.

Balloon Catheter Placement

Balloon angioplasty requires seating such that, during inflation, the balloon will not be ejected from, nor compressed forward past ("watermelon seed"), the coronary ostia (Fig. 11-1). Removal of the guide catheter into the aorta immediately before balloon inflation will permit the balloon to be inflated partly in the coronary ostium and the aorta and outside the guide catheter. The lesion will be appropriately spanned by the two ends of the balloon inflating at equal pressure. Inflation in the guide may result in failure of the distal end of the balloon to inflate properly. Stenting the ostial lesion may produce strut "hangout" into the main vessel, a common complication of ostial branch stenting, especially when angiographic angles do not allow good visualization of the takeoff. An anchor wire technique may obviate this problem.

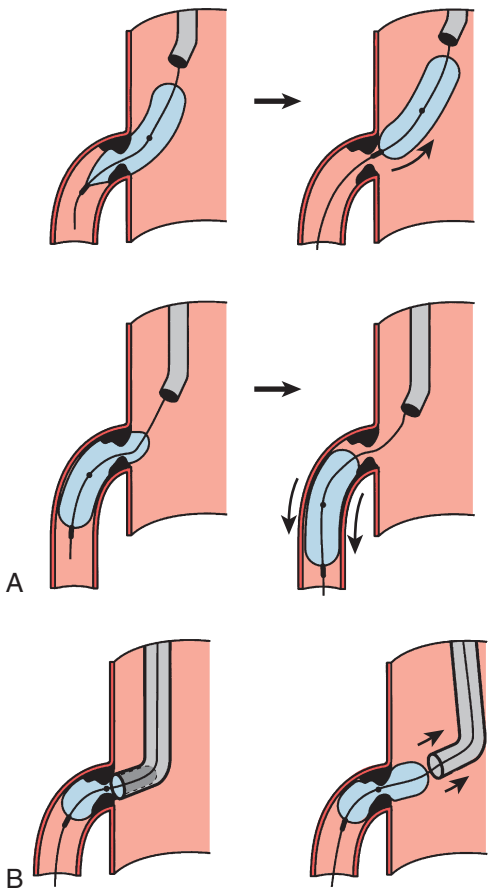


Figure 11-1 **A,** Effect of squeezing the balloon out of an ostial lesion. The top panels show the balloon being ejected from the ostium, and the lower panels show the balloon advancing inside the artery during inflation. **B,** Proper guide catheter positioning helps to seat the balloon in an ostial lesion. (Adapted from Safian R, Freed M, eds. *The manual of interventional cardiology,* 3rd ed. Birmingham, MI: Physicians' Press, 2001, p. 267.)

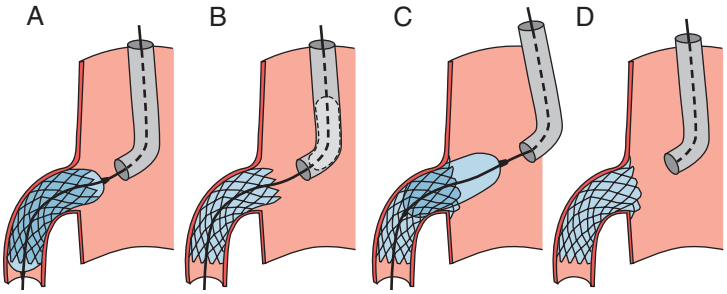


Figure 11-2 Aorto-ostial lesions: stent technique. **A,** Position the stent-delivery balloon so 1 to 2 mm of stent extends into the aorta. The guide must be retracted 1 to 2 cm before deploying the stent. **B,** Remove the delivery balloon while maintaining backward tension on the guide, to prevent it from advancing into the ostium and damaging the stent. **C,** Perform adjunctive percutaneous transluminal coronary angioplasty with a high-pressure balloon to ensure full stent expansion and apposition. Flaring the proximal end of the stent with a slightly larger balloon is useful. **D,** Final result. (From Freed M, Grines C, Safian R, eds. *The new manual of interventional cardiology.* Birmingham, MI: Physicians' Press, 1996.)

Figure 11-2 demonstrates good techniques for RCA ostial stenting. Recovering access to the main vessel after ostial stenting can be difficult depending on the angle of the ostium origin and the amount of stent. It may be helpful to leave the stent balloon catheter in place and advance the guide catheter over the balloon to minimize damage or disfiguration of the recently implanted stent.

The Back-Stop Technique

A strategy to prevent strut hangout uses a main vessel balloon inflated at low pressure (balloon:artery ratio 0.7:1), placed prior to branch stent deployment (Fig. 11-3). By pulling the ostial stent back against the inflated balloon and then deploying the stent, one prevents significant strut hangout into the main vessel.

For moderately or severely calcified lesions, rotational atherectomy is the technique of choice, followed by stenting.

Ostial or Very Proximal LAD Stenosis PCI

A complication of a very proximal or ostial LAD stenosis often involves the left main (LM) segment and can be life-threatening, especially if it involves the distal left main or LCX ostium. Balloon dilatation and stenting in part of the LM coronary artery segment may be unavoidable. As the circumflex branch is often diseased in patients with an ostial LAD stenosis, the potential for side-branch closure and the need for bifurcation technique should be carefully considered in advance.

Based on the historical incidence of LM dissection and the potential for abrupt vessel closure, stent placement (with or without preceding Rotablator) has superseded routine balloon angioplasty for ostial LAD lesions. However, even in the drug-eluting stent era, ostial LAD artery stenting still has a higher restenosis rate than non-ostial locations (> 15%). Key points for ostial lesion stenting are shown in Table 11-1.

The Szabo Technique for Precise Ostial Stent Placement

Precise localization of the edges of the ostium of any coronary artery or branch is among the most challenging of all angiographic image

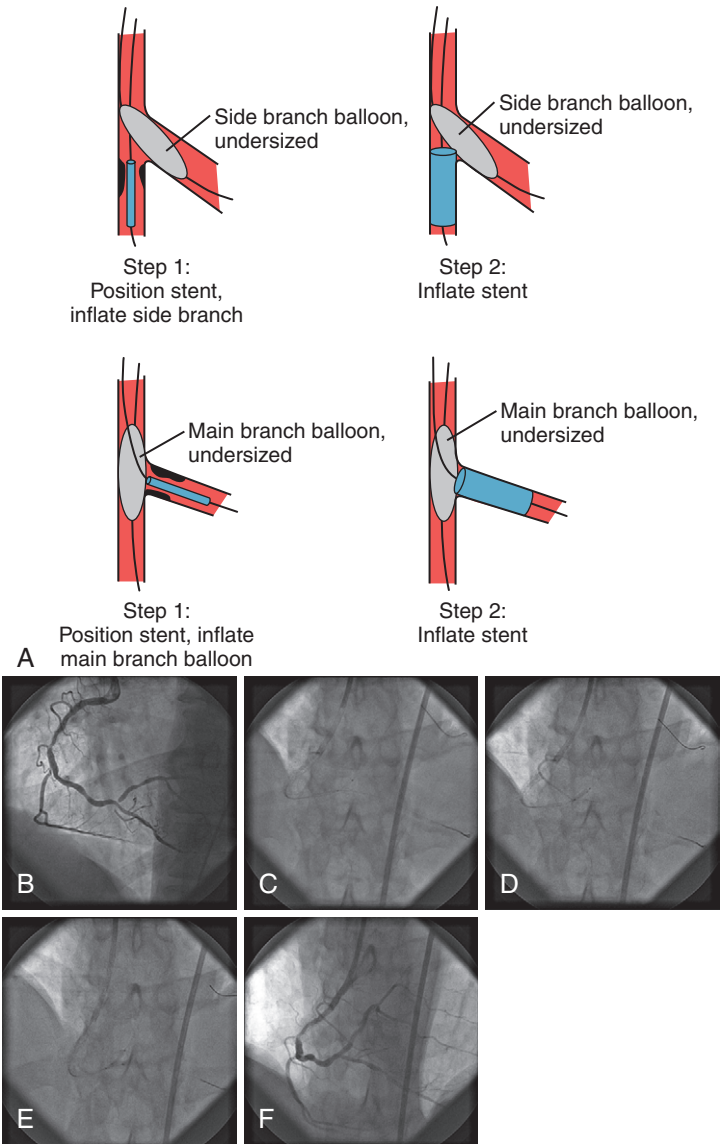


Figure 11-3 **A,** Back-stop technique for ostial stenting. **B,** Subtotal ostium of the posterior left ventricular (PLV) branch with an uninvolved posterior descending artery (PDA) at the bifurcation. **C,** Both vessels wired and undersized balloon is positioned across ostial PLV. **D,** PLV ostium is predilated. The balloon is then removed, reshaped, and inserted into the PDA for an undersized balloon backstop inflation. **E,** The undersized balloon is inflated in the PDA at low pressure. The stent is seated in the PLV and gently pulled back until a slight resistance is felt against the balloon in the PDA. The stent is then inflated at optimal atmospheres. The stent is deflated, and following deflation, the balloon is then deflated. **F,** Ostial PLV stent wall opposition is maximized, while PDA is protected from plaque encroachment. Barotrauma causing neointimal hyperplasia is minimized in the PDA by the undersized balloon at low inflation atm. The proximal RCA was treated by a direct stent. (Modified from Lunsford C. Advanced stenting strategies for complex coronary artery bifurcation lesions. *Cath Lab Digest,* June 19, 2008.)

Table 11-1

Techniques for Ostial Lesion PCI
Use Rotablator for calcified ostial lesions, especially of right coronary artery.
Use guide with side holes.
Use balloon long enough to span ostial lesion and remain inside artery and partly in aorta.
Use stents longer than 9 mm to prevent them from being "pulled out of position" by guide catheter manipulation.
Use larger balloon to flare aorto-ostial segment artery lesion.

PCI, percutaneous coronary intervention.

interpretations. Due to the limitations of angiographic imaging, there is commonly unavoidable stent overlap either too far inside or outside the ostium. Stents placed outside the true ostium may obstruct later catheter engagement, whereas stents inserted too deeply may miss the proximal edge of the lesion, resulting in a need for another stent or later restenosis.

In 2005, a technique to accurately place the stent and anchor it from advancing beyond the ostium of a lesion using a second angioplasty guidewire positioned in the aorta or opposing branch was reported. The technique using the most proximal end of a second guidewire passing it through the last cell of the stent inhibiting advancement and anchoring the stent position was first described in an abstract at the Transcatheter Cardiovascular Therapeutics conference by Szabo et al., but never brought forward into full publication. Our lab, and later others, described several cases for anchoring both the distal and proximal portions of the stent with the Szabo wire technique. The Szabo technique for aorto-ostial lesions (Fig. 11-4) and for bifurcation ostial lesions is described below:

Step 1: Begin with putting one wire into the target vessel and the anchor wire through the guide and into the aorta (or opposite branch). The very proximal end of the anchor wire is inserted through the last strut of stent. Take care on lifting the stent cell so as not to puncture the balloon.

Step 2: The stent is advanced over both the primary and anchor wires together. Remember the anchor wire is outside the ostium in the aorta (or in the opposite branch).

Step 3: The stent is advanced into the ostial lesion. The stent advancement is stopped by the anchor wire.

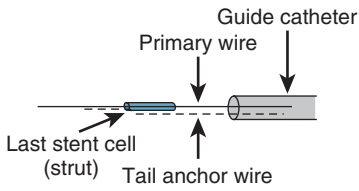
Step 4: Inflate the stent at low atm. Deflate the balloon. Remove the tail anchor wire and then perform a high atm balloon inflation.

While now in use for several years, there are several safety factors related to the use of the anchor wire method that should be considered:

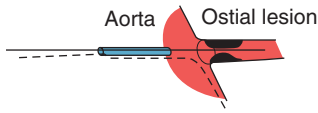
1. Before proceeding with the stent anchor, one should test the passage of the stent to the target lesion. By running the stent over the main guidewire to the lesion, the forthcoming double-wired stent movement will not be impeded by tortuosity, calcification, or other complicating features. Thus, after inserting the tail of the anchor wire into the last cell of the stent, the passage of the stent over the two wires should go smoothly.
2. Careful management of the guide catheter position is needed both on stent entry and anchor wire withdrawal. Resistance on anchor wire withdrawal should be of concern, especially if any kinking or excessive bending was present.
3. Any stent balloon might be damaged by the setup of capturing the last cell with the end of the anchor wire. Careful technique is needed to thread the end of the anchor wire through the stent cell without puncturing the balloon.

A

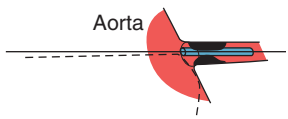
Step 1:
Anchor wire inserted through the last strut of stent.



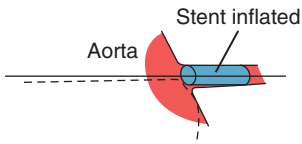
Step 2:
Stent advanced over both the primary wire and anchor wire which resides outside the ostium in the aorta.



Step 3:
Stent advanced into ostial lesion. The stent advancement is stopped by the anchor wire.

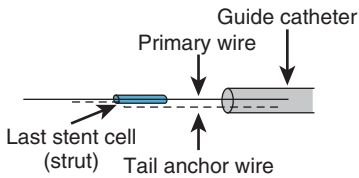


Step 4:
Inflate stent at low atm. Finalize by removing tail anchor wire and a high atm inflation.

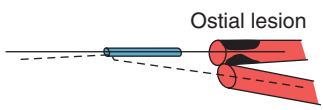


B

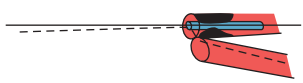
Step 1:
Anchor wire inserted through the last strut of the stent.



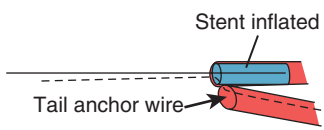
Step 2:
Stent advanced over both the primary wire and the anchor wire which resides in the other branch.



Step 3:
Stent is advanced in to the ostial lesion. The stent advancement is stopped by the anchor wire.



Step 4:
Inflate stent at low atm. Finalize by removing tail anchor wire and a high atm inflation.



C

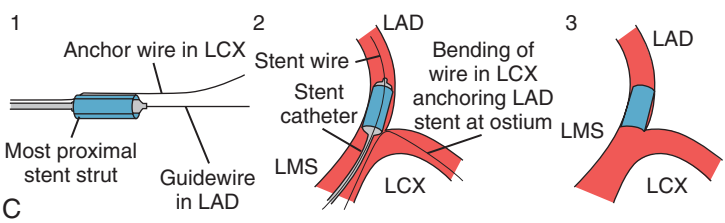


Figure 11-4 **A,** Aorto-ostial stent placement with the Szabo technique. **B,** Ostial bifurcation stent placement with the Szabo technique. **C,** LAD-LCX bifurcation stent placement with the Szabo Technique.

4. Guidewires with polymer coating or other coatings should be avoided because of the risk of stripping the coating with distal particulate embolization. Caution is emphasized if hydrophilic guidewires are used to minimize resistance of the anchor wire withdrawal. It is also unknown if the polymer coating on the drug-eluting stent plays a role in modifying the resistance to withdrawal of the anchor wire.

Other methods to assist in the exact ostial stent placement, such as metal spring feet on the end of the guide catheter (Ostial Pro), are emerging but the Szabo anchor wire technique appears to be an easy and cost-effective method for precise ostial lesion stenting.

Left Main PCI

The current and principal recommended management of significant atherosclerotic disease involving the LM is CABG surgery. However, bypass surgery is not innocuous and is associated with considerable morbidity. For PCI, there is a distinction between protected (i.e., previously bypassed LM) and unprotected LM (i.e., de novo or native) disease. Protected LM patients are at lower risk for PCI. PCI for unprotected LM disease needs to balance the alternative of CABG in the particular high-risk patient under consideration for intervention.

Use of the left internal mammary artery (LIMA) graft for CABG is highly beneficial and quite durable. However, CABG surgery for unprotected LM disease, in addition to using the LIMA, necessitates the use of alternative grafts for the remaining arteries (e.g., saphenous vein graft [SVG] or free radial artery). In fact, the SVG is the most frequently implanted surgical graft with patency rates nowhere near those of LIMA grafts. The combination of poor patency rates associated with the SVG along with progression of native coronary vessel disease has been documented in patients undergoing bypass surgery.

Results of PCI in treating unprotected LM disease differ depending on LM lesion location. LM lesions localized to the ostium or middle shaft are not as technically difficult to treat as distal LM disease, which often necessitates bifurcation stenting techniques. One study of 147 consecutive patients undergoing PCI of ostial or middle-shaft LM lesions using sirolimus-eluting or paclitaxel-eluting stents found cardiac mortality was 2.7% and target vessel revascularization (TVR) rate was 4.7% at the 3-year follow-up.

The results differ when treating predominantly distal LM bifurcation disease. The Scripps Clinic experience with unprotected LM disease included 50 patients with distal bifurcation disease, most (94%) treated with sirolimus-eluting stents. Multiple stents were used in 84% of the patients. Cardiac mortality was 2% and TVR rate was 14% (ischemia- or symptom-driven revascularization) at the 9-month follow-up. The TVR rates increase with technically challenging coronary anatomy. Bifurcation lesions often require double stenting, with less favorable long-term outcomes.

Anatomic factors that have been associated with worse outcomes include:

1. unprotected LM with a small diameter and significant quantities of calcium;
2. significant distal disease in the LAD and/or LCX requiring multilesion intervention; and
3. multiple downstream lesions, especially one or more total occlusions and/or disease of the RCA.

Despite more complicated LM coronary anatomy, the mortality rate associated with PCI of unprotected LM disease is comparable to CABG surgery. A meta-analysis of 17 published studies undergoing PCI for unprotected LM disease showed a mortality of 5.5% and TVR of

6.5% at 10 months. Selecting and treating those patients with optimal LM anatomy can potentially reduce high repeat revascularization rates.

Several studies have compared PCI and CABG surgery in terms of mortality and revascularization rates. The LEMANS trial showed a mortality benefit of PCI when compared to CABG (0.5 ± 0.8% vs. 3.3 ± 6.7%; $P = 0.047$ at 12 months). The SYNTAX trial showed a benefit of CABG surgery over PCI in patients with three-vessel and LM disease with respect to a combined primary end point (12.4% vs. 17.8%; $P = 0.002$ for MACCE at 12 months). However, a higher repeat revascularization rate in the PCI arm (13.5% vs. 5.9%; $P < 0.001$) predominately accounted for the difference. There was no difference in mortality between the two groups. The secondary outcomes of the SYNTAX trial also showed that the stroke rate was higher in the CABG group compared to PCI (2.2% vs. 0.6%; $P = 0.003$ at 12 months).

CABG surgery is often considered the conservative approach in patients with LM disease; however, given the surgical morbidity, a percutaneous management strategy for selected high-risk patients with LM disease will continue to be necessary and will evolve as techniques and tools improve.

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12

High-Risk Percutaneous Coronary Interventions

MICHAEL J. LIM · TODD K. ZYNDA · MORTON J. KERN · ARNOLD H. SETO · WILLIAM M. SUH

The risk of major complications such as myocardial infarction (MI), life-threatening arrhythmias, need for emergency coronary artery bypass surgery (CABG), and death during a percutaneous coronary intervention (PCI) is influenced by angiographic, patient-related, and clinical factors. Knowledge of these factors allows the interventionalist to identify the patient at high risk of complications and facilitates the essential discussion of the risks and benefits of the intervention with the patient, family, and hospital personnel (e.g., cardiac surgeons). Appropriate measures can then be taken before and during the high-risk PCI procedure to minimize the risk of a major adverse event, and the medical team can be optimally prepared to deal with complications should they occur.

Identifying the High-Risk PCI Patient

Retrospective studies and databases have been utilized to identify risk factors for adverse events occurring during PCI.

Angiographic Factors

The American College of Cardiology/American Heart Association (ACC/AHA) created a scoring system that classified lesions according to their complexity, likelihood of successful dilation, and the likelihood of an adverse event. Lesions were classified as either type A, B, or C, with C the highest risk lesions, based on lesion characteristics (Tables 12-1 and 12-2).

The ACC/AHA Lesion Classification Scheme has since been modified in that lesions with one "type B" characteristic are designated as "type B1" while lesions with two or more "type B" characteristics are designated as "type B2" lesions. Since this classification was first implemented in 1988, significant advances in PCI techniques have allowed treatment of more complex lesions with lower risks. In the current era of coronary stenting, it is primarily the type C lesions that are associated with lower success and higher complication rates.

In the mid-1990s, an era in which coronary stents and platelet glycoprotein IIb/IIIa inhibitors were frequently utilized, Ellis and coworkers analyzed a large database of patients undergoing PCI. Ten angiographic factors were identified that correlated with greater risk of complication. The two factors associated with the greatest increased risk were *degenerated saphenous vein grafts* (relative risk 4.18) and *nonchronic total occlusion* (relative risk 4.74). Other factors included long lesions, lesions with large filling defects, calcified angulated lesions, eccentric lesions, and old saphenous vein grafts (Table 12-2). The finding of marked increased risk in degenerated vein grafts supports the practice of using distal protection devices during PCI of such lesions.

Table 12-1

The ACC/AHA Lesion Classification Scheme

Type A Lesions
· Discrete
· Concentric
· Ready accessibility
· Location in a nonangulated segment (<45°)
· Smooth contour
· Little or no calcification
· Absence of total occlusion
· Nonostial location
· Absence of major branch involvement
· Absence of thrombus
Type B Lesions
· Tubular (10–20 mm in length)
· Eccentric
· Accessibility influenced by moderate tortuosity of proximal segment
· Location in moderately angulated segment (45°–90°)
· Irregular contour
· Moderate or severe calcification
· Presence of thrombus
· Ostial location
· Bifurcation lesion requiring double wiring
· Total occlusion <3 months old
Type C Lesions
· Diffuse disease (>20 mm in length)
· Excessive tortuosity of proximal segments
· Location in an extremely angulated segment (>90°)
· Total occlusion >3 months old
· Inability to protect major side branches
· Degenerated vein grafts

ACC, American College of Cardiology; *AHA,* American Heart Association.

Angiographic Risk Assessment Using the SYNTAX Score

The SYNTAX score, an angiographic grading tool to determine the complexity of coronary artery disease (CAD), was derived from pre-existing risk assessment classifications from numerous studies and expert consensus. The SYNTAX score is the sum of the points assigned to each individual lesion identified in the coronary tree with >50% diameter

Table 12-2

Lesion Characteristics and the Increased Risk of Ischemic Complications (Based on Multivariate Analysis)

Lesion Characteristic	Odds Ratio
Nonchronic total occlusion	4.74 (2.69–8.38)
Degenerated saphenous vein graft	4.18 (2.39–7.31)
Length ≥20 mm	2.77 (1.51–5.09)
Irregularity	1.88 (1.32–2.66)
Large filling defect	1.41 (1.17–1.70)
Length 10–20 mm	1.88 (1.26–2.82)
Moderate calcification with angulation >45°	4.44 (1.24–15.96)
Eccentric	2.12 (1.04–4.57)
Severe calcification	2.19 (1.04–4.57)
Saphenous vein graft age ≥10 years	1.81 (1.00–3.31)

Adapted from Ellis SG, Guetta V, Miller D, *et al.* Relation between lesion characteristics and risk with percutaneous intervention in the stent and glycoprotein IIb/IIIa era. *Circulation* 1999;100:1971–1976.

narrowing in vessels >1.5 mm diameter. The coronary tree is divided into 16 segments according to the AHA classification (see Fig. 12-1). Each segment is given a score of 1 or 2 based on the presence of disease, and this score is then weighted based on a chart, with values ranging from 3.5 for the proximal left anterior descending artery (LAD) to 5.0 for left main, and 0.5 for smaller branches. The branches <1.5 mm in diameter, despite having severe lesions, are not included in the SYNTAX score. The percent diameter stenosis is *not* a consideration in the SYNTAX score, only the presence of a stenosis from 50% to 99% diameter, <50% diameter narrowing, or total occlusion. A multiplication factor of 2 is used for non-occlusive lesions and 5 is used for occlusive lesions, reflecting the difficulty of PCI. Further characterization of the lesions adds points. (Fig. 12-1 shows the diagram of vessel segments used in the SYNTAX score.)

The SYNTAX score algorithm then sums each of these features for a total SYNTAX score. Table 12-3 summarizes the SYNTAX grade categories. A computer algorithm (available online at www.syntaxscore.com) is then queried, and a summed value is produced. Figure 12-2 shows two patients each with three-vessel CAD but very different PCI risk based on SYNTAX scores.

In patients with SYNTAX score <33, equal outcomes after revascularization were obtained with regard to major adverse cardiac events for both PCI and CABG. For higher SYNTAX scores, CABG had fewer adverse events than PCI. The conclusion of the SYNTAX study showed that the overall safety outcomes (death, cerebrovascular accident, MI) were similar in CABG and PCI patients at 12 months (7.7 vs. 7.6%). There was a higher rate of revascularization in the PCI group (13.7 vs. 5.9%), balanced by a higher rate of cerebrovascular accident in the CABG

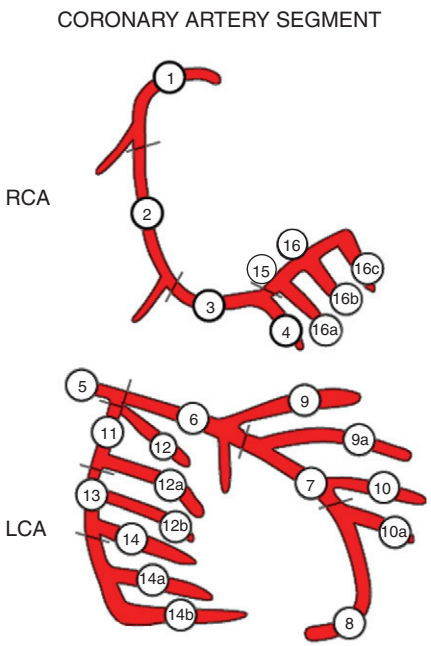

Figure 12-1 Definition of the coronary tree segments from the SYNTAX study
1. RCA (right coronary artery) proximal: from the ostium to one half the distance to the acute margin of the heart.
2. RCA mid: from the end of first segment to acute margin of heart.
3. RCA distal: from the acute margin of the heart to the origin of the posterior descending artery.
4. Posterior descending artery: running in the posterior interventricular groove.

Figure 12-1, cont'd

5. Left main: from the ostium of the LCA (left coronary artery) through bifurcation into left anterior descending and left circumflex branches.
6. LAD (left anterior descending) proximal: proximal to and including first major septal branch.
7. LAD mid: LAD immediately distal to origin of first septal branch and extending to the point where LAD forms an angle (RAO [right anterior oblique] view). If this angle is not identifiable, this segment ends at one half the distance from the first septal to the apex of the heart.
8. LAD apical: terminal portion of LAD, beginning at the end of previous segment and extending to or beyond the apex.
9. First diagonal: the first diagonal originating from segment 6 or 7.

9a. First diagonal a: additional first diagonal originating from segment 6 or 7, before segment 8.

10. Second diagonal: originating from segment 8 or the transition between segment 7 and 8.

10a. Second diagonal a: additional second diagonal originating from segment 8.

11. Proximal circumflex artery: main stem of circumflex from its origin of left main and including origin of first obtuse marginal branch.
12. Intermediate/anterolateral artery: branch from trifurcating left main other than proximal LAD or LCX (left circumflex). It belongs to the circumflex territory.

12a. Obtuse marginal a: first side branch of circumflex running in general to the area of obtuse margin of the heart.

12b. Obtuse marginal b: second additional branch of circumflex running in the same direction as 12.

13. Distal circumflex artery: the stem of the circumflex distal to the origin of the most distal obtuse marginal branch, and running along the posterior left atrioventricular groove. Caliber may be small or artery absent.
14. Left posterolateral: running to the posterolateral surface of the left ventricle. May be absent or a division of obtuse marginal branch.

14a. Left posterolateral a: distal from 14 and running in the same direction.

14b. Left posterolateral b: distal from 14 and 14a and running in the same direction.

15. Posterior descending: most distal part of dominant left circumflex when present. It gives origin to septal branches. When this artery is present, segment 4 is usually absent.
16. Posterolateral branch from RCA: posterolateral branch originating from the distal coronary artery distal to the crux.

16a. Posterolateral branch from RCA: first posterolateral branch from segment 16.

16b. Posterolateral branch from RCA: second posterolateral branch from segment 16.

16c. Posterolateral branch from RCA: third posterolateral branch from segment 16.

(From Sianos G, Morel MA, Kappetein AP, *et al.* The SYNTAX Score: an angiographic tool grading the complexity of coronary artery disease. *EuroIntervention* 2005;1:219–227.)

group (2.2 vs. 0.6%). Of note, the overall PCI major adverse cardiac and cerebrovascular event rate (MACCE) was higher (17.8 vs. 12.1%) primarily due to an excess need for repeat revascularization. If one accepts a repeat revascularization as part of the natural history of PCI and not an adverse event, then the difference between revascularization strategies becomes even less (Fig. 12-3).

Based on angiographic assessment and the operators' experience in the cath lab, the number and type of complex anatomic lesions determines which revascularization approach might be selected. However, the physiology of coronary lesions and stenting are strongly related to outcomes. A recent publication by Tonino *et al.* from the FAME study group reported on what truly constituted three-vessel and two-vessel CAD, making clear that one cannot equate angiographic three-vessel CAD with physiologic three-vessel CAD. Fractional flow reserve thus has important implications for the decision-making process in patients with multivessel disease.

Table 12-3

The SYNTAX Score Algorithm

1. Dominance
2. Number of lesions
3. Segments involved per lesion, with lesion characteristics
4. Total occlusions with subtotal occlusions
   a. Number of segments
   b. Age of total occlusions
   c. Blunt stumps
   d. Bridging collaterals
   e. First segment beyond occlusion visible by antegrade or retrograde filling
   f. Side branch involvement
5. Trifurcation, number of segments diseased
6. Bifurcation type and angulation
7. Aorto-ostial lesion
8. Severe tortuosity
9. Lesion length
10. Heavy calcification
11. Thrombus
12. Diffuse disease, with number of segments

Reprinted from Sianos G, Morel MA, Kappetein AP, *et al.* The SYNTAX score: an angiographic tool grading the complexity of CAD. *EuroIntervention* 2005;1:219–227. Copyright © 2009, with permission from Europa Edition.

Patient-Related Factors

Several clinical factors can be utilized to identify high-risk PCI, such as the presence of multivessel disease, angioplasty to more than one lesion, suboptimal activated clotting time (ACT), residual stenosis above 30%, depressed ejection fraction, old age (>65 years), unstable angina and recent MI (Table 12-4). A retrospective study from the Mayo Clinic, examining the risk of PCI with the use of glycoprotein IIb/IIIa inhibitors and coronary stents, found that clinical factors such as left main or multivessel disease, an ejection fraction below 35%, or a recent MI were more important than angiographic factors for predicting complications. Other studies have identified the presence of diabetes mellitus and renal disease as indicators of high-risk patients (Table 12-5).

Operator Experience

Another factor that has been correlated with PCI risk is operator volume and experience. Several studies have found that those operators with greater experience have lower complication rates, the correlate being

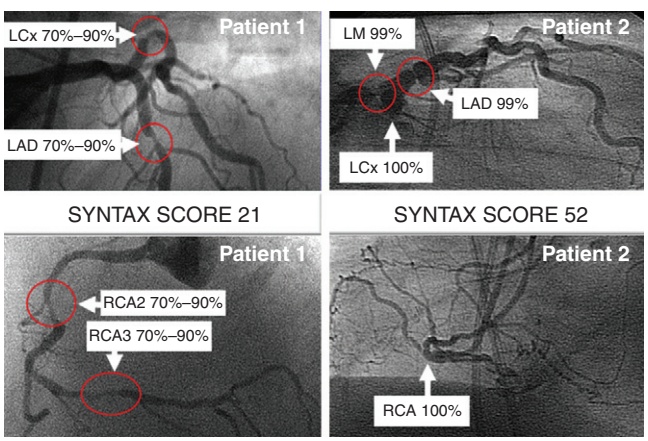

Figure 12-2 Angiographic examples of SYNTAX scores in patients undergoing PCI. Selected angiograms. (Reprinted from Sianos G, Morel MA, Kappetein AP, *et al.* The SYNTAX score: an angiographic tool grading the complexity of CAD. *EuroIntervention* 2005;1:219–227 with permission.)

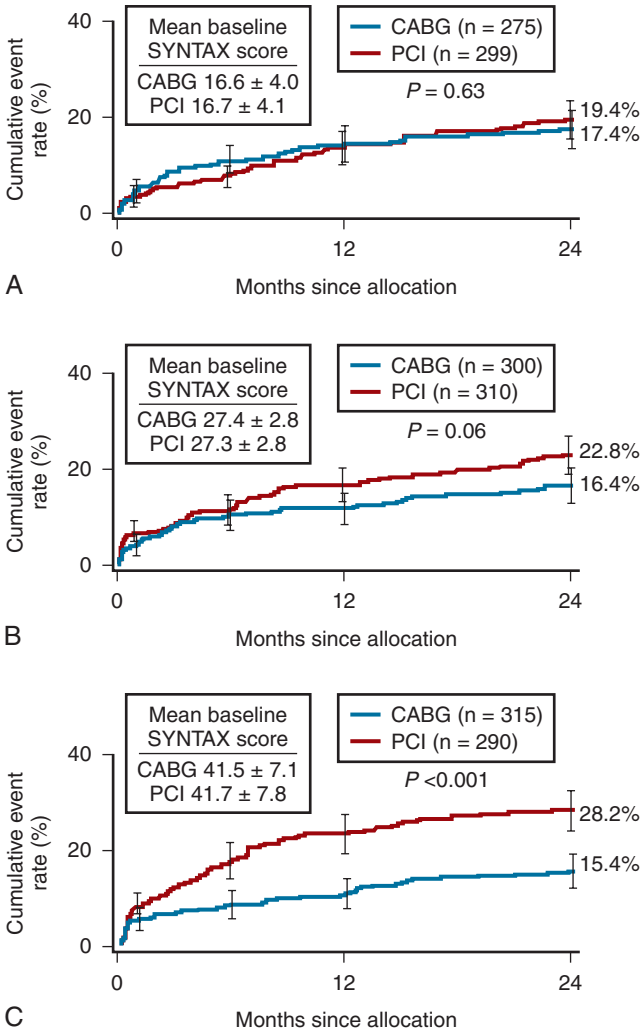

Figure 12-3 Outcomes of SYNTAX study by SYNTAX scores. Rates of major adverse cardiac or cerebrovascular events among the study patients, according to treatment group and SYNTAX score category. Kaplan-Meier curves are shown for the percutaneous coronary intervention (PCI) group and the coronary artery bypass grafting (CABG) group for major adverse cardiac or cerebrovascular events at 12 months. The 12-month event rates were similar between the two treatment groups for patients with low SYNTAX scores (0–22) (**A**) or intermediate SYNTAX scores (23–32) (**B**). Among patients with high SYNTAX scores (=33, indicating the most complex disease), those in the PCI group had a significantly higher event rate at 12 months than those in the CABG group. SYNTAX scores were calculated at the core laboratory. The I bars indicate 1.5 SE. *P* values were calculated with the use of the chi-square test. (Reprinted from Serruys PW, Morice, MC, Kappetein AP, *et al.* Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. *N Engl J Med* 2009;360(10):961–972.)

Table 12-4

Patient and Clinical Factors Associated With Higher Risk PCI
Presence of left main coronary artery or multivessel disease
PCI of more than one lesion
Suboptimal activated clotting time
Residual stenosis above 30%
Depressed ejection fraction (<35%)
Age over 65 years
Unstable angina and/or recent myocardial infarction
Severe comorbid disease

PCI, percutaneous coronary intervention.

Table 12-5

Elective PCI Patient and Lesion High-Risk Characteristics

High-Risk Patient

- Decompensated CHF (Killip Class 3-4)
- Recent (<8 weeks) cerebrovascular accident
- Known clotting disorder
- Left ventricular ejection fraction < or = 30%
- Renal failure (creatinine >2.0 mg/dL)
- Malignant ventricular arrhythmias

High-Risk Lesion

- Left main stenosis > or = 50% or three-vessel disease (>70% proximal or mid lesions)
- Unprotected by prior bypass surgery
- Target lesion that jeopardizes an extensive amount of myocardium (Jeopardy scoring systems, such as SYNTAX, may be useful in defining the extent)
- Diffuse disease (>20 mm length)
- Greater than moderate lesion calcification
- Extremely angulated segment or excessive proximal or in-lesion tortuosity
- Inability to protect side branches
- Older SVGs with friable lesion
- Thrombus in vessel or at lesion site
- Vessel characteristics that, in the operator's judgment, would impede stent deployment
- Chronic total occlusions

CHF, congestive heart failure; *SVG,* saphenous vein graft.
Modified from King SB, III, Walford G, for the New York State Cardiac Advisory Committee. Percutaneous coronary interventions in New York State, 2005–2007. Albany: New York State Department of Health, April 2010;1–52; and Dehmer GJ, Blankenship J, Wharton TP, Jr., *et al.* The current status and future direction of percutaneous coronary intervention without on-site surgical backup: an expert consensus document from the Society for Cardiovascular Angiography and Interventions. *Catheter Cardiovasc Interv* 2007;69:471–478.

that those with lower procedural volume and experience have higher complication rates. Operators with limited high-risk PCI volume and experience should consider referral to a tertiary center where advice and expertise are available.

Myocardium at Risk

In patients with depressed ejection fraction, it is particularly important to assess which myocardial territories (anterior, lateral, inferior) are akinetic and/or infarcted and which myocardial territories are doing the majority of the "work" of left ventricular function. In a patient with infarcted lateral and inferior walls in which the only functioning territory is the anterior wall and septum, PCI of the left anterior descending coronary artery carries extreme risk; if there is compromised blood flow during the procedure, the patient can be expected to tolerate this poorly. To some extent, a situation such as this should be considered as a "left main equivalent," and decisions regarding PCI and pharmacologic and/or mechanical support must be made accordingly.

Vascular Disease

An often underappreciated factor in the high-risk PCI patient is vascular access and vascular disease. During the high-risk PCI procedure, an intra-aortic balloon pump (IABP) may be placed either prophylactically or emergently, requiring knowledge of the presence of iliac/femoral arterial disease beforehand. Palpation of strong bilateral femoral pulses should be coupled with angiography. When possible,

angiography of the iliac and common femoral arteries should be performed prior to a high-risk PCI to determine if the patient is a candidate for IABP support.

Specific High-Risk Subsets

Left Main Coronary Artery PCI (also see Chapter 11)

Several registries and retrospective studies have examined procedural success and short- and intermediate-term complication rates in patients undergoing PCI of unprotected left main (UPLM) lesions. Some patients underwent PCI because they were poor candidates for CABG, some because of strong patient preference, and a few because of acute myocardial infarction (AMI).

The results of UPLM balloon angioplasty without stenting have been poor, with in-hospital mortality rates of up to 9.1% and a 3-year survival rate of 36%.

Reports of UPLM coronary stenting provide relatively encouraging data, including some with no in-hospital or late death attributable to the PCI procedure. However, in general, these reports are retrospective, limited to carefully selected patients, and from institutions with a high degree of experience and expertise. Thus, despite enthusiasm and encouraging results from small patient series, until randomized data are available comparing UPLM PCI to CABG, a UPLM stenosis should generally be considered a contraindication to PCI and should be preferentially treated with CABG.

In patients who are not candidates for, or who adamantly refuse, CABG, PCI of the left main appears to be a viable option but should be considered a very high–risk PCI, undertaken only with all the precautions discussed above. Any decision regarding UPLM PCI should be made in consultation with the cardiothoracic surgery service. Patients receiving successful UPLM PCI should undergo routine surveillance angiography during the restenosis window, in light of the high rate of mortality observed during the first 6 months after the procedure.

PCI for AMI

PCI for AMI can be performed before (primary PCI) or after thrombolysis (facilitated or rescue PCI). Primary PCI is the approach of choice for acute ST-segment elevation MI, but is not available in all facilities. Primary PCI for AMI is indicated in patients who present within 12 hours from the onset of symptoms and in whom the infarct vessel can be recanalized within 90 minutes of presentation. Primary PCI is also indicated for patients in whom thrombolytics are contraindicated and for patients in cardiogenic shock. Figure 12-4 shows angiograms of PCI for AMI.

The advantages of primary PCI include early and complete reperfusion, early identification of associated CAD, and reduced bleeding complications relative to thrombolytic therapy. The disadvantage is the delay in reperfusion therapy caused by on-call services. Primary PCI should not be performed in asymptomatic patients who present more than 12 hours after symptom onset and are hemodynamically and electrically stable.

PCI for AMI after thrombolysis for patients with continuing or recurrent myocardial ischemia is termed *rescue PCI.* Rescue PCI has resulted in higher rates of early infarct artery patency, improved regional infarct zone, wall motion, and greater freedom from adverse in-hospital and clinical events compared to a strategy of repeat thrombolysis. The REACT (Rescue Angioplasty Versus Conservative Treatment of Repeat Thrombolysis) trial was a randomized study that demonstrated significantly lower MACCE rates at 1 year in patients randomized to rescue PCI

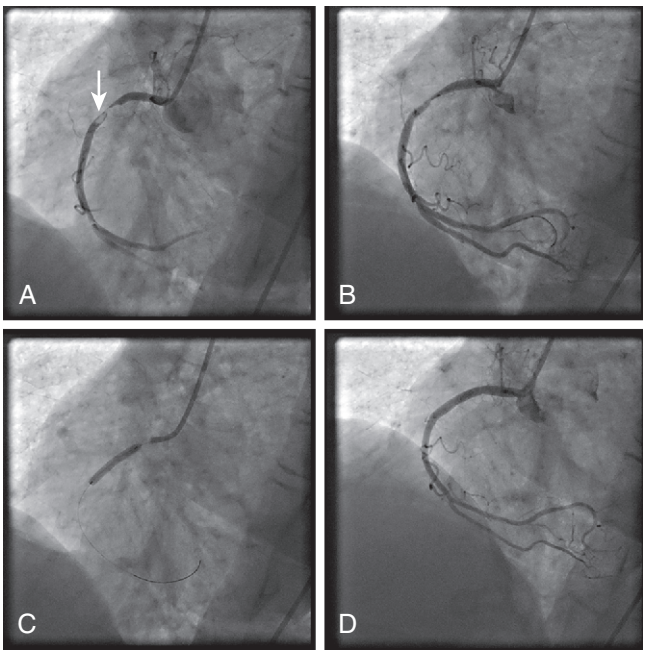

Figure 12-4 Angiograms of patient with acute inferior myocardial infarction (MI) with thrombus in the right coronary artery (RCA) (*top left,* **A**). **B** shows post balloon dilation, **C,** during stent implantation, and **D,** final result with no significant residual narrowing. (Courtesy of Drs. Wil Suh and Igor Palacios.)

after failed thrombolysis. Improvement in the TIMI grade flow from 2 to 3 may offer additional clinical benefit.

PCI in AMI patients immediately after successful thrombolysis (called *facilitated PCI*) has shown no benefit with regard to salvage of jeopardized myocardium or prevention of reinfarction or death. In some studies, this approach was associated with increased adverse events, including bleeding, recurrent ischemia, emergency coronary artery surgery, and death. Routine PCI immediately after thrombolysis may increase the chance of vascular complications at the access site and hemorrhage into the infarct related vessel wall (Table 12-6).

In contrast to trials of facilitated PCI, in which PCI occurred within 2 hours after thrombolysis at a PCI-capable facility, two recent trials (CARESS-in-AMI and TRANSFER-AMI) have addressed the management of patients who present to a non-PCI facility and receive thrombolytics. In these trials, ST-segment elevation MI patients with any high-risk features (e.g., anterior MI, extensive or >2 mm ST-segment elevation or depression, congestive heart failure, or low ejection fraction) were randomized to immediate transfer to a PCI-capable facility for planned PCI (within 6 hours), or to transfer only if rescue PCI was required. Patients transferred immediately after thrombolysis for a PCI had a reduction in

Table 12-6

Key Points for Acute Myocardial Infarction PCI

1. Prepare for complications such as heart block, hypotension, and arrhythmia. Venous access is helpful for delivery of ACLS medications and if temporary pacing is required.
2. Consider aspiration or rheolytic thrombectomy for large amount of thrombus.
3. Balloon-dilate and then observe for no reflow.
4. Stent, observe, and treat no reflow.
5. Insert pulmonary artery catheter, intra-aortic balloon pump, or temporary pacemaker to assist future management in the coronary care unit.

MACCE, with a number needed to treat of 16-17 in both trials, and demonstrated no increase in bleeding. As a result, PCI performed as part of a pharmacoinvasive strategy for high-risk AMI patients has received a IIa ACC/AHA guideline recommendation.

Technical Considerations for PCI in AMI

Anticoagulation (also see Chapter 5)

As AMI always involves thrombosis with both thrombin and platelet activation, the simultaneous use of both antithrombotic and antiplatelet agents is required. Dual oral antiplatelet therapy with aspirin and a thienopyridine (e.g., clopidogrel) is mainstay therapy. Heparin is traditionally used with glycoprotein receptor IIb/IIIa inhibitors, although the benefit of IIb/IIIa inhibitors may be limited in patients preloaded with clopidogrel. Higher doses of heparin are associated with increased bleeding.

The HORIZONS-AMI trial demonstrated that monotherapy with bivalirudin, a direct thrombin inhibitor, was associated with a significant reduction in bleeding complications as well as a significant reduction in mortality when compared to the combination of heparin and IIb/IIIa inhibitor. Premedication with dual oral antiplatelet therapy is necessary. The downside of using bivalirudin is that there is no reversal antidote.

Rapid Angiography in AMI

Although there is pressure to achieve a door-to-balloon time <90 minutes, complete diagnostic angiography of the entire coronary arterial system is recommended. Based on which artery the electrocardiogram suggests is the culprit artery, the operator should first perform angiography of the non–infarct-related artery with a diagnostic catheter, followed by angiography of the infarct-related artery with a guiding catheter. Findings on angiography may influence the decision of whether or not hemodynamic support will be needed for PCI or whether CABG may be a more appropriate strategy.

Before angiography, the operators should anticipate proceeding to intervention and thus initiate the procedure with a 6F or larger arterial sheath. The operator may anticipate a need for venous access so that a pulmonary artery balloon-tipped catheter for hemodynamic monitoring and/or a temporary pacemaker can be inserted. Additional arterial access in the contralateral femoral artery with a 5F sheath may be useful if hypotension is likely to require balloon pump support.

High-Risk Multiple-Vessel PCI

Multiple-vessel PCI approaches a series of stenoses one at a time, using any and all methods applicable to simple and complex single-vessel PCI. Multivessel stenting compares favorably with surgical revascularization in patients with low or intermediate angiographic complexity (i.e., Syntax scores <33). However, it appears that freedom from cardiovascular events is directly related to completeness of overall revascularization.

Abdominal angiography should be performed before beginning PCI to identify patients who are not candidates for intra-aortic balloon placement. All stents, guiding catheters, wires, and sheaths should be selected beforehand, and alternative equipment and support supplies (e.g., intravenous dopamine) should be ready for immediate use. An IABP or Impella LV support device may be inserted prophylactically or be available on standby for immediate insertion for hypotension or shock. Evidence favoring for the prophylactic insertion of support devices is lacking, but preparation for the need for rapid institution of support is prudent.

Cardiogenic Shock

The highest clinical risk factor associated with PCI is cardiogenic shock. Despite recent advances in pharmacotherapy, the incidence of

Table 12-7

Key Points for Cardiogenic Shock PCI

1. Establish systolic pressure >80 mm Hg. Use dopamine, norepinephrine, intra-aortic balloon pump, Impella.
2. Use intubation as required sooner rather than later.
3. Use rapid approaches for PCI as in acute myocardial infarction.
4. Anticipate VT/VF. Use amiodarone, cardioversion, intubation, and cardiopulmonary resuscitation as needed.
5. Dilate and stent essential lesion(s) and if not stabilized, treat remaining ischemic related lesions.
6. If possible, limit duration of procedure in lab. Stabilize the patient and manage clinically in coronary care unit.

PCI, percutaneous coronary intervention; *VT/VF,* ventricular tachycardia/ventricular fibrillation.

cardiogenic shock as a complication of acute coronary syndromes has not diminished over time, nor has its treatment decreased mortality rates.

Cardiogenic shock occurs in approximately 2% to 3% of patients presenting with non–ST-segment elevation acute coronary syndrome ("unstable angina" or "non-Q wave" MI) and approximately 5% to 8% of patients presenting with ST-segment elevation MI. Mortality for this condition is approximately 60%. At least 14 single-institution retrospective studies have suggested that, in patients with cardiogenic shock who underwent PCI, mortality was reduced. The average successful reperfusion rate in these studies was 73%. Mortality in such patients was 44%. Mortality was 30% if reperfusion was successful but 80% if reperfusion attempts were unsuccessful. The overall lower mortality rates with PCI reported in these studies were, however, potentially subject to selection bias, in that cardiogenic shock patients with fewer comorbid conditions and those believed more likely to survive may have been preferentially selected to undergo cardiac catheterization and PCI.

The SHOCK trial provided randomized data of the role of PCI in patients with cardiogenic shock. In this multicenter trial, urgent revascularization was compared to initial medical stabilization in 302 patients with cardiogenic shock from AMI. In patients who underwent urgent revascularization, 64% had angioplasty and 36% were revascularized via CABG. At 30 days, the mortality was 46.7% and 56.0% for the revascularization and the medical therapy groups, respectively (P = NS). At 6 months, however, the mortality was significantly lower in the revascularized group (50.3% vs. 63.1%), and this difference remained significant at 1-year follow-up. Of note, in the prespecified group of patients older than 75 years, there was no benefit from revascularization. Based on the SHOCK trial and prior reports, PCI for elderly cardiogenic shock patients may not be beneficial (Table 12-7).

Pharmacologic Support

Pharmacotherapy must be implemented both prophylactically and during complications in high-risk PCI patients. To achieve this efficiently, at least one, and ideally two, large-bore functioning peripheral intravenous lines should be present in high-risk patients. Although discouraged in most routine PCI procedures (due to an increased risk of bleeding complications), femoral venous sheaths should be strongly considered in patients with a high risk of needing aggressive anti-ischemic, vasopressor, and/or inotropic support, or transvenous pacing.

Anti-ischemic Agents

Although nitroglycerin (intravenous or intracoronary) is commonly utilized during PCI, it has not been demonstrated to provide prolonged ischemic benefit. Nitroglycerin may, however, reduce coronary spasm

in selected situations. When using nitroglycerin, it is important to maintain an adequate margin of blood pressure (mean arterial pressure >70 mm Hg) so that transiently induced ischemia does not reduce blood pressure below a critical perfusion level (mean arterial pressure <60 mm Hg), leading to a downward ischemic spiral. High-risk PCI patients should be well hydrated before the procedure (i.e., adequate LV filling pressures) so that nitroglycerin does not cause an excessive decrease in blood pressure.

Beta blockers and calcium channel blockers may reduce local myocardial ischemia through a regional decrement in myocardial oxygen consumption. This benefit has little clinical impact, particularly in the era of brief balloon inflations and coronary stenting. Pretreatment with these agents may become counterproductive if the patient "crashes" during the high-risk PCI procedure, as these agents act as negative inotropes and/or vasodilators.

During high-risk PCI, operators should have immediate access to drugs that at least partially reverse the actions of beta blockers and calcium channel blockers. Calcium chloride (1 ampule; 13.6 mEq) may reduce some of the vasodilatory effects of calcium channel blockers and, perhaps to a lesser degree, the negative inotropic and negative chronotropic effects. Glucagon (1 mg) may partially reverse the actions of beta blockers.

Antiplatelet Agents (Oral)

Aspirin markedly decreases the incidence of abrupt vessel closure and is mandatory in all patients undergoing routine as well as high-risk PCI. In patients who have true aspirin allergy, pretreat with clopidogrel, either started several days before the procedure (75 mg daily) or given as a loading dose (300 mg) the night before (if possible) or early on the morning of the procedure (at least 6 hours preprocedure). Patients pretreated with clopidogrel hours to days before their procedure (in those who are also being treated with aspirin) have a lower incidence of complications than those not receiving clopidogrel before the procedure. Although this would seem to suggest that all high-risk PCI patients should receive pre-procedure clopidogrel, the nature and design of these studies does not permit definite conclusions.

Clopidogrel increases the risk of bleeding during surgery and, as an irreversible platelet inhibitor, exerts its effects for days. Therefore, pending further data, in the high-risk patient where there is a reasonable chance that the patient may require emergency CABG, it may be prudent to defer clopidogrel pretreatment until PCI has been successfully completed. To decrease the incidence of subacute stent thrombosis, patients who do undergo successful PCI with coronary stent placement should be treated with clopidogrel (300-600 mg loading dose given immediately postprocedure if patient has not yet been treated with clopidogrel; then 75 mg daily) in addition to aspirin therapy.

Antiplatelet Agents (Intravenous)

The platelet glycoprotein IIb/IIIa inhibitors block platelet aggregation and adhesion. Intravenous administration of these agents usually leads to 80% to 95% inhibition of platelet aggregation. These agents reduce ischemic complications in patients undergoing PCI. The greatest absolute of risk reduction is in those with high-risk angiographic and/or clinical features. Therefore, these agents should be strongly considered during high-risk PCI. Chapter 5 provides detailed information on platelet glycoprotein IIb/IIIa inhibitor characteristics and dosing regimens.

Antithrombin Therapy

Unfractionated heparin is the antithrombin most commonly used during PCI. In current practice, in patients treated with IIb/IIIa inhibitors, the ACT should be maintained at 200 to 300 seconds. Although some patients undergo PCI on enoxaparin therapy, experience in high-risk

patients is limited, and the inability to monitor anti-Xa levels in the lab is a concern.

The direct thrombin inhibitor bivalirudin (Angiomax) has been compared to unfractionated heparin (with or without IIb/IIIa inhibitor) in the REPLACE-2, ACUITY, and HORIZONS-AMI studies. In REPLACE-2, bivalirudin and provisional IIb/IIIa therapy were associated with a lower risk of bleeding than unfractionated heparin and routine IIb/IIIa use, but were associated with a trend toward slightly higher rates of MI. Similarly, in the HORIZONS-AMI trial, there was reduction in bleeding events but an increase in acute stent thrombosis within 24 hours. Pretreatment with clopidogrel significantly reduced ischemic complications with bivalirudin use in the REPLACE-2 study. Based on these trials, it seems prudent to consider bivalirudin in patients at very high risk for bleeding complications but to preferentially utilize unfractionated heparin and IIb/IIIa therapy for patients at very high risk of ischemic complications.

Vasopressors and Inotropic Agents

For high-risk PCI, vasopressors and inotropic agents should be readily available. In very high–risk PCI procedures, at least one vasopressor agent should be premixed and available for immediate infusion (Table 12-8). Commonly used vasopressors include dopamine and norepinephrine.

Dopamine produces primarily renal and splanchnic vasodilation at low doses, exerts a positive inotropic and chronotropic effect at moderate doses, and exerts a vasoconstrictive effect at higher doses. A starting dose in symptomatic hypotensive patients is 5 mcg/kg/min. A higher starting dose (10 mcg/kg/min) can be considered in the severely hemodynamically compromised patient.

Norepinephrine can be given either via intermittent intravenous boluses or continuous infusion. In our laboratory, for high-risk PCI, we always have premixed intermittent boluses of norepinephrine (2.5–5 mcg) available. This produces rapid improvement in blood pressure, is easily titratable, and has a relatively short half-life.

If necessary, dobutamine may be considered for inotropic support. However, because as a beta-receptor agonist it can also lead to peripheral dilation, it is not ideal for the hypotensive patient. Usual doses of dobutamine are 2.5 to 10 mcg/kg/min.

Table 12-8

Medications and Dosing Regimens for Arrhythmias and Hypotension During High-Risk PCI

Bradycardia
• Atropine 0.5–1.0 mg—can repeat as indicated every 3–5 min up to total dose of 2.0 mg
Stable Ventricular Tachycardia
• Amiodarone—can administer in one of two regimens, as dictated by clinical setting —Regimen 1: 150 mg over 10 min, followed by infusion rate of 1 mg/min —Regimen 2: 300 mg IV over 10 min after dilution in 20–30 mL fluid—can give additional 150-mg boluses in similar manner if indicated • Lidocaine 1.0–1.5 mg/kg IV bolus—can give additional boluses of 0.5–0.75 mg/kg IV as indicated, up to total dose of 3.0 mg/kg
Pulseless Ventricular Tachycardia/Ventricular Fibrillation
• Epinephrine 1 mg IV bolus—can repeat every 3–5 min • Amiodarone 300 mg IV rapid infusion after dilution in 20–30 mL fluid—can give additional 150-mg rapid infusions in similar manner as indicated • Lidocaine 1.0–1.5 mg/kg IV bolus—can give additional boluses of 0.5–0.75 mg/kg IV as indicated, up to total dose of 3.0 mg/kg

Transvenous Pacing

Prophylactic pacemaker insertion is determined by (1) the patient's risk of developing a bradyarrhythmia and (2) the patient's ability to tolerate the arrhythmia should it occur. Conditions in which a prophylactic pacemaker may be considered include:

- Severe fascicular block
- Heart block greater than first degree
- Marked sinus bradycardia
- PCI involving the (dominant) artery supplying the arteriovenous node (particularly if the right coronary artery is occluded during a left circumflex artery PCI and vice versa).

A balloon-tipped pacing catheter reduces the potential for right ventricular perforation.

Hemodynamic Support

In patients with hypotension, mitral regurgitation, multivessel disease, or decreased left ventricular function, hemodynamic support should be instituted before the procedure begins. After successful PCI for acute infarction, IABP is associated with reduced recurrent ischemia. Other percutaneous hemodynamic support devices such as TandemHeart and Impella have been used for high-risk PCI, but the ease and speed of placing the IABP still makes it the most attractive device for AMI procedures.

Intra-aortic Balloon Pump (IABP)

IABP counterpulsation increases myocardial oxygen supply and decreases myocardial oxygen demand. IABP balloon inflation at the onset of diastole (at the dicrotic notch on the central arterial pressure tracing) results in augmentation of diastolic pressure, which increases coronary artery (and systemic) perfusion. Deflation of the balloon just before systole (end diastole on the arterial pressure tracing) results in decreased ventricular afterload, which decreases myocardial oxygen consumption and increases cardiac output. These effects are illustrated in Figure 12-5. An example of the arterial waveform during correctly timed intra-aortic balloon counterpulsation is shown in Figure 12-6.

With an IABP, there appears to be a 20% to 30% increase in cardiac output in patients with low-output syndromes and a significant

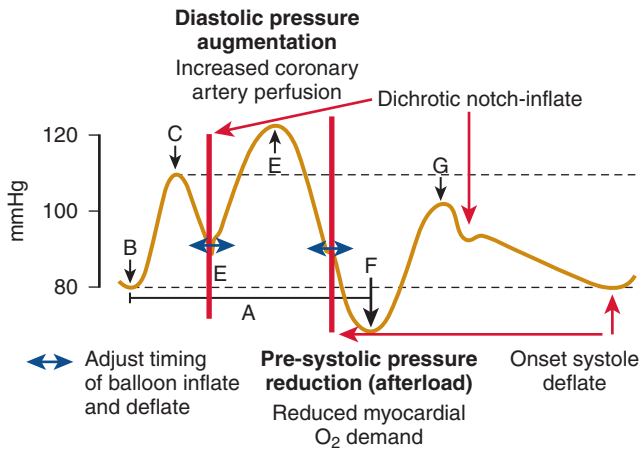

Figure 12-5 Arterial waveforms during 2:1 intra-aortic balloon pump (IABP) counterpulsation. **A,** one complete cardiac cycle; **B,** unassisted aortic end-diastolic pressure; **C,** unassisted aortic systolic pressure; **D,** dicrotic notch (balloon inflation); **E,** diastolic augmentation; **F,** assisted aortic end-diastolic pressure; **G,** assisted systole.

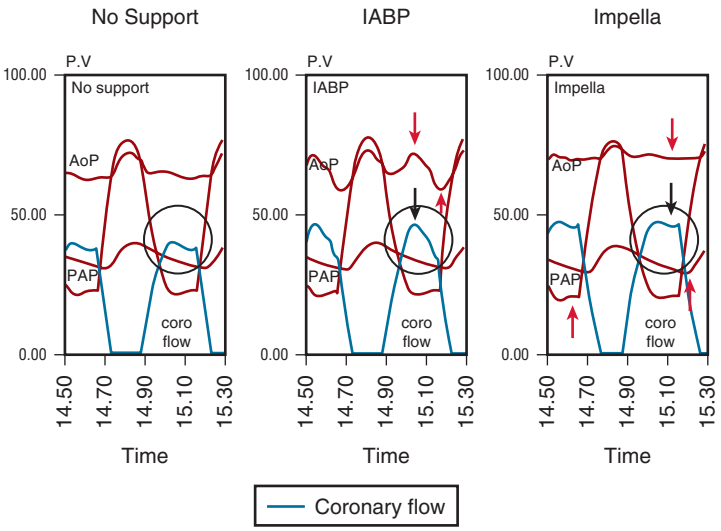

Figure 12-6 Hemodynamic simulator-predicted coronary flow enhancement (*blue line*) with the Impella (*right*) compared to the baseline (*left*) and intra-aortic balloon pump (IABP) (*center*). Diastolic augmentation of IABP increases coronary artery perfusion while deflation of the balloon just before the onset of systole decreases afterload, which results in decreased myocardial oxygen demand, decreased cardiac workload, and increased cardiac output. Adapted from Hunziker 2006, as reproduced in Weber DM, Raess DH, Henriques J, Siess T. Principles of Impella Cardiac Support. *Cardiac Interventions Today*, August/September 2009: 3–16.

amount of afterload reduction as demonstrated in reduction of mitral regurgitation. Direct measurement of coronary blood flow during IABP function has demonstrated augmentation in nondiseased and post-angioplasty vessels, but no increase in vessels distal to significant stenosis.

The indications and contraindications for IABP counterpulsation during high-risk PCI are shown in Table 12-9. Before a diagnostic cardiac catheterization or interventional procedure, the patient should be treated medically to optimize hemodynamics and reduce myocardial ischemia. Hypotension (not responding to volume loading or intravenous vasopressors) and medically refractory angina are important indications for IABP placement. Contraindications to IABP placement must be factored into decisions on whether to proceed with a high-risk PCI.

In unstable patients and very high–risk patients, an IABP may be required before proceeding with the catheterization; however, there is scant evidence that routine prophylactic IABP insertion reduces complications. In the BCIS-1 trial, 301 patients with low ejection fraction (EF) (<30%) and extensive myocardium at risk were randomized to routine or bailout IABP insertion, and no difference in MACCE was seen. Bailout IABP was required in 12% of control patients.

Routine IABP support after PCI is also not indicated. In a prospective randomized study of 1100 patients with AMI (437 of which were high risk), Stone *et al.* found that routine IABP support for 36 to 48 hours after PCI did not improve the combined end point of death, reinfarction, infarct-related artery reocclusion, stroke, new-onset heart failure, or sustained hypotension compared to patients in the control arm.

Although routine insertion may not be indicated, the ACC/AHA guidelines give IABP support a Class I recommendation for refractory cardiogenic shock, so the ability to rapidly initiate support during high-risk PCI is required.

Notes on the IABP insertion technique:

Recall that the normal puncture site should be about 2 cm below the inguinal ligament (or centered near the middle of the femoral head). For IABP insertion, a puncture slightly more proximal than a

Table 12-9

Indications and Contraindications for IABP Counterpulsation During High-Risk PCI

Indications for Prophylactic Balloon Pump Placement
• Severely depressed ejection fraction
• PCI of sole remaining or primary remaining coronary artery or bypass graft
• Unprotected left main coronary artery PCI (especially if the right coronary artery is occluded)
• Ongoing ischemia
• Intractable ventricular arrhythmia believed due to ischemia
• Hemodynamic instability
• Hypotension
• Cardiogenic shock
Indications for "Rescue" Balloon Pump Placement
• Hemodynamic instability, hypotension, or cardiogenic shock
• Intractable ventricular arrhythmia believed due to ischemia
• Abrupt vessel closure (particularly if TIMI 3 flow cannot be quickly restored)
Contraindications
• Severe iliac/femoral atherosclerotic disease or tortuosity
• Aortic dissection or aneurysm
• Moderate or severe aortic regurgitation
• Bleeding diathesis
• Bypass grafting to femoral arteries or aorta
• Patent ductus (augments the abnormal shunting)
• Sepsis

IABP, intra-aortic balloon pump; *PCI,* percutaneous coronary intervention; *TIMI,* thrombolysis in myocardial infarction.

standard femoral puncture for cardiac catheterization may be helpful. A puncture lower than the prescribed site may introduce the balloon into a superficial femoral artery too small to accept the large IABP catheter.

As discussed previously, iliac-femoral angiography (or distal aortic angiography with runoff) should be performed at the time of diagnostic catheterization, or at least, preceding high-risk PCI. The IABP balloon is inserted into either groin using standard Seldinger technique, as described in detail by Kern (2011). *The Cardiac Catheterization Handbook,* 5th edition. Some manufacturers are making small caliber or "sheathless" IABP balloon catheters, which are especially useful in the elderly and those with peripheral vascular disease. Fluoroscopic observation of the balloon inflated above the renal arteries confirms optimal placement.

Complications of IABP most commonly result from a low puncture site, perforation of the superficial femoral artery, or forceful advancement of the catheter damaging the arterial entry site. The most serious complication of IABP is lower extremity ischemia, which occurs in approximately 5% to 10% of patients. Prolonged intra-aortic balloon counterpulsation is also associated with hemolysis and platelet destruction, and thus the blood counts of patients should be closely monitored.

Despite the use of IABP during angioplasty in high-risk patients, there remains an in-hospital mortality of 6% to 19%, with a rate of vascular complications of 2% to 14%.

Impella LV Support Device

The Impella LV support device is an alternative to IABP and cardiopulmonary support. The Impella 2.5 is a minimally invasive, catheter-based cardiac assist device which directly unloads the left ventricle, reduces myocardial workload and oxygen consumption, and increases cardiac output and coronary and end-organ perfusion.

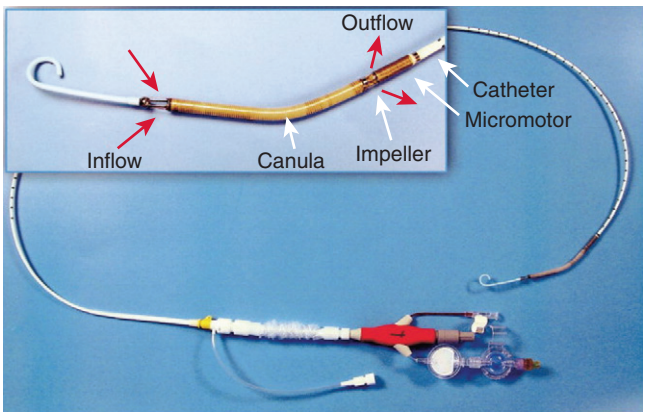

Figure 12-7 Impella system. 13F catheter is shown with ports for infusion to cool impeller. Insert shows the inflow and outflow ports with their protective cages, cannula structure, and impeller motor.

The Impella 2.5 can be inserted into the left ventricle over a 0.018-inch stiff guidewire through the femoral artery, across the aortic valve and into the left ventricle. The tip of the catheter has a "pigtail" that facilitates safe positioning in the left ventricle. The impeller motor draws blood into the cannula and expels it into the aorta, thereby generating pressure, and flows up to 2.5 L/min (Fig. 12-7). This compares with the IABP, which provides 0.2-0.4 L/min of support. A 13F femoral sheath is required for insertion of the Impella 2.5. Peripheral vascular disease and aortic valve disease are contraindications to the Impella.

Unloading of the LV by the Impella increases aortic and intracoronary pressure, hyperemic flow velocity, and coronary flow velocity reserve, and decreased microvascular resistance. The Impella-induced increase in coronary flow probably results from both an increased perfusion pressure and a decreased LV volume-related intramyocardial resistance.

Clinical trials comparing the IABP with the Impella 2.5 have demonstrated improvements in hemodynamic parameters but no improvements in survival or MACE. In the ISAR-SHOCK trial of 26 patients with AMI and cardiogenic shock, when compared with patients receiving IABP patients with Impella had increases in mean arterial pressure and cardiac index, and decreases in lactate levels, but no difference in 30-day mortality. Recently, the PROTECT-II trial of Impella 2.5 versus IABP for high-risk PCI was stopped halfway (305 patients) due to futility.

Despite these early setbacks, based on its relative ease of use and high level of circulatory support, the Impella remains a promising device for use in selected patients for high-risk PCI or refractory shock.

The TandemHeart Pump System

The TandemHeart percutaneous ventricular assist device is designed for short-term mechanical LV support. The TandemHeart involves the placement of a 21F catheter inserted into the left atria from the femoral vein via a transseptal puncture. Blood is withdrawn from the left atrium by an external centrifugal pump and infused into the femoral artery via a 14–19F catheter. The TandemHeart can provide up to 4.5 L/min of cardiac support. As with IABP and Impella, iliac-femoral angiography must be performed prior to canula insertion. Figure 12-8 shows the TandemHeart system.

Like the Impella, compared with the IABP the TandemHeart has been shown to improve hemodynamic parameters in two small trials. However, there is a high rate of complications with its use, including bleeding, tamponade, and vascular complications. The complexity of its insertion (30–45 minutes) and higher complication rate compared

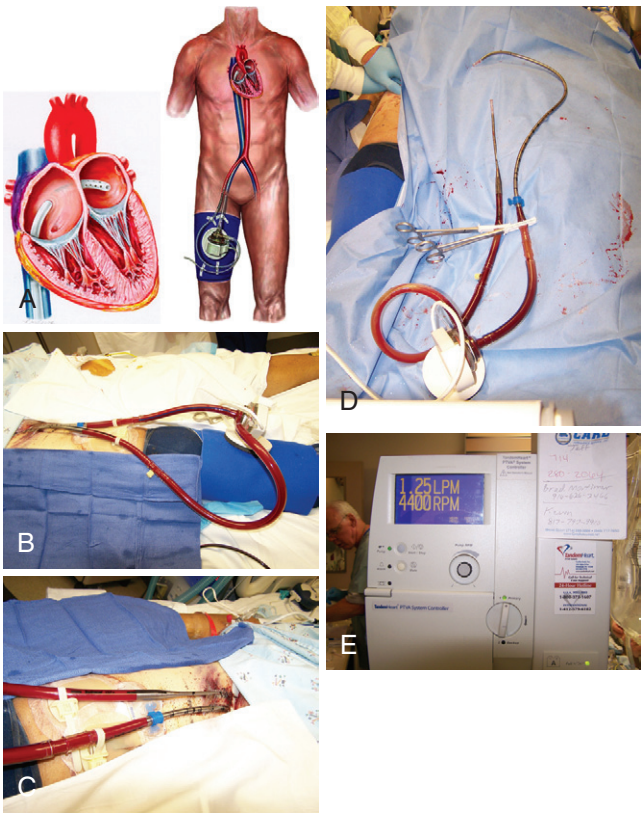

Figure 12-8 **A,** TandemHeart system. **B, C,** Arterial and venous canula system in right femoral artery and vein with centrifugal pump secured on thigh. **D,** Canula after removal from leg to show different lengths and sizes. **E,** TandemHeart console.

with the Impella or IABP likely will limit the role of the TandemHeart to patients with aortic valve disease, or to severe cardiogenic shock refractory to IABP support.

Management of Complications in High-Risk PCI Patients

Hypotension

Hypotension may result from myocardial ischemia, coronary perforation with cardiac tamponade, arrhythmia, contrast- or medication-induced anaphylaxis, or acute occult bleeding (e.g., retroperitoneal hematoma). This differential diagnosis of hypotension must be evaluated quickly and therapy directed to the cause of the hypotension. After the first step of aggressive fluid resuscitation with normal saline, support blood pressure with inotropic agents such as dopamine (initial starting infusion rate of 5 to 10 mcg/kg/min depending on degree of hypotension) or bolus dose norepinephrine (2.5–5 mcg IV boluses as needed). An emergent echocardiogram will help assess for cardiac tamponade or valvular dysfunction. The treatment of anaphylaxis is discussed below (Table 12-10).

Bradyarrhythmias and Heart Block

Bradyarrhythmias may occur as a result of ischemia of the sinus node (most commonly supplied via the right coronary artery). Symptomatic sinus bradycardia can initially be treated with atropine (0.5–1.0 mg IV),

Table 12-10

Treatment of Severe Anaphylactoid Reactions: Recommendations From the Society of Cardiac Angiography and Interventions

Initial Pharmacological Therapy
• Epinephrine 10 mcg/min IV until desired blood pressure response, then 1–4 mcg/min to maintain desired blood pressure, given simultaneously with large volumes of normal saline • Diphenhydramine 50–100 mg IV • Hydrocortisone 400 mg IV
If unresponsive to initial therapy:
• H_2-blocker therapy —Cimetidine 300 mg in 20 mL normal saline administered IV over 15 min —Ranitidine 50 mg in 20 mL normal saline administered IV over 15 min • Dopamine 2–15 mcg/kg/min IV infusion

with repeat doses every 3 to 5 min as indicated, up to a usual total maximal dose of 2.0 mg (see Table 12-8).

Heart block may occur as a result of occlusion of the "dominant" artery (either the right coronary artery or the left circumflex artery) that supplies the atrioventricular node. Although there are no data to support this, intuitively one might believe that a patient with abrupt closure of the right coronary artery is more likely to develop heart block if the left circumflex artery is already occluded (and vice versa). Complete heart block with a slow ventricular escape rhythm should not be treated with atropine. Dopamine (initial infusion 5 mcg/kg/min) may, in certain circumstances, ameliorate sinus bradycardia or heart block.

Patients on beta blockers or calcium channel blockers can be treated with glucagon (1 mg) or calcium chloride (1 ampoule, 13.6 mEq), although the effects of such therapy are more theoretical than established. For both bradycardia and heart block, severely symptomatic patients can be treated with transcutaneous or transvenous pacing. Ultimately, the treatment for these conditions includes restoration of the compromised coronary artery blood flow.

Ventricular Tachyarrhythmias

Ventricular tachycardia (VT) and ventricular fibrillation (VF) may result from severe myocardial ischemia. Patients who develop VT and are hemodynamically stable can first be treated with intravenous antiarrhythmic therapy, specifically amiodarone and lidocaine (see Table 12-8). Stable patients not responding to antiarrhythmic therapy can be treated with synchronized cardioversion (beginning at 100 J and increasing stepwise up to 360 J as necessary).

Patients who develop unstable or pulseless VT or VF have been treated with a precordial thump. However, immediate defibrillation is indicated (at 200 J biphasic energy). Chest compressions are indicated to support coronary perfusion pressure and should be continued with minimal interruptions. Patients who do not convert after defibrillation should be treated with epinephrine (1 mg IV, repeated every 3–5 min) or vasopression (40 units IV × 1) and repeat defibrillation afterward. Patients who still do not respond can then be treated with amiodarone (300 mg IV bolus after dilution in 20 mL fluid) or lidocaine (1.0–1.5 mg/kg IV bolus). The advanced cardiac life support (ACLS) algorithm for the treatment of pulseless VT/VF is presented in Figure 12-9.

During resuscitative efforts, coronary access, as well as guidewire position across the lesion, should be maintained to complete the ultimate coronary recanalization. It is unknown how defibrillation affects the coronary artery with the guidewire in place.

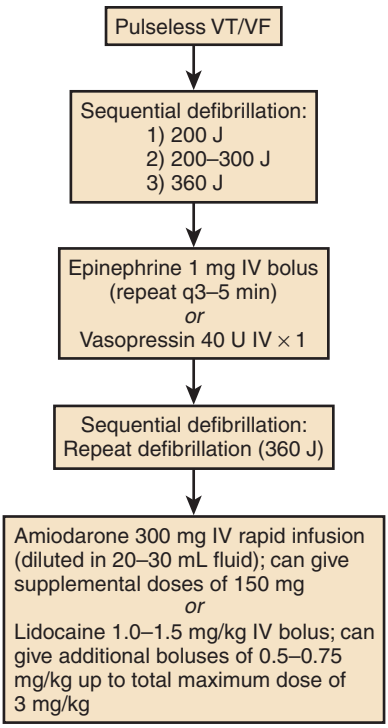

Figure 12-9 An ACLS algorithm for the treatment of pulseless ventricular tachycardia (VT) or ventricular fibrillation (VF).

Pulselessness

Asystole is usually the result of extensive myocardial ischemia. Asystole should be confirmed in two leads because it can be difficult to distinguish fine ventricular fibrillation from asystole. If the diagnosis is unclear, one should assume that fine ventricular fibrillation is present and treat it accordingly. Atropine (1 mg) and epinephrine (1 mg) should be given and can be repeated every 3 to 5 minutes if necessary. Metabolic abnormalities, including hyperkalemia or severe preexisting acidosis, may contribute to the arrhythmia and may respond to the use of buffers.

Electromechanical dissociation (also called pulseless electrical activity [PEA]) is a condition that is almost uniformly fatal unless the underlying cause can be identified and immediately treated. General treatment includes the use of epinephrine (1 mg every 5 min). Bicarbonate may be considered. If PEA or asystole is refractory, emergency cardiopulmonary bypass may be considered.

Underlying causes of PEA include:

1. Hypovolemia, especially resulting from bleeding.
2. Pericardial tamponade, especially in patients with AMI recent cardiac biopsy, recent endocardial pacer insertion, or uremia; if tamponade is suspected, emergency pericardiocentesis is warranted.
3. Enhanced vagal tone in patients with ischemic heart disease. Consider this whenever the heart rate is inappropriate for the degree of hypotension. Atropine is indicated.
4. Massive pulmonary embolism.
5. Tension pneumothorax, especially in patients on ventilators or in patients with central venous access above the diaphragm. Emergency needle decompression is indicated.

Pulmonary Edema

Pulmonary edema during high-risk PCI may be the result of ischemia-induced depression of myocardial function and/or volume overload due to intravenous fluids. Initial measures may include administration of furosemide 20 to 40 mg intravenously (which initially acts as a venodilator well before its diuretic actions become significant) and/or intravenous nitroglycerin (which also acts primarily via venodilation). Inotropic support can be considered utilizing dobutamine (2.5 advanced cardiac life support (ACLS 10 mcg/kg/min). Patients refractory to these measures, particularly those with severely compromised left ventricular function, may require intubation, IABP support, or intravenous afterload reduction.

Anaphylactoid Reactions

Anaphylactoid reactions to contrast agents may include hypotension and shock. Although such reactions are exceedingly rare during PCI procedures, the operator should understand the treatment of this life-threatening condition. Recommendations by the Society for Cardiac Angiography and Intervention for treatment include intravenous epinephrine with large volumes of normal saline, diphenhydramine, hydrocortisone, and, if unresponsive to therapy, an H_2 blocker and dopamine. Specific dosing regimens are given in Table 12-10.

Abrupt Vessel Closure and Thrombosis (Fig. 12-10)

Abrupt vessel closure is an uncommon complication since the introduction of stents. It is often due to dissection in association with intracoronary thrombosis. In these cases, immediate relief of the dissection with stenting of the inflow flap is indicated. In other cases, acute stent thrombosis may occur as a result of an inadequate anticoagulation or antiplatelet regimen, or from suboptimal stent deployment.

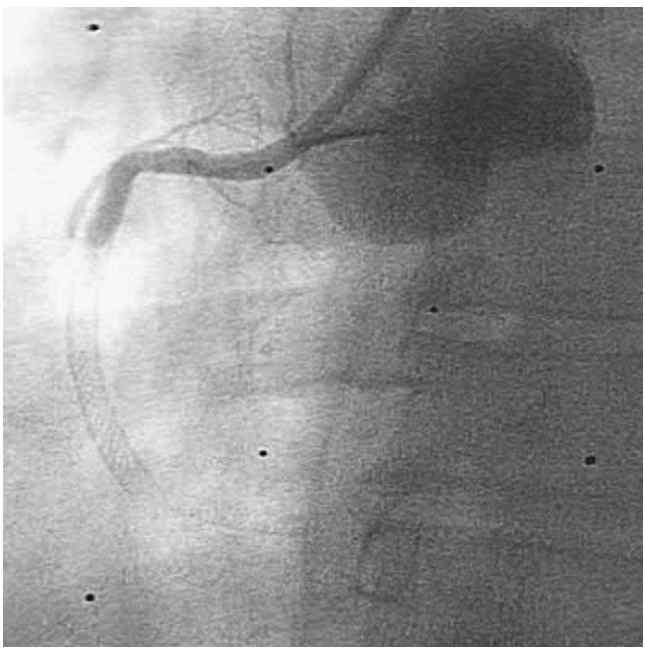

Figure 12-10 Angiogram of acute stent thrombosis.

Although multiple studies have demonstrated that initiation of platelet IIb/IIIa inhibitor therapy at the time of PCI decreases ischemic complications, there are no data on the degree of benefit from the "bailout" use of platelet IIb/IIIa inhibitors once a complication such as abrupt vessel closure has occurred. Nevertheless, the pathophysiology of abrupt vessel closure supports initiating platelet IIb/IIIa therapy. In patients who are may require emergency CABG, the operator should balance the benefit of IIb/IIIa inhibitors against the possibility that CABG will be delayed or precluded by their use.

In addition to thrombosis aspiration, the operator must ensure adequate anticoagulation. ACT should be checked in patients being treated with either unfractionated heparin or bivalirudin and, if it is low, the heparin dose should be repeated. The ACT does not reflect the degree of anticoagulation in patients who have been treated with enoxaparin. Patients who have received a subcutaneous dose of enoxaparin (1 mg/kg) within the previous 8 hours usually have therapeutic levels of anti-factor-Xa activity. Those who have received their last dose 8 to 12 hours prior to intervention may benefit from an additional dose (0.3 mg/kg IV, if they have not already received this "booster" dose at the time of PCI).

The data on administration of intracoronary thrombolytic therapy are conflicting. This route is rarely used in current practice, particularly given the availability of platelet IIb/IIIa inhibitors.

Slow Flow and No Reflow

Slow flow refers to the phenomenon in which blood flow (as assessed by contrast dye flow) in a treated and non-occluded artery decreases from TIMI 3 to TIMI 1 or 2 after intervention. *No reflow* refers to TIMI grade 0 flow after PCI. The occurrence of slow flow during PCI is usually accompanied by severe chest pain, ST-segment elevations, and sometimes hemodynamic and/or electrophysiological deterioration. The mechanisms for no reflow or slow reflow are only partially understood but appear to involve a variable combination of:

- Microcirculatory vasoconstriction
- Plugging from fibrin, platelets, thrombus, and leukocytes
- Microcirculatory structural damage or edema

Treatment recommendations for slow or no reflow are as follows. Given the contribution of platelets and thrombus to slow flow (and no reflow), rescue or emergent administration of a platelet IIb/IIIa inhibitor is prudent (despite few if any data). The ACT should be rechecked and additional boluses of antithrombin therapy given if the ACT is subtherapeutic. (However, there are again no data that show that this benefits slow flow or no reflow.)

Vasodilator therapy directed at the coronary microcirculation can include one or more of the following agents administered intracoronary:

- Verapamil (125–250 mcg boluses)
- Nitroglycerin (100–200 mcg boluses)
- Nitroprusside (50–100 mcg boluses)
- Adenosine (18–40 mcg boluses)

Preparation and administration of these medications is given in Table 12-11.

Atherosclerotic emboli appear to play a major role in the slow-flow phenomenon during treatment of degenerated saphenous vein grafts. Distal protection devices (FilterWire, Spider) decrease the incidence of complications during saphenous vein graft PCI. A proximal protection device (Proxis) has been shown to reduce complications on the same order as distal protection devices and is indicated when graft anatomy precludes distal protection. These devices should be considered for prophylactic use when possible. However, there is no role for these devices once atheroembolization has occurred.

Table 12-11

Preparation and Administration Guidelines for Intracoronary Vasodilators Used for "Slow Flow" and "No Reflow"

Verapamil
• Usually comes in preparation of 5 mg/2 mL • Take 1 mL of verapamil (2.5 mg) and mix in 19 mL = 2.5 mg/20 mL = 125 mcg/mL • Administer 250 mcg–2 mL
Adenosine
• Usually comes in preparation of 6 mg/2 mL • Take 1 mL (3 mg) of adenosine and mix in 500 mL D_5W = 3 mg/500 mL = 6 mcg/mL • Administer 24 mcg (4 mL) boluses
Nitroglycerin
• Usually comes in concentration of 5 mg/mL • Take 0.2 mL (1 mg) and mix in 10 mL = 100 mcg/mL • Administer 200 mcg (2 mL)
Nitroprusside
• Usually comes in preparation of 50 mg/2 mL (25 mg/mL) • Take 2 mL (50 mg) and mix in 500 mL bag = 100 mcg/mL • Administer 100 mcg (1 mL) condition

Coronary Perforation

Coronary perforation becomes of major clinical significance when it leads to cardiac tamponade. Treatment begins with prolonged inflation of a PTCA (percutaneous transluminal coronary angioplasty) balloon at the perforation site. Placement of a coronary stent graft to "seal" the perforation may ultimately be needed. Proximal balloon inflation relative to the perforation may also work provided there are no large distal collaterals. Continued brisk flow from a perforation despite these interventions may require placement of a covered stent graft (Jomed).

Treatment of cardiac tamponade requires pericardiocentesis. Reversal of anticoagulation may facilitate hemostasis at the site of perforation and efflux of blood into the pericardium, but this benefit must be balanced against the risk of thrombosis occurring in the coronary artery being treated.

Major Bleeding

Decisions as to whether to "reverse" anticoagulation and antiplatelet therapy in patients with major bleeding complications must balance the risk of further bleeding with the risk of coronary arterial thrombosis. The anticoagulant effects of unfractionated heparin can be reversed with protamine sulfate (1 unit protamine per 100 units heparin). Protamine should be used with caution in patients who have received NPH insulin or are postvasectomy. Protamine partially reverses the anticoagulant effects of low-molecular-weight heparin. Patients who have been treated with subcutaneous enoxaparin can be treated with 1 mg protamine per 1 mg enoxaparin when the last enoxaparin dose is within 0 to 8 hours of PCI, and 0.5 mg protamine per 1 mg enoxaparin when the last enoxaparin dose was 8 to 12 hours prior to PCI. Protamine is not effective in patients treated with a direct thrombin inhibitor (such as bivalirudin).

Both aspirin and clopidogrel are irreversible platelet inhibitors whose antiaggregatory effects can be reversed only with platelet transfusion. As abciximab is an antibody fragment that binds tightly to the IIb/IIIa receptor, and as less free abciximab molecules are in circulation

than molecules of tirofiban or eptifibatide, the effects of abciximab on platelet aggregation are reversed to a greater degree with platelet transfusion than those of either tirofiban or eptifibatide.

Summary

Careful evaluation of angiographic, patient-related, and clinical factors can identify the high-risk PCI patient. Use of pharmacologic and mechanical therapies may serve to decrease the risks of major complications during high-risk PCI. Adequate planning and laboratory preparation are essential to quickly address complications when they occur. Familiarity with both pharmacotherapy and mechanical therapy is essential when attempting high-risk PCI.

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13

Nonangiographic Coronary Lesion Assessment: FFR, IVUS, OCT, NIRS

MORTON J. KERN · JOHN M. HODGSON · ARNOLD H. SETO

The rationale for using nonangiographic lesion assessment tools arises from two principles: (1) that revascularization (via percutaneous coronary intervention [PCI] or coronary artery bypass graft [CABG]) is justified best by the presence of ischemia, which depends on the hemodynamic significance of a lesion; and (2) that the coronary angiogram frequently fails to establish the hemodynamic significance of coronary stenoses with accuracy, particularly the intermediately narrowed (between 30% and 80% diameter stenosis) lesions. This limitation of angiography has been documented repeatedly by poor correlations to stress testing and is attributable to the anatomical complexity of the atherosclerotic lumen (Fig. 13-1).

Coronary angiography can only produce a two-dimensional silhouette image of the three-dimensional vascular lumen. Angiographic accuracy is further limited by the inability to identify diffusely "diseased" and "normal" vessel segments. In addition, unlike intravascular ultrasound (IVUS), angiography does not provide vascular wall detail sufficient to characterize plaque size, length, and eccentricity. The eccentric lumen produces conflicting degrees of angiographic narrowing when viewed from different angulations, causing uncertainty related to lumen size and its impact on coronary blood flow. Moreover, there are at least six morphologic features that determine resistance to flow, most of which can be measured from the angiogram or even IVUS (Figs. 13-1, 13-2). Additional artifacts, including contrast streaming, branch overlap, vessel foreshortening, calcifications, and ostial origins, further contribute to uncertain angiographic lesion interpretation.

The uncertainty of angiographic lesion assessment is a significant clinical problem. When evidence of ischemia is lacking, before stenting all intermediate lesions indiscriminately, the functional significance of a stenosis by fractional flow reserve should be identified as the first step in PCI. After the lesion is shown to be flow limiting, the anatomical and morphologic features of the stenosis and reference vessel segment can be assessed by IVUS. More detail on structure and composition can be obtained by optical coherence tomography (OCT) and, in the future, a determination of the plaque character (e.g., lipid pool content with near-infrared spectroscopy [NIRS]) may assist in appropriate stenting in regions beyond the most stenotic segment.

Thus, the three most common technologies for nonangiographic coronary lesion assessment tools available at this time are the (1) coronary pressure wire, (2) IVUS, and (3) OCT. The Doppler flow wire as a research tool to study the microcirculation and new imaging modalities such as NIRS imaging will be addressed briefly.

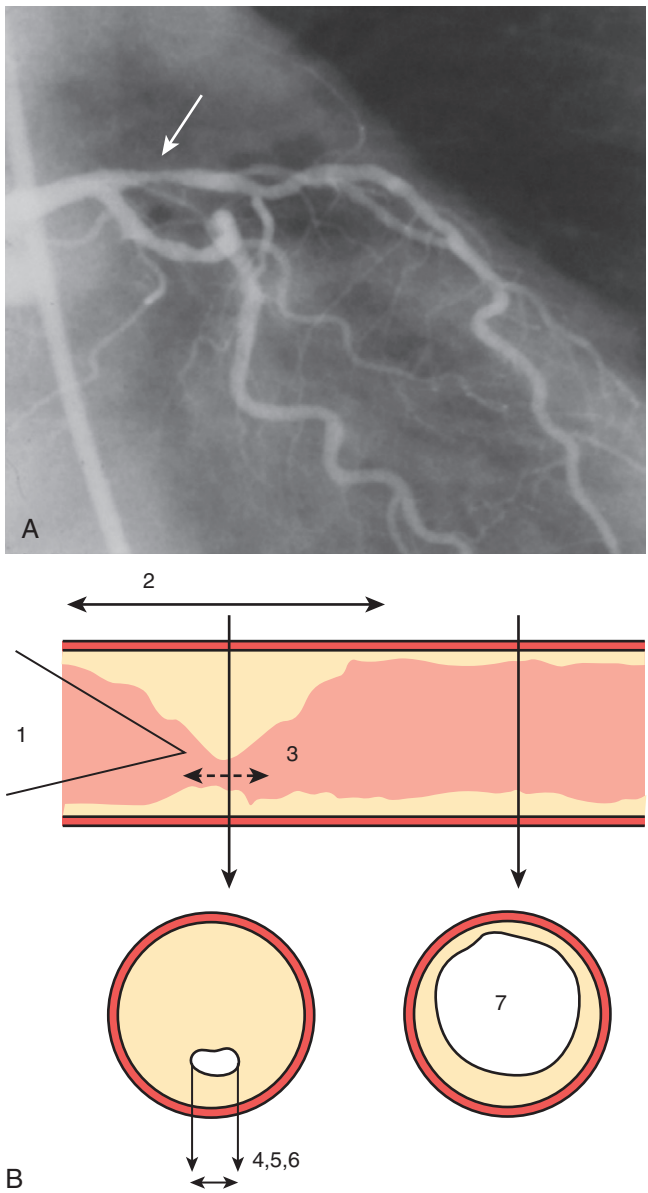


Figure 13-1 **A,** Frame from cineangiogram of left coronary artery (LCA) with an intermediate left anterior descending (LAD) lesion. Arrow indicate LAD narrowing. **B,** Diagram of regions of stenosis resistance causing poststenotic pressure loss. (*1*) Entrance angle, (*2*) Length of disease, (*3*) Length of stenosis, (*4*) Minimal lumen diameter, (*5*) Minimal lumen area, (*6*) Eccentricity of lesion, (*7*) Area of reference vessel segment.

Coronary Pressure and Fractional Flow Reserve

Pijls and De Bruyne developed and validated an index for determining the physiologic impact of coronary stenoses, called the fractional flow reserve (FFR). FFR is measured as the ratio of mean distal coronary pressure divided by the mean proximal aortic pressure during maximal hyperemia.The coronary pressure beyond the stenosis is measured with a 0.014-inch guidewire with a high-fidelity pressure transducer

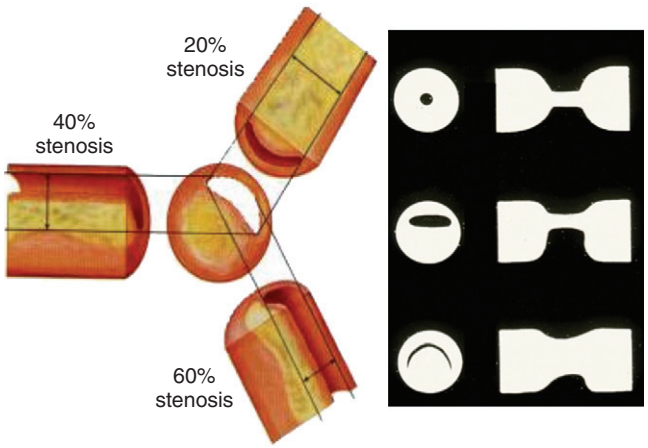


Figure 13-2 Diagram of angiographic projections demonstrating markedly different diameter narrowings illustrating the greatest limitation of angiography for eccentric lesions (*left*). Orthogonal projections of different orifice configurations that complicate determination of physiologic impact of narrowing (*right*).

mounted 3 cm from the tip of the wire, at the junction of the radiopaque and radiolucent segments. A full discussion of the FFR method and results can be found elsewhere (see Suggested Readings).

Concept of FFR

FFR is defined as the ratio of maximal hyperemic flow across an epicardial coronary stenosis compared with maximal hyperemic flow in the same artery without the stenosis. FFR is expressed as the percentage of normal maximal flow through the stenotic artery. FFR can be separately computed for the myocardium (FFR_m), the epicardial coronary artery (FFR_c), and the collaterals, (FFR_{collat}), based on translesional pressure measured during maximal hyperemia and in some cases coronary occlusion wedge pressure. Figures 13-3 and 13-4 illustrate the concept and data used to derive FFR. Table 13-1 lists the calculations for FFR and Table 13-2 lists the thresholds for clinical applications of FFR.

FFR differs from absolute coronary flow reserve (CFR, maximal flow/basal flow) since it does not depend on basal flow levels but is computed only at maximal flow (hyperemia). FFR has several advantages over CFR:

1. It has an absolute normal value of 1.0 for every artery, every patient.
2. It is not affected by changing hemodynamics or status of the microcirculation.
3. It is specific for epicardial coronary stenoses.

Technique of FFR

FFR can be easily measured using a 5F or 6F guide catheter and either of two available pressure wire systems (St. Jude Medical, Minneapolis, MN or Volcano Therapeutics, Rancho Cordova, CA). After diagnostic angiography with a catheter seated in the coronary ostium, the steps to measure FFR are as follows:

1. The pressure wire is connected to the system's pressure analyzer and calibrated and zeroed outside the body.
2. Anticoagulation intravenous (IV) heparin (usually 40 U/kg) and intracoronary (IC) nitroglycerin (100–200 µg bolus) are administered.
3. The wire is advanced through the guide to the coronary artery. The pressure wire signal and the guide pressure are matched

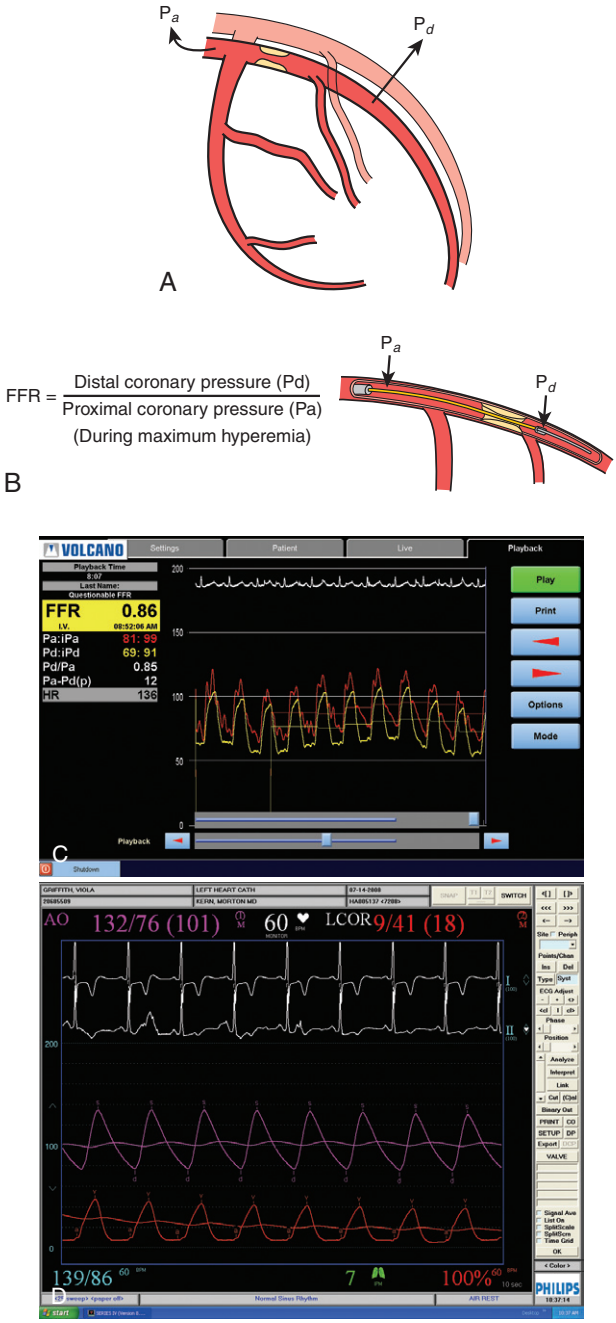
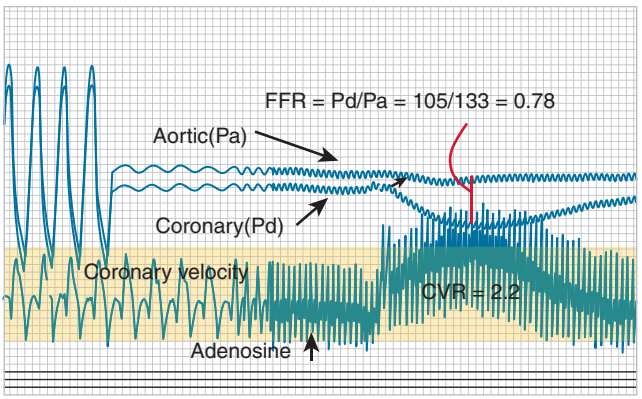


Figure 13-3 **A,** Diagrams of the theory of fractional flow reserve (FFR). FFR is the ratio of maximal myocardial perfusion in the stenotic territory divided by maximal hyperemic flow in that same region in the hypothetical case the lesion was not present (dotted artery behind solid lines). FFR represents that fraction of hyperemic flow that persists despite the presence of the stenosis. This ratio of two flows is calculated solely from the ratio of mean coronary pressure (Pd) divided by mean aortic pressure (Pa) provided both pressures are recorded under conditions of maximal hyperemia. Pa is the same along the length of the normal vessel. FFR is defined as myocardial flow (Qs) across stenosis/myocardial flow (Qn) without stenosis. To derive FFR, assume resistance = P/Q, then flow, Q = P/R, and that Qs/Qn = (Pd/Rs)/(Pa/Rn), where Rs, Rn is resistance in stenotic and normal bed which are identical at maximal hyperemia. If Rs = Rn, then Qs/Qn = Pd/Pa, which is FFR = Qs/Qn = Pd/Pa. **B,** Pressure signals used to calculate FFR. Pa and Pd are recorded at rest and then during hyperemia induced by adenosine, in this case intracoronary. The nadir of distal pressure is used for the FFR calculation. Shown under the yellow band is the flow velocity signal, which illustrates that the peak flow corresponds to the nadir of distal pressure. **C,** Screen from FFR monitor showing colored signals of Pa (*red*) and Pd (*yellow*) for FFR of 0.86. **D,** Hemodynamic display of FFR across severe stenosis with FFR of 0.40. Note very low distal pressure.



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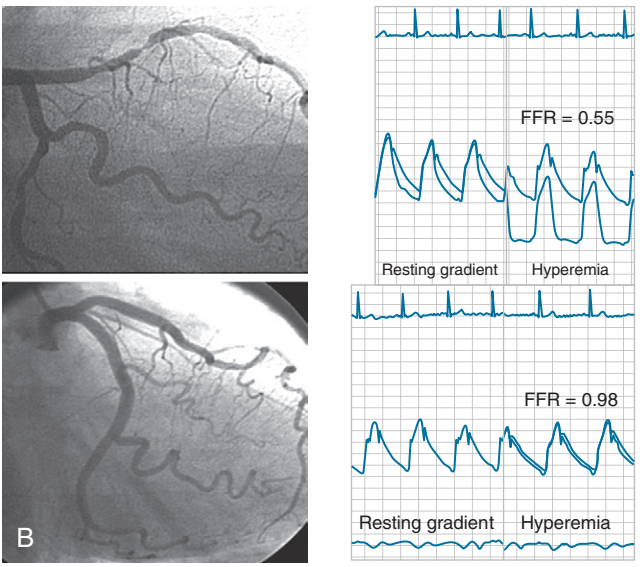


Figure 13-4 **A** (top pannel) pressure and flow velocity signals used to measure FFR. CVR = coronary vasodilatory reserve. **B** (lower pannel) Translesional pressure measurements before (*top*) and after (*bottom*) LAD stent placement. Resting gradients do not always indicate severity of lesion. Prestent FFR = 0.55 despite small resting gradient. Poststent FFR = 0.98, a normal value. (Courtesy of Dr. Bernard DeBruyne.)

Table 13-1

Calculations of Fraction Flow Reserve From Pressure Measurements Taken During Maximal Arterial Vasodilation

Myocardial fraction flow reserve (FFR_{myo}):
$FFR_{myo} = 1 - \Delta P/P_a - P_v$
$= P_c - P_v/P_a - P_v$
$= P_c/P_a$
Coronary fractional flow reserve (FFR_{cor}): $FFR_{cor} = 1 - \Delta P(P_a - P_w)$
Collateral fractional flow reserve (FFR_{coll}): $FFR_{coll} = FFR_{myo} - FFR_{cor}$

Note: All measurements are made during hyperemia except P_w.
P_a, mean aortic pressure; P_c, distal coronary pressure; ΔP, mean translesional pressure gradient; P_v, mean right atrial pressure; P_w, mean coronary wedge pressure or distal coronary pressure during balloon inflation.
From Pijls NHJ, van Som AM, Kirkeeide RL, *et al.* Experimental basis of determining maximum coronary, myocardial, and collateral blood flow by pressure measurements for assessing functional stenosis severity before and after percutaneous transluminal coronary angioplasty. *Circulation* 1993;87:1354–1367.

Table 13-2

Physiologic Criteria Associated With Clinical Applications

Indication	CFR	rCFR	HSRv*	FFR
Ischemia detection	<2.0	<0.8	>0.8	<0.75
Deferred angioplasty	>2.0	—	—	>0.80
End point of angioplasty	>2.0–2.5†	—	—	>0.90
End point of stenting	—	—	—	>0.90

*mm Hg/cm/sec
†With <35% diameter stenosis.
CFR, coronary vasodilatory reserve, *FFR,* fractional flow reserve, *rCFR,* relative CFR, *HSRv,* hyperemic stenosis resistance index.
From Kern MJ, Lerman A, Bech JW, *et al.* Physiological assessment of coronary artery disease in the cardiac catheterization laboratory: a scientific statement from the American Heart Association Committee on Diagnostic and Interventional Cardiac Catheterization, Council on Clinical Cardiology. *Circulation* 2006;114;1321–1341.

(i.e., equalized, also called normalized) before crossing the stenosis. By early convention, the guidewire transducer was positioned at the end of the guide catheter. In fact, it does not matter exactly where the wire is in relation to the guide catheter or coronary ostium except that both should be in the aortic sinus when equalizing the signals.

4. The wire is then advanced across the stenosis about 2 cm distal to the coronary lesion.
5. Maximal hyperemia is induced with IV adenosine (140 μg/kg/min) or IC bolus adenosine (20–30 μg for the right coronary artery, 60–100 μg for the left coronary artery). Alternative hyperemic agents are rarely used but include IC papaverine (10 mg), nitroprusside (50–100 μg), or ATP (50–100 μg). FFR is measured at 2 min for IV adenosine and at 15 to 20 seconds after IC adenosine.
6. The ratio of the mean distal pressure to mean proximal pressure during maximal hyperemia is calculated as the FFR. An FFR <0.80 has a strong ischemic correlation and is an indication to proceed with PCI. If a PCI is deemed necessary, it can be performed using the pressure wire as the angioplasty guidewire. After the procedure, FFR can be remeasured to assess the adequacy of the intervention.
7. Finally, at the end of the procedure (either the assessment or the PCI), the pressure wire should be pulled back into the guide to confirm equal pressure readings, or the lack of pressure wire drift. Table 13-2 shows the criteria for FFR and associated clinical situations.

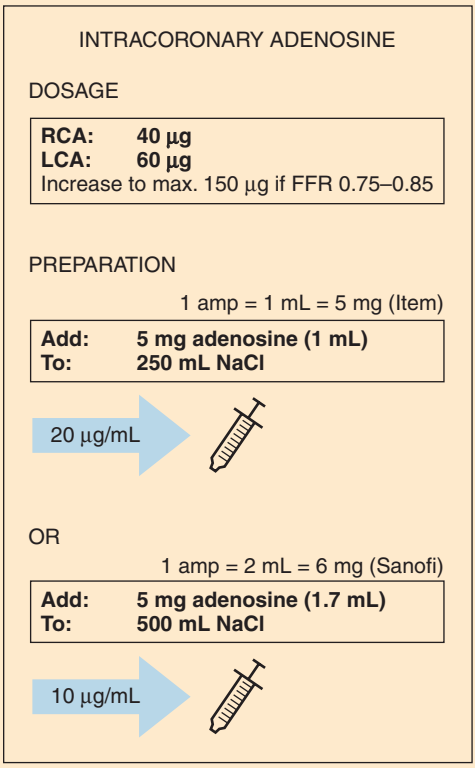
Coronary Hyperemia for FFR

IV adenosine is weight based, operator independent, and the preferred method of inducing hyperemia. By providing a prolonged hyperemic stimulus, IV adenosine allows for a slow pullback of the pressure wire, useful for identifying the exact location of the pressure dropoff or the presence of diffuse disease. It is also required for assessment of aortoostial narrowings to permit maximal coronary flow without guide catheter obstruction (Box 13-1, Table 13-3A, Box 13-2, Table 13-3B).

While IC adenosine is equivalent to IV infusion for determination of FFR in a large majority of patients, in a small percentage of cases, coronary hyperemia may be suboptimal with IC adenosine. Jeremias *et al.* compared IC (15–20 μg in the right, and 18–24 μg in the left coronary artery) with IV adenosine (140 μg/kg/min) in 52 patients with 60 lesions. There was a strong and linear relationship between IC and IV adenosine ($r = 0.978$ and $P < 0.001$). The mean measurement difference for FFR was -0.004 ± 0.03. In 8.3% of stenoses, FFR with IC adenosine differed by 0.05 or more compared with IV adenosine, suggesting an inadequate hyperemic response.

BOX 13-1

Intracoronary Adenosine



(Modified from Volcano Therapeutics.)

Pitfalls of FFR

As a cautionary note, catheters with side holes should not be used to measure FFR, as proximal pressure gradients may occur, complicating distal gradient evaluations. Larger guide catheters can partially occlude the coronary ostium as hyperemia is induced, impairing maximal flow. Removing the guide catheter from the coronary ostium after giving the hyperemic agent will avoid this pitfall.

The errors in the performance of accurate FFR involve hemodynamic artifacts and failure to induce maximal hyperemia. Tables 13-4, 13-5, and 13-6 list these problems. Figures 13-5, 13-6, 13-7, and 13-8 show artifacts that may produce false FFR readings.

Use of FFR for Specific Angiographic Subsets

Intermediate Coronary Lesion

FFR assists the operator in deciding to treat or not treat coronary lesions based on ischemia. Some operators are concerned that not stenting intermediate but hemodynamically insignificant lesions will result in harm to the patient later. This concern is unfounded based on the 5-year outcomes of the DEFER study. The DEFER study randomized 325 patients scheduled for PCI into three groups: a deferral group ($n = 91$) in whom an FFR was ≥ 0.75 and medical therapy was continued; or despite an FFR > 0.75, the PCI performance group ($n = 90$), in which the lesions were treated with stents. The third group was the reference group ($n = 144$) who had an FFR < 0.75 and stents were placed as

Table 13-3A

Intracoronary Adenosine	
Effects:	
· Peak effect:	≤10 seconds after administration.
· Duration of plateau:	<20 seconds.
Side Effects:	
· AV block.	Short and rapidly transient. Usually after injection in the RCA.
Comments:	
Hyperemia generally	
· Just before inducing hyperemia, give nitrates, if appropriate for the patient, as per regular coronary intervention.	Avoids performing measurements influenced by spasm.
I.C. bolus injection generally	
· Guide catheters with side holes should NOT be used.	Unknown amounts of the drug may spill into the aorta.
· Guide catheters that are too large (tight) for the ostium should NOT be used.	Pressure damping may occur. This can be recognized by a ventricularized aortic pressure curve.
I.C. adenosine specifically	
· NO pullback curve possible.	No steady-state hyperemia. Overestimation of FFR (underestimation of stenosis severity) may occur if only mean pressure is recorded.
· Interruption of aortic pressure (Pa) should be as short as possible.	If too long, hyperemia will be over before aortic pressure can be measured again.
· Successive measurements using IC adenosine may be performed.	The effects of adenosine wear off quickly. Wait between measurements just long enough for the previous dose to cease to have effect.
· Ensure that maximum effects of the hyperemic stimulus have been achieved.	In case of suboptimal hyperemia, overestimation of FFR (underestimation of stenosis severity) may occur. If FFR 0.75-0.85, check for pitfalls and repeat measurement, increase dose or switch to I.V. adenosine or another drug. In 10-15% of patients only submaximum hyperemia can be achieved using I.C. adenosine. FFR may be underestimated due to e.g., caffeine and theophylline (adenosine are inhibited by adenosine receptor antagonists, such as methylxanthines).

(Modified from Volcano Therapeutics.)

planned. For the deferred and performed groups, the event-free survival was the same (80% and 73% respectively, $P = 0.52$), and both were significantly better than in the reference group (63%, $P = 0.03$). The composite rate of cardiac death and acute myocardial infarction (MI) in the deferred, performed, and reference groups was 3%, 8%, and 16% respectively ($P = 0.21$ for deferred vs. performed and $P = 0.003$ for reference vs. both of the deferred and performed groups) (Fig. 13-9). The percentage of patients free from chest pain on follow-up was not different between the deferred and performed groups. The 5-year risk of cardiac death or MI in patients with a normal FFR is <1% per year and is not decreased by stenting. Treating patients with intermediate lesions assisted by FFR is associated with a low event rate, comparable to event rates in patients with normal noninvasive testing. Figure 13-10 is an example of FFR for intermediate lesion assessment. Similar outcomes for deferment of lesions with FFR > 0.80 were also reported in patients in the FAME study described in the next section.

BOX 13-2

Intravenous Adenosine

INTRAVENOUS ADENOSINE*

DOSAGE

IV infusion: 140 µg/kg/min
Increase to 180 µg/kg/min if FFR 0.75–0.85

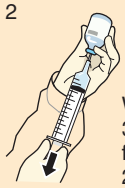
PREPARATION

1 vial = 30 mL = 90 mg adenosine
1 saline bag = 100 mL NaCl

1

WITHDRAW
40 mL NaCl from
100 mL saline IV
bag and discard.

2



WITHDRAW
30 mL (= 90 mg adenosine)
from vial/ampules (use 15 x
2 mL vials or 3 x 10 mL vials).

3

ADD
30 mL (= 90 mg adenosine)
to saline bag.

LABEL
and hang IV bag
90 mg in 90 mL normal saline.

1 mg/mL

DOSAGE TABLE Adenosine intravenous infusion 1 mg/mL (90 mg/90 mL) 140 µg/kg/min = 8.4 mg/kg/hr			DOSAGE TABLE Adenosine intravenous infusion 1 mg/mL (90 mg/90 mL) 180 µg/kg/min = 10.8 mg/kg/hr		
Weight (kg)	(lbs)	Infusion rate (mL/hr)	Weight (kg)	(lbs)	Infusion rate (mL/hr)
45	99	378	45	99	486
50	110	420	50	110	540
55	121	462	55	121	594
60	132	504	60	132	648
65	143	546	65	143	702
70	154	588	70	154	756
75	165	630	75	165	810
80	176	672	80	176	864
85	187	714	85	187	918
90	198	756	90	198	972
95	209	798	95	209	1026
100	220	840	100	220	1080
105	231	882	105	231	1134
110	243	924	110	243	1188
115	254	966	115	254	1242
120	265	1008	120	265	1296
125	276	1050	125	276	1350
130	287	1092	130	287	1404
135	298	1134	135	298	1458
140	309	1176	140	309	1512

*The dosage for Adenosine Triphosphate (ATP) is the same for adenosine.

(Modified from Volcano Therapeutics.)

Table 13-3B

Intravenous Adenosine

Effects:	
• Peak effect:	≤2 minutes after administration in central vein.
• Duration of effect:	Effect disappears within 2 minutes after infusion stopped.
• *The effects of Adenosine Triphosphate (ATP) are condsidered equivalent to adenosine.*	
Side Effects:	
• AV block.	Rarely.
• Do NOT use in patients with bronchoconstrictive or bronchospastic lung disease (e.g., asthma).	Risk for bronchospasm.
• Decrease in blood pressure and increase in heart rate by 10-20%	A slight increase in blood pressure often precedes the decrease.
• Unpleasant angina-like or burning sensation in chest or throat during infusion.	Disappears rapidly after ending the infusion. Harmless and does not indicate ischemia. Inform and reassure the patient in advance.
Comments:	
Hyperemia generally:	
• Just before inducing hyperemia, give nitrates, if appropriate for the patient, as per regular coronary intervention.	Avoids performing measurements influenced by spasm.
I.V. infusion generally	
• Use volume-controlled infusion pump with sufficient capacity.	Inadequate infusion may result in suboptimal hyperemia.
• Infuse in femoral or large antecubital vein. If brachial vein is used for infusion, avoid kinking of brachial vein caused by bending of the patient's forearm. Patient's arm should be extended.	Improper infusion may result in fluctuations in pressure.
I.V. adenosine specifically	
• Pullback curve possible.	Steady-state hyperemia.
• Instruct patient to breath normally. The patient should avoid Valsalva-like maneuvers.	Decrease of venous return = pressure signal fluctuations—overestimation of FFR.
• Ensure that maximum effects of the hyperemic stimulus have been achieved.	In case of suboptimal hyperemia, overestimation of FFR (underestimation of stenosis severity) may occur. If FFR 0.75-0.85, check for pitfalls and repeat measurement, increase dose, or switch to another drug. Only submaximum hyperemia can be achieved in approximately 8% of patients using IV adenosine. FFR may be underestimated due to e.g., caffeine and theophylline (adenosine is inhibited by adenosine receptor antagonists, such as methylxanthines).

(Modified from Volcano Therapeutics.)

Table 13-4

Reasons for Nonischemic Fractional Flow Reserve (FFR) Despite an Apparently Severe Stenosis

Physiologic Explanations
Stenosis hemodynamically nonsignificant despite angiographic appearance
Small perfusion territory, old myocardial infarction, little viable tissue, small vessel
Abundant collaterals
Severe microvascular disease (rarely affecting FFR)
Interpretable Explanations
Other culprit lesion, diffuse disease not focal stenosis
Chest pain of noncardiac origin
Technical Explanations
Insufficient hyperemia
Guiding catheter related pitfall (deep engagement, small ostium, side holes)
Electrical drift
Actual False Negative FFR
Acute phase of ST-segment elevation myocardial infarction
Severe left ventricular hypertrophy
Exercise-induced spasm

From Koolen JJ, Pijls NHJ. Coronary pressure never lies. *Catheter Cardiovasc Interv* 2008;72:248–256.

Table 13-5

Factors Involved in Fractional Flow Reserve Accuracy

Hemodynamic Artifacts or Errors

1. Signal drift. This is rare and can be determined by careful observation of pressure waveform and presence of dicrotic notch. If suspicious, check with re-matching of signals on pullback to aortic location.
2. Incorrect height of pressure transducer.
3. Loss of pressure due to guidewire introducer. Remove and tighten Touhey-Borst valve.
4. Damping of pressure by guiding catheter. Observe aortic pressure wave. Use IV adenosine and keep catheter in aorta, not coronary ostium.
5. Guiding catheters with side holes produce pseudostenosis across the catheter into the coronary ostium. Use IV adenosine and keep catheter in aorta, not coronary ostium.
6. Pressure damping with 4F or 5F catheters if not flushed with saline. Contrast media viscosity will produce unreliable aortic pressure wave.

Failure to Induce Hyperemia

A. Adenosine, intracoronary bolus administration
   1. Submaximum stimulus in some patients. Very rare; if suspected select alternative agent (e.g., nitroprusside, papaverine, adenosine triphosphate [ATP]).
   2. Failure to capture pressure change at peak hyperemia. Maximum gradient underestimated when calculated from mean signal, unless it is taken on beat-to-beat basis.
   3. No pullback curve possible with bolus administration.
   4. Guiding catheter failure to seat and delivery drug.
   5. Guide catheter flow obstruction.
   6. Incorrect dose mix or dilution.

B. Adenosine, IV adenosine
   1. Check infusion, pump system, and lines.
   2. Infuse through central vein.
   3. Avoid Valsalva maneuver during infusion.
   4. Decrease of blood pressure by 10%–15%.
   5. Burning or angina-like chest pain during infusion. This is a harmless effect and does not indicate ischemia. IV adenosine not to be used in patients with severe obstructive lung disease (bronchospasm).
   6. If peripheral vein is used, avoid kinking of arm/elbow.
   7. Avoid Valsalva maneuvers.

Table 13-6

Most Common Reasons for False Negative and False Positive Fractional Flow Reserve (FFR)

False Negative
Pressure Damping
No hyperemia
Wrong drug, not mixed not delivered (IV) or side holes
False Positive
Small artery, small territory
pressure signal drift
Cautionary considerations: pathophysiologic conditions theoretically limiting FFR
Left Ventricular Hypertrophy
Exercise-Induced Vasoconstriction
Microvascular Disease and Myocardial Infarction

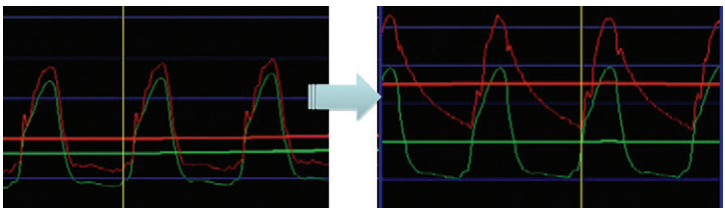


Figure 13-5 Example of pressure signal damping (*left*) and after withdrawal of guide catheter (*right*).

Multivessel Disease PCI

The FAME (FFR vs. Angiography for Multivessel Evaluation) trial by Tonino *et al.* compared a physiologically guided PCI approach (FFR-PCI) to a conventional angiographic guided PCI (Angio-PCI) in patients with multivessel coronary artery disease (CAD). A total of 1005 patients with multivessel CAD undergoing PCI with drug-eluting stents were enrolled. Operators identified all lesions by visual angiographic appearance (>50% diameter stenosis) to be treated in advance of randomization to a stenting strategy. For the FFR-PCI group ($n = 496$), all lesions had FFR measurements and only those with FFR < 0.80 were stented. For the Angio-PCI group ($n = 509$), all lesions identified were stented. Clinical characteristics and angiographic findings were similar in both groups with average SYNTAX scores of 14.5 (indicating low-intermediate risk patients).

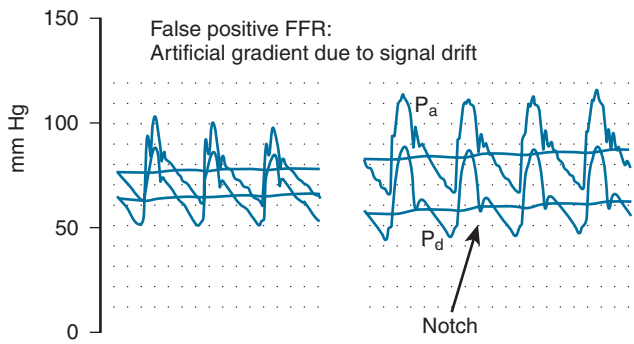


Figure 13-6 Example of pressure signal drift as a cause for false positive fractional flow reserve (FFR). Note preservation of dicrotic notch on distal pressure indicating normal transmission of pressure.

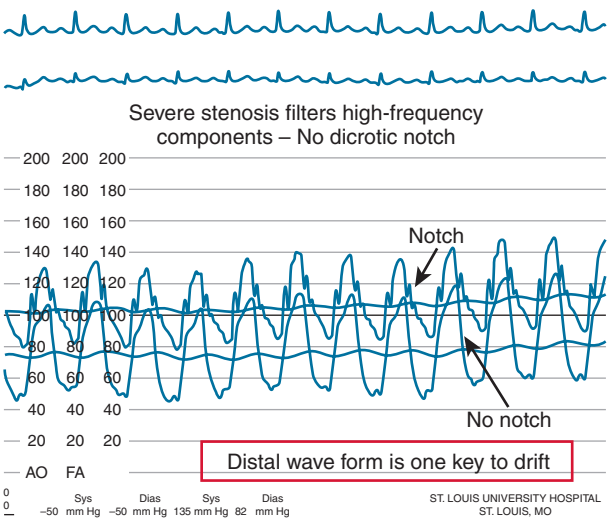


Figure 13-7 Example of distal pressure across severe stenosis. Note distal pressure wave configuration with wide pulse pressure and loss of dicrotic notch indicative of severe stenosis.

Compared with the Angio-PCI group, the FFR-PCI group used fewer stents per patient (1.9 ± 1.3 vs. 2.7 ± 1.2, $P < 0.001$) and less contrast (272 mL vs. 302 mL, $P < 0.001$), had a lower procedure cost (US$ 5,332 vs. US$ 6,007, $P < 0.001$), and had a shorter hospital stay (3.4 vs. 3.7 days, $P = 0.05$). More importantly, the 2-year rates of mortality or MI were 13% in the Angio-PCI group compared with 8% in the FFR-PCI group ($P = 0.02$). Composite rates of death, nonfatal MI, or revascularization were 22% and 18%, respectively ($P = 0.08$). For lesions deferred on the basis of FFR > 0.80, the rate of MI was only 0.2% and the rate of revascularization was 3.2 % after 2 years (Fig. 13-11).

FAME demonstrated that PCI guided by FFR in patients with multivessel CAD significantly reduces mortality and MI at 2 years when compared with standard angiography-guided PCI. A related cost-effectiveness evaluation showed that FFR-guided PCI not only improved outcomes, but did so at a significantly lower cost.

Significance of Abnormal FFR after PCI

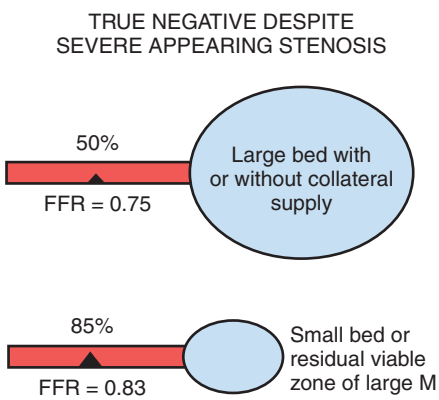


Figure 13-8 Illustration of bed size on fractional flow reserve (FFR). Because flow is related to myocardial bed size, a moderate lesion (*top,* 50%) serving a large territory could have low FFR (0.75) while a more severe appearing lesion (*bottom,* 85%) serving a small bed (such as after infarction) could have high FFR (0.83).

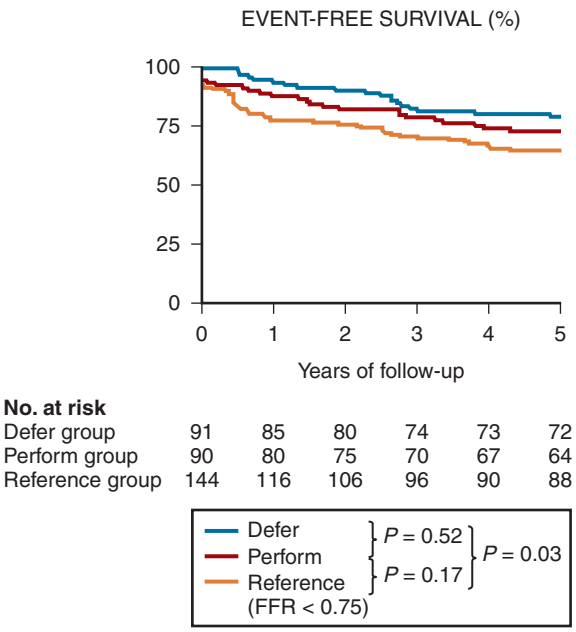


Figure 13-9 The DEFER study results. Kaplan-Meier survival curves for freedom from adverse cardiac events during 5 years of follow-up for the defer group (*blue line*), treatment group (*red line*), and reference group (*black line*). (From Pijls NHJ *et al. J Am Coll Cardiol* 2007;49:2105–2111.)

FFR after bare-metal stenting predicts adverse cardiac events at follow-up. Pijls *et al.* examined 750 patients with angiographically satisfactory PCI using postprocedural FFR. At 6 months, 76 patients (10%) suffered an adverse event. FFR immediately after stenting was the most significant independent variable related to all types

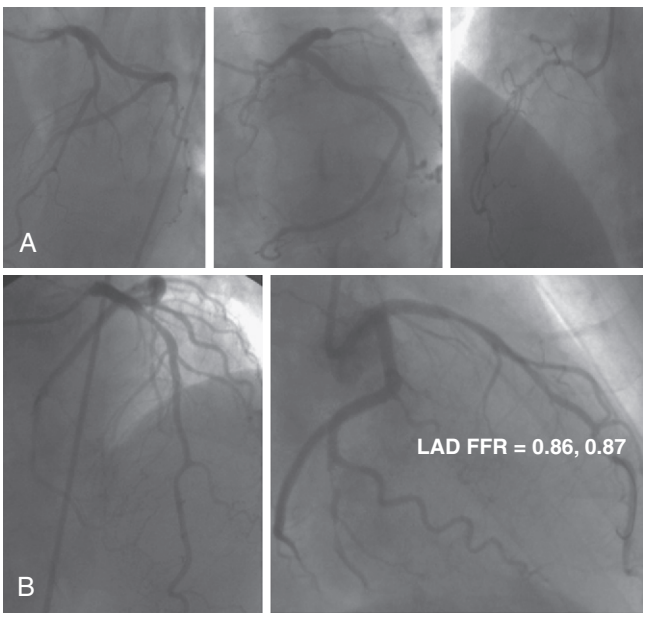


Figure 13-10 Angiograms of patient with intermediate LAD and severe OM1 branch lesion. **A,** LAO view of LAD (*left*), LAO caudal view of LCA (*middle*), and occluded RCA of 2 years ago (*right*). **B,** RAO cranial shows intermediate LAD (*left*), severe OM1 branch stenoses (*right*). FFR of LAD is 0.86, 0.87.

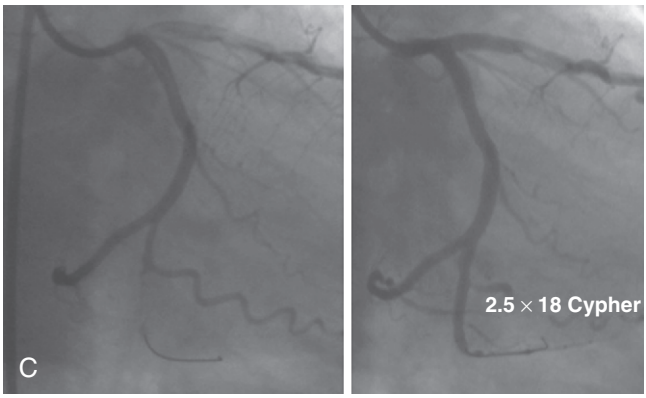


Figure 13-10, cont'd **C,** Pre-PCI of OM1 (*left*) and post-PCI (*right*). Patient became pain free and did well. *FFR,* fractional flow reserve; *LAD,* left anterior descending; *LAO,* left anterior oblique; *LCA,* left coronary artery; *OM1,* first obtuse marginal; *PCI,* percutaneous coronary intervention; *RAO,* right anterior oblique; *RCA,* right coronary artery.

of events. In 36% of patients, FFR normalized (>0.95) and patients had an event rate of only 5%. In 32% of patients with postprocedure FFR between 0.90 and 0.95, the event rate was 6%. In the remaining 32% with FFR <0.90, the event rate was 20%, and was 30% among those patients with FFR <0.80. These data suggest that both edge stent abnormalities (e.g., occult dissection) and diffuse disease are associated with a worse long-term outcome after bare-metal stenting. Outcome correlations with FFR after drug-eluting stenting have not yet been reported.

Left Main Stenosis

Accurate assessment of the hemodynamic significance of left main coronary lesions is of critical importance when patients face possible CABG surgery. Because of the inherent limitations discussed earlier, angiography alone may not be reliable in intermediate left main stenoses, and FFR is useful for decision making.

Numerous studies of FFR support its use in equivocal left main CAD (Table 13-7). Most recently, Hamilos *et al.,* in a large multicenter prospective trial, examined FFR and 5-year outcomes in 213 patients with an angiographically equivocal left main coronary artery stenosis. When FFR was >0.80, patients were treated medically or another stenosis was treated by coronary angioplasty (nonsurgical group; $n = 138$). When FFR was <0.80, CABG surgery was performed (surgical group; $n = 75$). The 5-year survival estimates were 90% in the nonsurgical (FFR > 0.80) group and 85% in the surgical (FFR < 0.80) group ($P = 0.48$). The 5-year event-free survival estimates were 74% and 82% in the two groups, respectively ($P = 0.50$) (Fig. 13-12). Of note, only 23% of patients with a diameter stenosis >50% had a hemodynamically significant left main stenosis as measured by FFR. Table 13-7 lists studies with FFR for left main stenosis.

Figure 13-13 shows an example of FFR in multivessel CAD.

Ostial- and Side-Branch Lesions

Ostial narrowings of side branches or newly produced narrowing in side branches within stents ("jailed" branches) are particularly difficult to assess by angiography because of their overlapping orientation relative to the parent branch, stent struts across the branch, and image foreshortening (Fig. 13-14*A*). Koo *et al.* compared FFR to angiography in 97 "jailed" side-branch lesions (vessel size >2.0 mm, percent stenosis >50% by visual estimation) after stent implantation. No lesion with

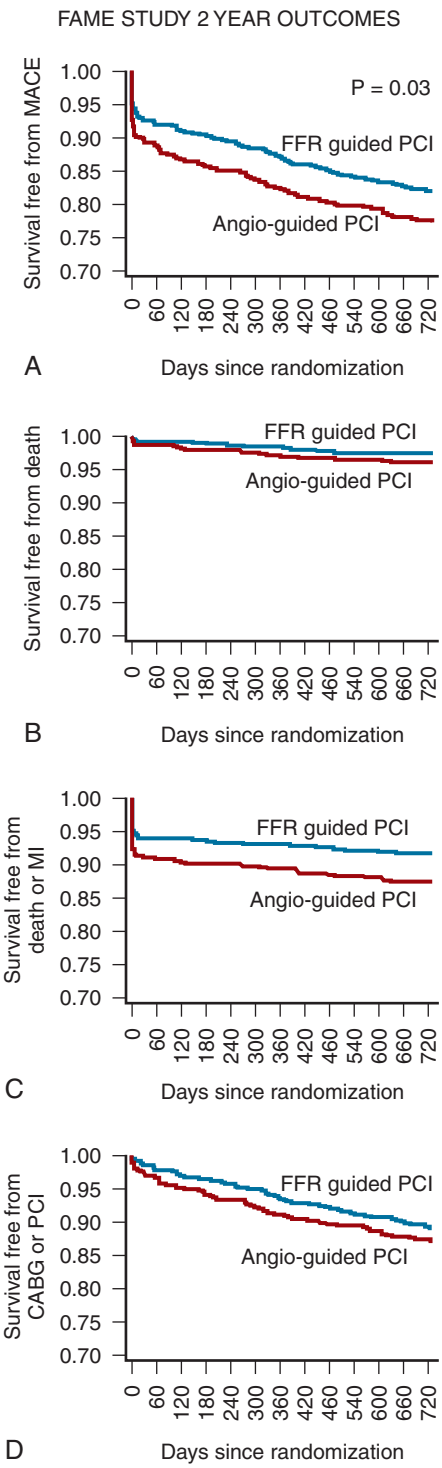


Figure 13-11 The FAME study results. Kaplan-Meier survival curves according to study group for 2-year outcomes. *CABG,* coronary artery bypass graft; *FFR,* fractional flow reserve; *MACE,* major adverse cardiac event; *MI,* myocardial infarction; *PCI,* percutaneous coronary intervention. (From Tonino PAL *et al. N Engl J Med* 2009;360:213–224.)

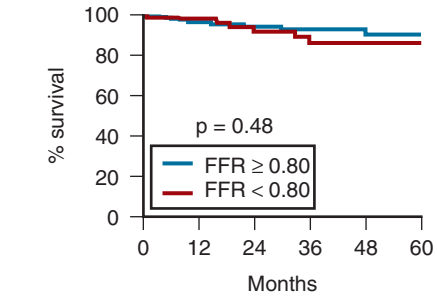
Table 13-7

Fractional Flow Reserve (FFR) to Assess Intermediate Left Main Coronary Stenoses

			Medical Therapy			Surgical Therapy			
Study	**FFR Threshold**	**N**	**N (%)**	**MACE**	**Death**	**n (%)**	**MACE**	**Death**	**Follow-up Time (mo)**
Hamilos *et al.* (2009)	0.8	213	136 (65%)	26%	9 (6.5%)	73 (35%)	17%	7 (9.6%)	35 25
Courtis (2009)	075 surg 08 med	142	82 (58%)	13%	3 (3.6%)	60 (42%)	7%	3 (5%)	14 11
Lindstraedt (2006)	0.75 surg 0.8 med	51	24 (47%)	31%	0	27 (53%)	34%	5 (19%)	29 16
Suemaru (2005)	0.75	15	8 (53%)	0	0	7 (47%)	29%	0	33 10
Legutko (2005)	0.75	38	20 (53%)	10%	0	18 (46%)	11%	2	24 mean
Jimenez-Navaro	0.75	27	20 (74%)	10%	0	7 (26%)	29%	2	2 12
Bech, Droste, Pijls *et al.* (2001)	0.75	54	24(44%)	24%	0	30 (56%)	17%	1	29 15

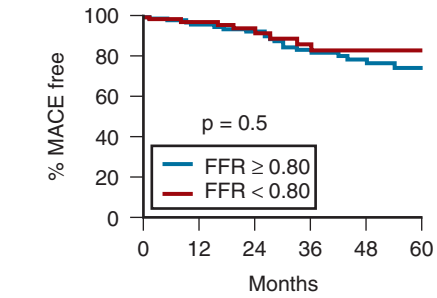
From Lokhandwala J, Hodgson JM Assessing intermediate left main lesions with IUVS or FFR. *Cardiac Interventions Today* Oct 2009.

Bech GJ, Droste H, Pijls NH, et al. Value of fractional flow reserve in making decisions about bypass surgery for equivocal left main coronary artery disease. *Heart*. 2001;86:547–552.
Jimenez-Navarro M, Hernandez-Garcia JM, Alonso-Briales JH, et al. Should we treat patients with moderately severe stenosis of the left main coronary artery and negative FFR results? *J Invas Cardiol*. 2004;16:398–400.
Legutko J, Dudek D, Rzeszutko L, et al. Fractional flow reserve assessment to determine the indications for myocardial revascularization in patients with borderline stenosis of the left main coronary artery. *Kardiol Pol*. 2005;63:499–509.
Lindstaedt M, Spiecker M, Lawo T, et al. Angiographic assessment of functionally insignificant left main coronary artery stenoses: Reliability compared to intracoronary pressure measurement. *Dtsch Med Wochenschr*. 2006;131:2134–2138.
Suemaru S, Iwasaki K, Yamamoto K, et al. Coronary pressure measurement to determine treatment strategy for equivocal left main coronary artery lesions. *Heart Vessels*. 2005;20:271–277.
Courtis J, Rodes-Cabau J, Larose E, et al. Usefulness of coronary fractional flow reserve measurements in guiding clinical decisions in intermediate or equivocal left main coronary stenoses. *Am J Cardiol*. 2009;103:943–949.



No at risk						
FFR ≥ 0.80	136	103	72	52	38	26
FFR < 0.80	73	56	41	30	14	10

A



No at risk						
FFR ≥ 0.80	136	106	77	57	42	30
FFR < 0.80	73	56	40	29	15	10

B

Figure 13-12 The left main fractional flow reserve (FFR) 5-year outcome study. **A,** Total survival. **B,** Major adverse cardiac event (MACE) free survival by Kaplan-Meier mortality curves in the two study groups. (Modified from Hamilos M. *et al. Circulation* 2009;120:1505–1512.)

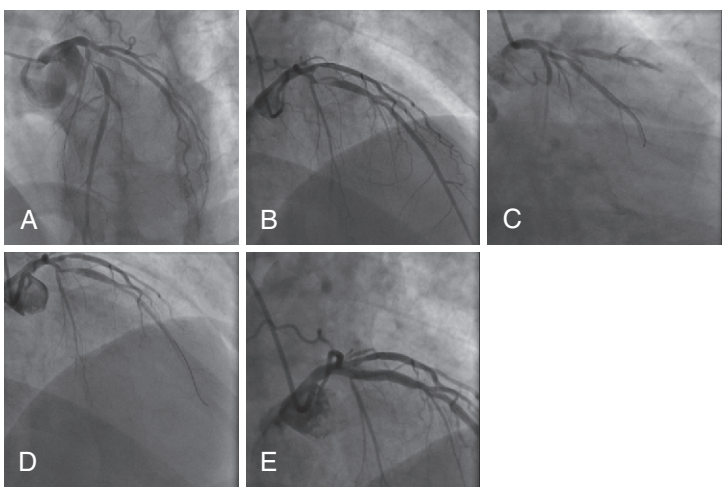


Figure 13-13 Cine frames from multivessel PCI guided by FFR. **A,** LAO cranial view of LCA showing severe and moderate lesions in LAD and CFX. **B,** RAO view of LCA. **C,** FFR of CFX was 0.88. **D,** PCI of LAD performed. **E,** Mid LAD lesion assessed by FFR at 0.68. An additional stent was placed, and IVUS was performed. Final result of fully deployed stents with FFR 0.89. *CFX,* circumflex artery; *FFR,* fractional flow reserve; *IVUS,* intravascular ultrasound; *LAD,* left anterior descending; *LAO,* left anterior oblique; *LCA,* left coronary artery; *PCI,* percutaneous coronary intervention; *RAO,* right anterior oblique; *RCA,* right coronary artery.

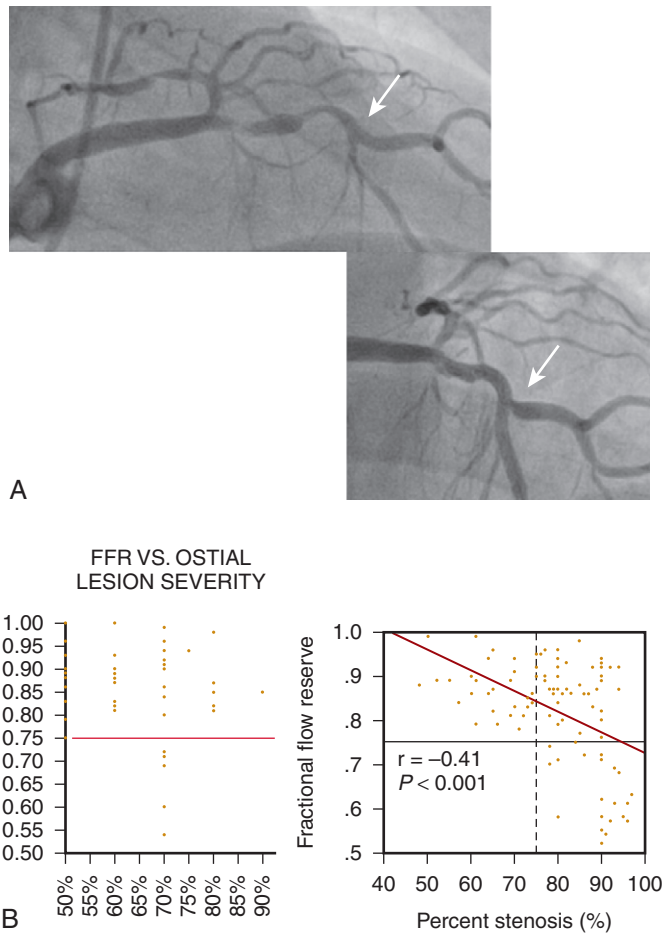


Figure 13-14 **A,** Angiographic frames showing jailed side branch before (*left*) and after (*right*) LAD stenting. White arrows point to side branch at location of new narrowing. **B,** Comparison of FFR and percent stenosis for ostial lesions (*left*). (From Zaiee A, *et al.* FFR vs. ostial lesion severity *AJC* 2004;93:1404–1407). Comparison of FFR and percent stenosis for jailed side branches (*right*). (Data from Koo BK, *et al. J Am Coll Cardiol* 2005;46:633–637.)

<75% stenosis had FFR <0.75. Among 73 lesions with ≥75% stenosis, only 20 lesions (27%) were functionally significant. Of 91 patients, side-branch intervention was performed in 26 of 28 patients with FFR < 0.75. In this subgroup, FFR increased to >0.75 despite residual stenosis of 69 ±10%. At 9 months, functional restenosis was 8% (5/65) with no difference in events compared with 110 side branches treated by angiography alone (4.6% vs. 3.7%, $P = 0.7$) (Fig. 13-14*B*). Measurement of FFR for ostial- and side-branch assessment thus identifies the minority of lesions that are functionally significant, reducing the need for complex, time-consuming, and potentially detrimental side-branch interventions.

Saphenous Vein Graft Lesions

When assessing a lesion in a saphenous vein graft (SVG), recall that there are three sources of coronary blood flow to the myocardium: the epicardial artery, the bypass conduit, and collateral flow (Fig. 13-15*A*). The FFR is the summed responses of three competing flows (and pressure) from (1) the native vessel, (2) the CABG conduit, and (3) the collateral flow induced from long-standing native coronary occlusion. In

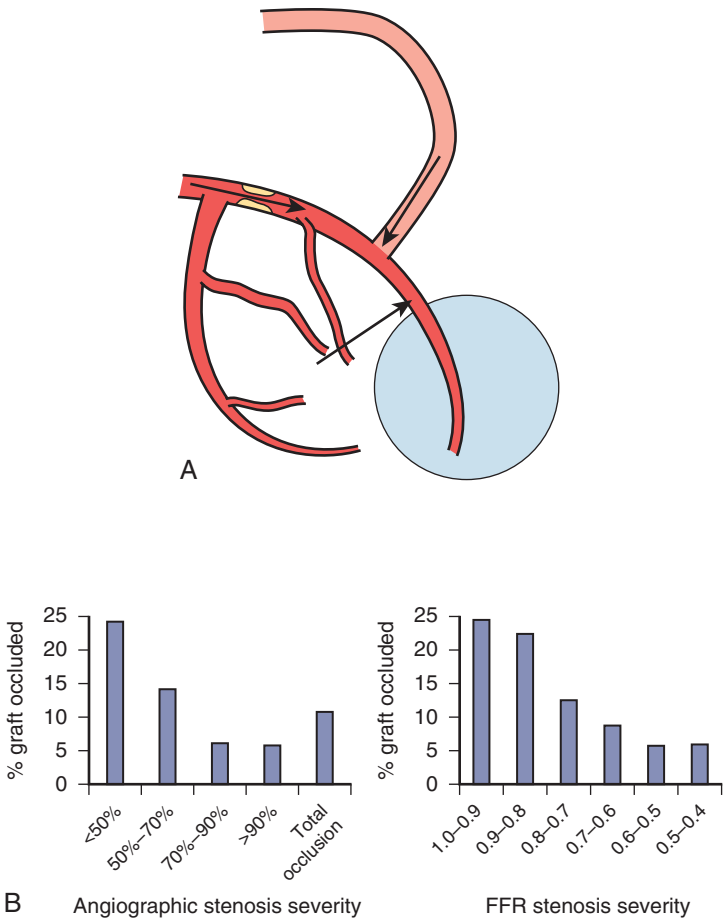


Figure 13-15 **A,** Diagram of saphenous vein graft (SVG) and resulting fractional flow reserve (FFR). There are three pressure inputs from native vessel, SVG, and collateral source which add to produce the net FFR. **B,** The fate of bypass grafts and FFR at time of surgery. High FFR is associated with high occlusion rates. (From Botman CJ *et al*. *Ann Thorac Surg* 2007;83:2093–2097.)

the most uncomplicated situation of an occluded native vessel with minimal distal collateral supply, the theory of FFR will apply just as much to a lesion in an SVG as to a native right coronary artery feeding a normal myocardial bed. For more complex situations, the FFR will reflect the summed responses of the three supply sources and yield a net FFR indicating potential ischemia in that region.

Interesting is the fate of SVG conduits implanted distal to hemodynamically *insignificant* lesions. Surgeons and cardiologists have recognized that late patency is reduced and native CAD can be accelerated by placement of an unneeded graft. Although most surgical consultants typically recommend bypassing all lesions with >50% diameter narrowing in patients with multivessel disease, the patency rate of SVGs on vessels with hemodynamically nonsignificant lesions has rarely been questioned. Botman *et al.* found that there was a 20% to 25% incidence of graft closure in 450 CABGs when placed on nonhemodynamically significantly stenosed arteries (preoperative FFR >0.80) at the 1-year follow-up (Fig. 13-15*B*). In patients requiring CABG for multivessel revascularization, angiographic lesions of uncertain significance would benefit from FFR assessment, providing prognosis of graft patency and potentially reducing unnecessary graft placement.

Coronary Lesions in Acute Coronary Syndrome

In acute coronary syndrome settings and especially in acute MI, the pathophysiology of the infarcted artery and its subtended microvascular bed is both dynamic and complex. The predictive ability of FFR in acute coronary syndrome has several limitations: (1) The microvascular bed in the infarct zone may not have uniform, constant, or minimal resistance, (2) the severity of stenosis may evolve as thrombus and vasoconstriction abate, and (3) FFR measurements are not meaningful when normal perfusion has not been achieved. Thus, FFR has limited utility in the infarct-related artery during the first 24 to 48 hours after acute coronary syndrome. However, FFR has demonstrated value in remote lesion assessment and in target lesion assessment during the recovery phase of MI.

De Bruyne *et al.* compared single-photon emission computed tomography (SPECT) myocardial perfusion imaging and FFR (obtained before and after PCI) in 57 patients with an MI >6 days (mean 20 days) prior to evaluation. Patients with positive SPECT before PCI had a significantly lower FFR than patients with negative SPECT (0.52 ± 0.18 vs. 0.67 ± 0.16; $P = 0.0079$), but a significantly higher left ventricular ejection fraction (63% ± 10% vs. 52% ± 10%; $P = 0.0009$) (Fig. 13-16). The best FFR cutoff for determining peri-infarct ischemia was 0.78. In a similar

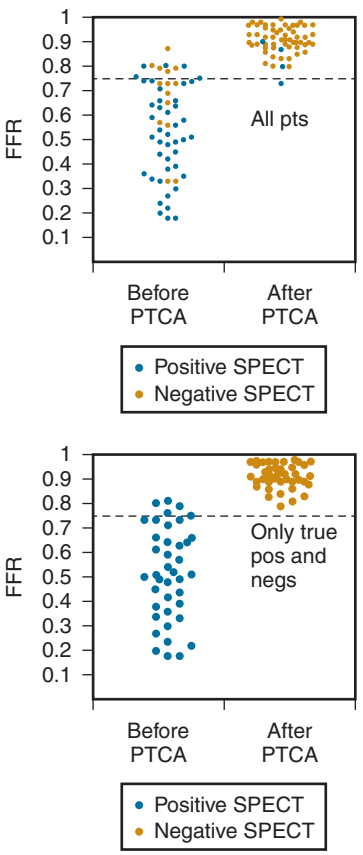


Figure 13-16 Fractional flow reserve (FFR) after acute MI. Values of FFR before and after angioplasty according to results of sestamibi SPECT myocardial perfusion imaging in patient population as a whole (*top*) and in patients with truly positive and truly negative SPECT imaging (*bottom*). *MI,* myocardial infarction; *PTCA,* percutaneous transluminal coronary angioplasty; *SPECT,* single photon emission computed tomography. (From DeBruyne B, *et al. Circulation* 2001;104:157–162.)

study Samady *et al.* compared FFR to SPECT and myocardial contrast echo in 48 patients 3.7 ± 1.3 days after infarction. The optimal FFR value for discriminating inducible ischemia on noninvasive imaging was also 0.78, similar to the findings of DeBruyne *et al.* These studies suggest that within 3 to 6 days following acute MI, FFR of the infarct-related artery correlates with noninvasive stress testing.

For patients with unstable angina or non–ST-elevation myocardial infarction, FFR measurement at the time of angiography may be superior to a SPECT strategy. Leesar *et al.* randomized 70 patients who received at least 48 hours of medical stabilization and had an intermediate single-vessel stenosis to one of two strategies: angiography followed by SPECT the next day, or FFR-guided revascularization at the time of angiography. Compared with the SPECT strategy, the FFR-guided approach had a reduced hospital stay (11 ± 2 hours vs. 49 ± 5 hours, $P < 0.001$) and reduced cost (US$ 1,329 ± US$ 44 vs. US$ 2,113 ± US$ 120, $P < 0.05$), with no increase in procedure time, radiation exposure time, or clinical event rates at 1-year follow-up.

Serial (Multiple) Lesions in a Single Vessel

When more than one discrete stenosis is present in the same vessel, the hyperemic flow and pressure through the first lesion will be attenuated by the second and vice versa (Fig. 13-17). One stenosis will mask the true effect of its serial counterpart. When the distance between two lesions is greater than six times the vessel diameter, the stenoses generally behave independently and the overall pressure gradient is the sum of the individual pressure losses at any given flow rate.

The interaction between two stenoses is such that the FFR of each lesion cannot be calculated by the simple equation for isolated stenoses applied to each separately, but can be predicted by more complete equations taking into account P_a, P_m, P_d, and coronary occlusion pressure, P_w. The requirement for the coronary occlusion pressure makes this approach unsuitable for most for diagnostic purposes.

In clinical practice, the use of a pressure pullback recording is particularly well suited to identify the specific regions of a vessel with large pressure gradients which may benefit by treatment. The one stenosis with the largest gradient can be treated first and the FFR remeasured for the remaining stenoses to determine the need for further treatment (Fig. 13-18).

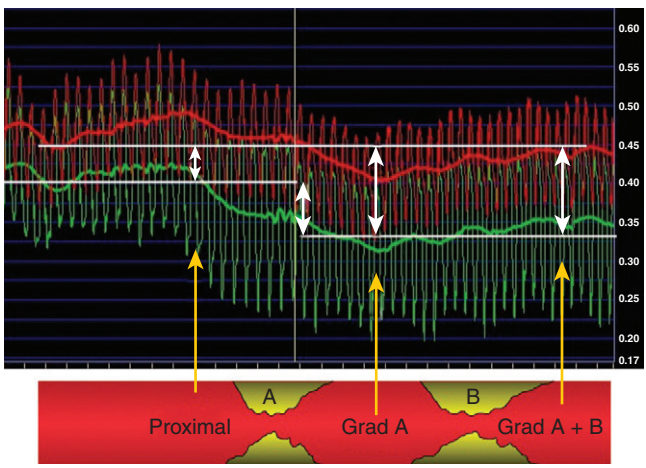


Figure 13-17 Example of serial lesion fractional flow reserve (FFR). Individual lesion FFR cannot be determined without a coronary occlusion wedge pressure. In practice, treatment of largest translesional gradient is performed, and then reassessment of remaining lesion will determine treatment approach.

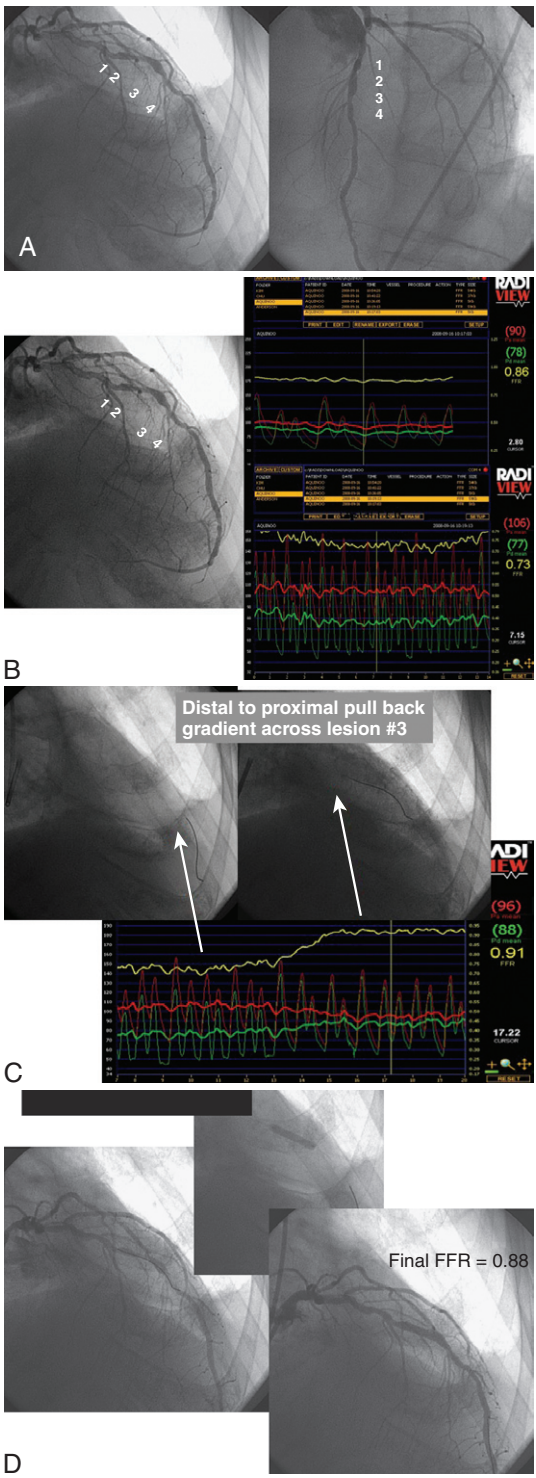


Figure 13-18 **A,** Example of serial lesion assessment. RAO (*left*) and LAO (*right*) angiogram of LAD showing four lesions in series. **B,** Angiogram (*left*). Resting pressure across all lesions (*top right*) and FFR across all lesions (*bottom right*). FFR = 0.73. **C,** Distal to proximal pressure wire pullback shows step-up of pressure gradient was present only across lesion #3. **D,** Angiographic frames of PCI for lesion #3. Final FFR was 0.88. *FFR,* fractional flow reserve; *LAD,* left anterior descending; *LAO,* left anterior oblique; *PCI,* percutaneous coronary intervention; *RAO,* right anterior oblique.

Diffuse Coronary Disease

Using FFR_{myo} during continuous pressure wire pullback from a distal to proximal location, the impact of diffuse atherosclerosis can be documented. Diffuse atherosclerosis, rather than a focal narrowing, is characterized by a continuous and gradual pressure recovery during pullback, without any abrupt increase in pressure related to a focal region. The pressure pullback recording at maximum hyperemia will provide the necessary information to decide if and where stent implantation may be useful (Fig. 13-19). The location of a focal pressure drop superimposed on the diffuse disease can be identified as an appropriate location for treatment.

Assessing Collateral Flow

The pressure-derived fractional collateral flow is defined as the mean coronary wedge pressure (distal coronary pressure during balloon occlusion) divided by the mean aortic pressure (if the central venous pressure is abnormal, then it should be subtracted from both the wedge and aortic pressures). In general, a pressure-derived fractional collateral flow of 0.25 or more suggests sufficient collaterals to prevent ischemia during PCI. Furthermore, these patients have a significantly lower adverse event rate during follow-up compared with those with insufficient collaterals at the time of PCI (pressure-derived collateral flow <0.25). Pressure-derived collateral flow has also been studied in patients with acute MI and has been shown to be the major determinant of left ventricular recovery after primary PCI. Unfortunately, this technique for assessing collaterals is limited by the requirement for coronary artery occlusion.

Assessing the Microcirculation: Index of Microcirculatory Resistance Using Coronary Thermodilution Blood Flow Measurements

Software has been developed that allows simultaneous measurement of FFR, CFR, and the index of microcirculatory resistance (IMR) using the pressure wire. CFR and IMR are measured using a novel coronary thermodilution technique, whereby the pressure transducer serves as

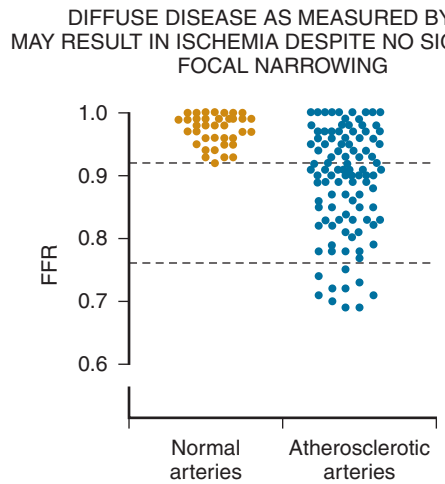


Figure 13-19 Fractional flow reserve (FFR) in diffuse coronary artery disease. Graphs of individual values of FFR in normal arteries and in atherosclerotic coronary arteries without focal stenosis on arteriogram. Upper dotted line indicates the lowest value of FFR in normal coronary arteries. Lower dotted line indicates the 0.75 threshold level. (From DeBruyne B, Hersbach F, Pijls NHJ, et al. Abnormal epicardial coronary resistance in patients with diffuse atherosclerosis but "normal" coronary angiography. *Circulation* 2001; 104: 2401–2406.)

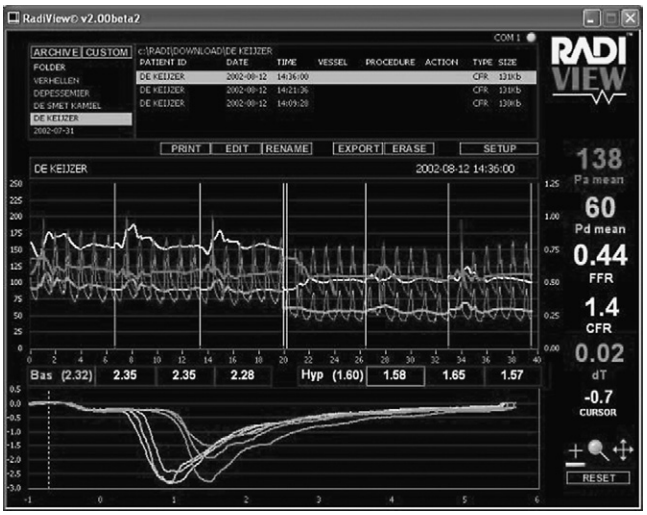


Figure 13-20 Example of simultaneous pressure and temperature tracings. The top tracings represent central aortic pressure (Pa) and distal coronary pressure (Pd), and FFR (Pd/Pa). The lower tracings are temperature tracings recorded by the proximal (shaft) and distal sensors. The half-time of injection was derived from the proximal thermodilution curve. Coronary flow volume is calculated from the distal thermodilution. Tmn at hyperemia, CFR = V/Tmn at hyperemia, V/Tmn at rest CFR = Tmn at rest. (Courtesy of St. Jude Medical, Minneapolis, MN (Figure formerly provided by Radi Medical, Uppsala Sweden), Uppsala, Sweden.)

a distal thermistor and the shaft of the pressure wire as a proximal thermistor. In this manner, the resting mean transit time of room-temperature saline injected down the coronary artery can be measured with the pressure wire and compared with the hyperemic mean transit time. The ratio of resting to hyperemic mean transit times serves as an estimate of CFR. FFR using the standard technique can be measured simultaneously (Fig. 13-20). Coronary thermodilution CFR was initially validated in an in vitro model and in vivo animal model. Subsequently, it has been shown to correlate with coronary flow velocity reserve (CFVR) measured with a Doppler wire in humans. A similar wire system that measures pressure-derived FFR and Doppler-derived CFVR is also available.

The ratio of distal coronary pressure to the inverse of the mean transit time during maximal hyperemia defines IMR. IMR is superior to CFR because it is not affected by resting hemodynamics, making it more reproducible, even after hemodynamic perturbations. It is also specific for the microvasculature, whereas CFR is affected by epicardial stenosis. IMR, when used to measure for ST-elevation myocardial infarction immediately after primary PCI, predicts the amount of myocardial damage, as well as left ventricular recovery better than other indices, such as CFR, ST-segment resolution, or TIMI myocardial perfusion grade. IMR can also be useful for identifying microvascular dysfunction in patients with chest pain and no epicardial artery disease.

IVUS

IVUS is inherently different from physiologic measurements. IVUS provides only anatomical information, including plaque characteristics, lesion length, and lumen dimensions. It is complementary to both angiography and physiology, allowing a more thorough investigation of the disease within the vessel wall. By better determining plaque characteristics, IVUS also is useful in guiding selection of interventional equipment, such as the need for plaque debulking. AHA/ACC/SCAI recommendations for coronary IVUS are shown in Table 13-8.

Table 13-8

Recommendations for Coronary Intravascular Ultrasound

	Level of Evidence
Class IIA	
1. Evaluation of lesion severity at a location difficult to image by angiography in a patient with a positive functional study and a suspected flow-limiting stenosis	C
2. Assessment of a suboptimal angiographic result after coronary intervention	C
3. Diagnostic and management of coronary disease after cardiac transplantation	C
4. Assessment of the adequacy of deployment of a coronary stent, including the extent of stent apposition and determination of the minimal luminal diameter within the stent	B
Class IIB	
1. Determination of plaque location and circumferential distribution for guidance of directional coronary atherectomy	C
2. Further evaluation of patients with characteristic anginal symptoms and a positive functional study with no focal stenoses or mild coronary artery disease (CAD) on angiography	C
3. Determination of the mechanism of stent restenosis (inadequate expansion vs. neointimal proliferation) and to enable selection of appropriate therapy (plaque ablation vs. repeat balloon expansion)	C
4. Preinterventional assessment of lesional characteristics as a means to select an optimal revascularization device	C
Class III	
When angiographic diagnosis is clear and no interventional treatment is planned	

(From Scanlon PJ, Faxon DP, Audet AM, *et al.* ACC/AHA guidelines for coronary angiography: executive summary and recommendations. A report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines (Committee on Coronary Angiography) developed in collaboration with the Society for Cardiac Angiography and Interventions. *Circulation* 1999;99:2345–2357, with permission from the American Heart Association.)

Two types of IVUS systems exist, both utilizing 20- to 40-MHz silicon piezoelectric crystals: (1) a mechanical system that relies on a rotating internal cable, and (2) a solid-state system externally mounted on a catheter and controlled electronically (Fig. 13-21). With the mechanical systems, the imaging core rotates via a flexible drive shaft to sweep the transducer continuously through a 360-degree arc in the vessel. The rotation rate is 1800 rpm, generating 30 images per second. The solid-state catheter (Volcano Therapeutics, Rancho Cordova, CA) has 64 ultrasound transducers arranged circumferentially around the catheter tip and sequentially activated to produce a 360-degree image. Both IVUS catheters range in size from 3.2 F to 3.5 F and have a tapered tip and shaft. They are designed to fit through a 6 F guide catheter. The IVUS catheter connects to a console, which displays and records the images digitally. Images from both systems are displayed in a tomographic, real-time video format. Currently, IVUS has a resolution of approximately 100 to 150 μm.

Common clinical applications for IVUS include:

1. Assessment of lesion calcium
2. Vessel and lesion dimensions
3. Confirmation of atherosclerotic plaque
4. Adequacy of stent deployment

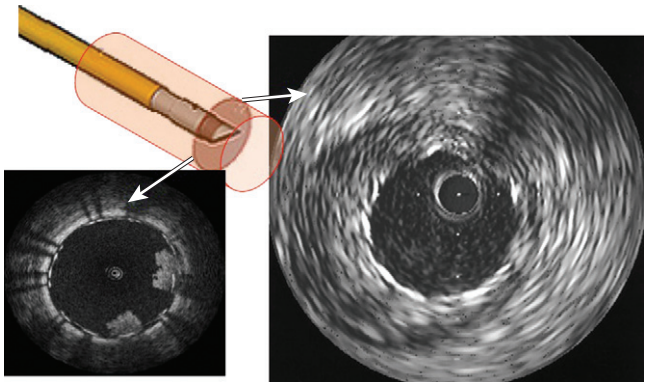


Figure 13-21 Intravenous ultrasound (IVUS) catheter has either rotating imaging core or multiple microtransducers at tip to generate IVUS image (*right*). Optical coherence tomographic imaging uses a rotating core of the imaging fibers to generate image (*left*).

Technique of IVUS

The technique of IVUS is identical to that of PCI balloon catheter advancement. After administration of heparin and positioning of a standard angioplasty guidewire in the distal coronary vessel, IC nitroglycerin is given to avoid vasospasm. The IVUS catheter is then advanced along the guidewire until the transducer is beyond the region of interest. The catheter can then be pulled back either manually or with an automated pullback device. An accurate pullback run is necessary to determine lesion length and volumetric analyses.

The mechanical system requires an initial flush of saline to remove air microbubbles from the plastic sheath housing the imaging core. Non-uniform rotational distortion can occur with the mechanical system due to uneven drag on the catheter drive shaft leading to changes in the rotational speed. This artifact most commonly occurs in tortuous vessels and manifests as a smearing of one side of the image. A ring-down artifact, seen with the solid-state system, results in white circles surrounding the ultrasound catheter and precluding near-field imaging and is due to acoustic oscillations in the transducer, resulting in high amplitude signals. Adjustments can now be made on the newer solid-state systems to minimize this problem.

Setup

Integration of IVUS into the laboratory is critical for optimal use of the technology (Fig. 13-22). To minimize problems, it is important for several members of the support staff to take specialized training and assume responsibility for the equipment. There are now commercially available IVUS systems which are fully integrated into the angiographic imaging system and do not require transport of a separate console into the laboratory. The following preparations make use of IVUS most efficient:

1. Specialized support staff familiar with operation of the equipment and image interpretation.
2. Use of an automated pullback device, which standardizes the procedure to prevent too rapid scanning and eliminate much of the physician operator effect on image quality.
3. A system of maintenance for IVUS-related records, videotapes, and CD-ROMs.
4. An image review station that is separate from the IVUS machine itself. Direct transfer of the DICOM images to an image-archival network allows review at many stations.

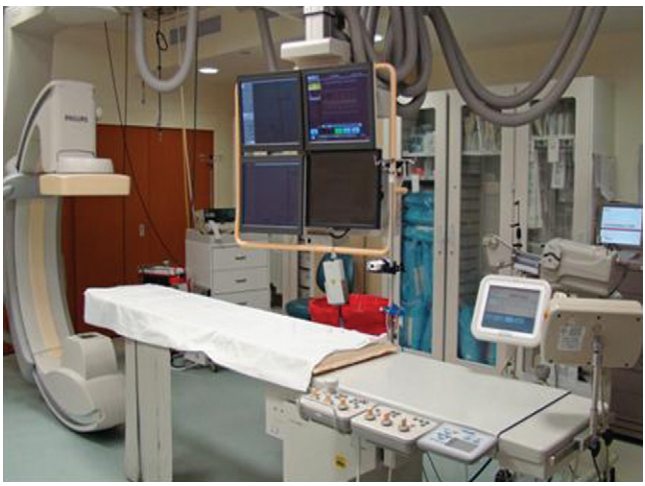


Figure 13-22 Cath lab with integrated intravenous ultrasound (IVUS) and fractional flow reserve (FFR) into monitors.

Image Features

Regardless of the imaging system used, the basic image features are listed here from the center outward. A normal IVUS image is shown in Figure 13-23.

1. Dead zone. The black circular ring in the middle of the image is caused by the space occupied by the catheter.
2. Catheter artifact. A "halo" artifact around the catheter usually encroaches onto lumen areas and therefore may affect analysis. It may also encroach onto the signals transmitted from the vessel wall. These artifacts are related to either the imaging sheath or a property of ultrasonic imaging termed *ringdown* (disorganized near-field echo signals).

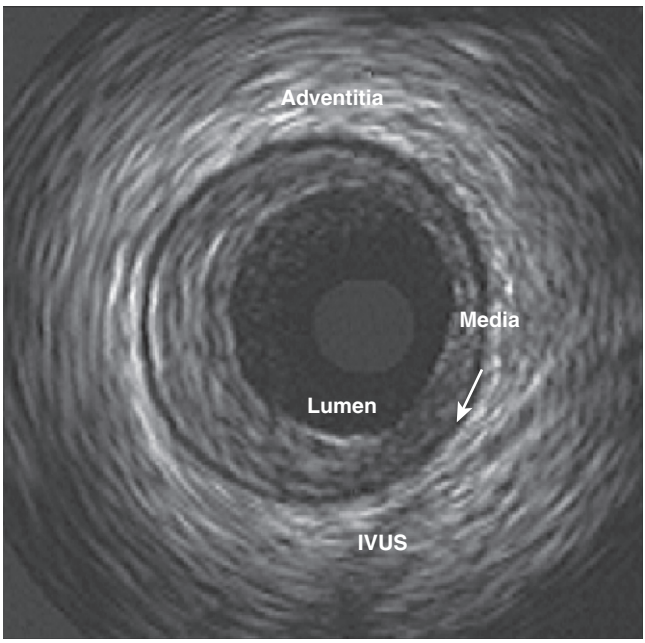


Figure 13-23 Normal intravascular ultrasound (IVUS) image, demonstrating the three normal layers of the coronary artery—the adventitia is the outermost, separated by a dark echolucent line between the media and the lumen. This an abnormal artery with eccentric plaque from 4 o'clock to 11 o'clock.

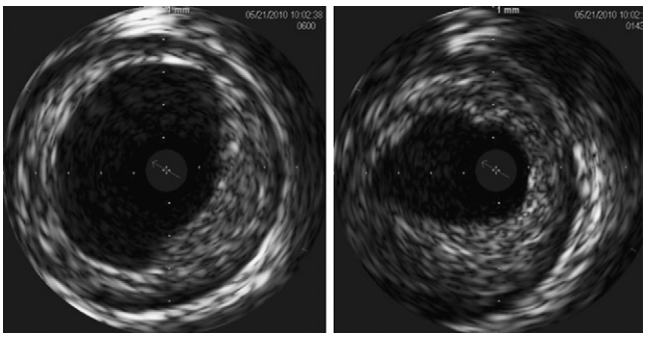


Figure 13-24 Eccentric plaque by IVUS in large ecstatic vessel.

3. Lumen. The dark, echolucent area surrounding the catheter artifact signal is the lumen. With some higher frequency scanners or under conditions of slow blood velocity, a fine speckle pattern may be seen in the lumen (Fig. 13-24).
4. Inner layer. In a normal artery, the intima is often too thin to be seen reliably. The thin inner echogenic layer surrounding the lumen usually represents the internal elastic lamina. In a diseased coronary artery, the atheromatous intima is seen as a thick echogenic layer surrounding the lumen. In vessels with mild to moderate atherosclerosis, a thin echodense layer at the intima-media interface can be seen, correlating histologically to the internal elastic lamina. This may be obscured in severely diseased atherosclerotic arteries.
5. Middle hypoechoic layer. The media, packed with smooth muscle cells and a few elastin fibers, appears as a relatively echolucent area. The external elastic lamina may sometimes be seen as an echodense layer at the media-adventitia interface.
6. Outer echogenic layer. The adventitia is seen as an echodense layer surrounding the hypoechoic media. The adventitia shows increased echodensity due to both the inhomogeneous histologic structures and the high elastin and collagen content. This structure has the most intense echoes in normal arteries. Echoes that are more intense than the adventitia are therefore abnormal. In this region, perivascular structures may also be observed (i.e., veins and pericardium).

Dimensional Measurements

One of the major advantages of IVUS is its ability to provide precise measurements (Figs. 13-25, 13-26, 13-27). Several studies have analyzed the accuracy of ultrasound images for measuring lumen size and wall thickness. Correlations with histologic measurements have been uniformly

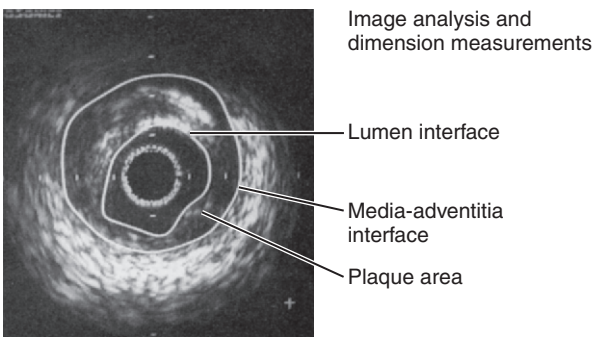


Figure 13-25 Intravascular ultrasound (IVUS) images showing how ultrasound-derived measurements are obtained from planimetry of the lumen and media-adventitia interfaces. *Halo* is the term given for lucency around the central black space of the IVUS catheter. (Courtesy of John M. Hodgson, MD.).

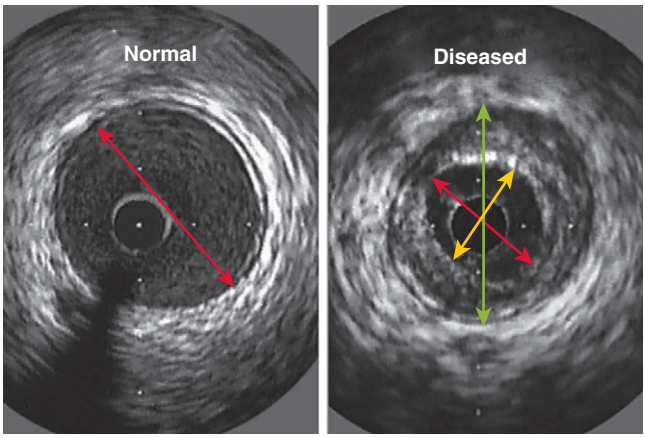


Figure 13-26 Intravascular ultrasound (IVUS) measurements for dimensions in normal (*left*) and diseased (*right*) coronary artery. Interdot distance = 1 mm. Vessel diameter computed from leading edge to leading edge adventitia (*red arrow*). Lumen diameter on right has two dimensions of an eccentric plaque (*yellow and red arrows*). Vessel dimension here is from green arrow.

high, although measurements of the dimensions of the layers and overall wall thickness have been reported to be less accurate than lumen area determinations. The lumen-intima and media-adventitia interfaces are generally accurate through means of ultrasound scanning; both interfaces show a relatively large increase in acoustic impedance as the beam passes through the layers. The intima-media interface may also provide a significant change in impedance, particularly in the presence of prominent internal elastic lamina. At this interface, however, there is a "trailing-edge" effect that can result in the spreading or blooming of the intimal image. The net result is that the transition is obscured, the intima appears thicker than by histologic determination, and the media appears correspondingly thinner. However, wall thickness using the combined intima and media corresponds closely to the histologic dimensions.

All ultrasound measurements are performed on end-diastolic images, unless specified otherwise. Artery lumen dimensions are quantified from images of proximal, distal, or reference vessel segments and within the target lesion(s) or stent. The flowing measurements are routinely obtained.

1. **Lumen and vessel diameters.** Minimal, maximal, and mean diameters may be obtained.
2. **Percentage diameter or area stenosis** is the lumen diameter or area within the lesion segment divided by the lumen diameter or area within the reference segment. This is similar to the measurements made by angiography.
3. **Total vessel area.** The vessel cross-sectional area is the area confined within the external elastic lamina or the media-adventitia interface.

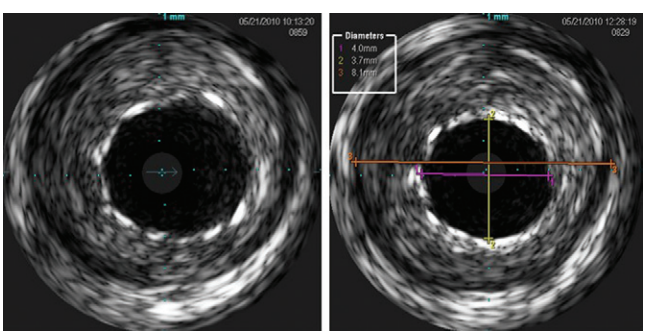


Figure 13-27 Intravascular ultrasound (IVUS) measurements made after stent implantation.

4. **Lumen area** is the integrated area central to the leading-edge echo. The area is confined within the lumen-intima interface. If the catheter is tangential, the lumen area is slightly overestimated.
5. **Wall area (intima and media)** equals total area minus lumen area. In abnormal vessels, this is the plaque area (also called plaque plus media area).
6. **Percentage plaque area** (also called plaque burden or percentage cross-sectional narrowing [%CSN]) equals total vessel area minus lumen area divided by total vessel area: Percentage plaque area = (total area - lumen area/total area) × 100.
7. **Indices of Eccentricity.** A lesion eccentricity index (L_{ECC}) is calculated by lumen dimensions: L_{ECC} = maximum diameter/minimum diameter.

Plaque distribution is classified into three categories:

1. Concentric plaque. Maximum plaque thickness (leading edge plus sonolucent zone) <1.3 times minimum plaque thickness
2. Moderately eccentric plaque. Maximum plaque thickness (leading edge plus sonolucent zone) 1.3 to 1.7 times minimum plaque thickness
3. Severely eccentric plaque. Maximum plaque thickness (leading edge plus sonolucent zone) >1.7 times minimum plaque thickness.

Intravascular Ultrasound Plaque Morphology

In general, plaque may be classified as "soft" or "hard" based on whether the echodensity is less than or similar to the adventitia.

Soft Plaque. More than 80% of the plaque area in an integrated pullback throughout the lesion is composed of thickened intimal echoes with homogeneous echo density less than that seen in adventitia (Fig. 13-28).

Fibrous Plaque. More than 80% of plaque in an integrated pullback throughout the lesion is composed of thick and dense echoes involving the intimal leading edge, with homogeneous echo density greater than or equal to that seen for adventitia.

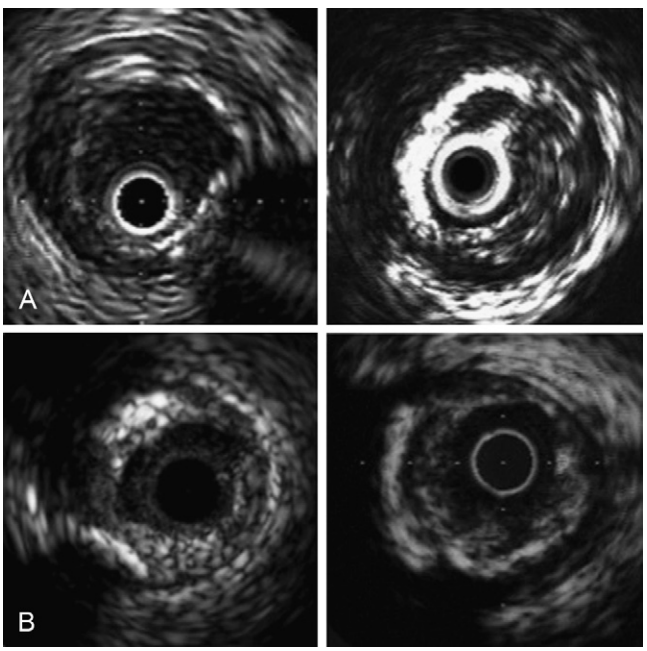


Figure 13-28 Intravascular ultrasound images for various types of coronary arterial disease. **A,** Normal vessel. **B,** Mild atherosclerosis. (Courtesy of John M. Hodgson, MD.)

Calcified Plaque. Bright echoes within a plaque demonstrate acoustic shadowing and occupy more than 90% of the vessel wall circumference in at least one cross-sectional image of the lesion. The extent of calcification, defined as the presence of any hyperechogenic structure that shadows underlying ultrasound anatomy, is reported as the degree of circumference in which shadowing is present. Calcium is also classified as deep or superficial (Fig. 13-29). Detection of calcium

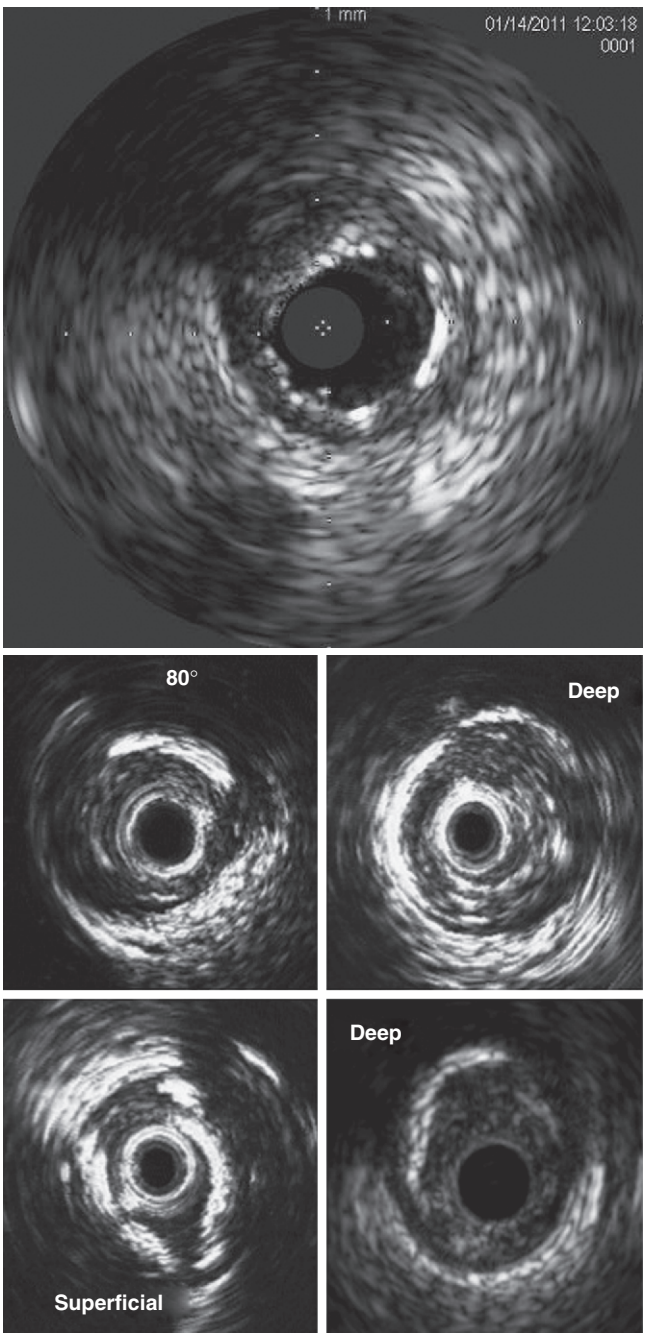


Figure 13-29 Calcium is quantified by measuring the "arc" it encompasses. Calcium is classified by its location within the plaque. Superficial calcium is closer to the lumen than to the adventitia. Deep calcium is closer to the adventitia than to the lumen.

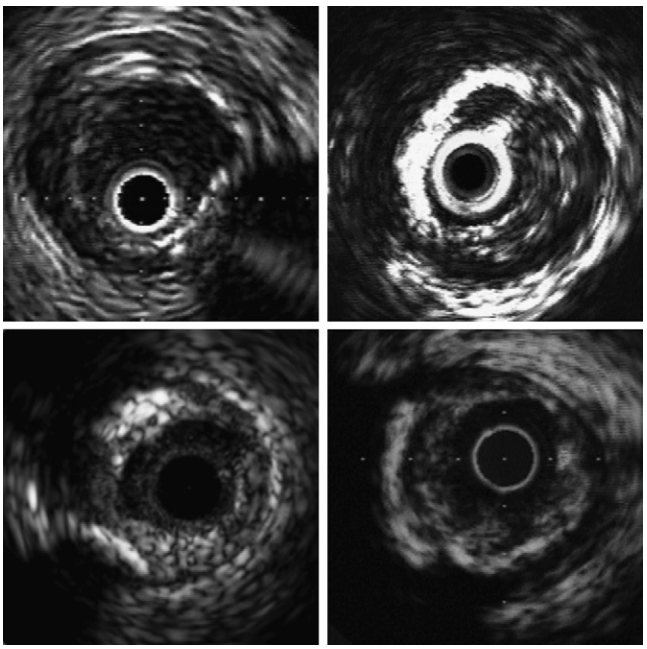


Figure 13-30 Mixed plaque types. Soft plaque (*upper left*); calcified plaque (*upper right*); mixed calcified and fibrous plaque (*lower left*); Soft fibrous plaque (*lower right*).

by means of IVUS can guide appropriate device selection, such as the need for high-speed rotational atherectomy.

Mixed Plaque. Bright echoes with acoustic shadowing encompass less than 90% of the vessel wall circumference, or a mixture of soft and fibrous plaque is seen with each component occupying less than 80% of the plaque area in an integrated pullback through the lesion (Fig. 13-30).

Subintimal Thickening. Subintimal thickening involving reference vessel segments is defined as a concentric prominent leading edge echo and a widened subintimal echolucent zone with a combined thickness of more than 500 μm.

Additional Plaque Features

Plaque Location. Plaque may be described as concentric or eccentric, with or without ulceration. In describing a nonconcentric plaque, its location is noted in relation to a clock, that is, "plaque is present, extending from the 8 o'clock position to the 11 o'clock position, with calcium deposits seen at 9 o'clock."

Intimal Flap or Dissection. This is seen as a linear structure with or without a free edge. True and false channels can also be visualized. The characteristic motion of an intimal flap may be seen within the lumen. Radiographic contrast injection can assist in defining the lumen and indicating whether there is communication of the lumen with an echo-free area below a flap. In some systems, blood flow can be colorized and may assist in defining dissections (Fig. 13-31).

Thrombus. Fresh thrombus is a low to moderately echogenic or granular mass that occupies part of the lumen and adjoins the adjacent wall; often it is mobile and has an irregular border. Edge definition is possible with contrast injection.

Aneurysm. Aneurysmal areas are expanded, thin-walled structures adjoining the lumen. They can be mistaken for branches, which have a similar appearance.

Side Branches. Side branches appear as "buds" with a loss of the intimal border. The location of the lesion in relation to branch vessels and, in particular, in relation to the coronary ostium, can be well visualized with IVUS, which can aid in decisions regarding stent placement.

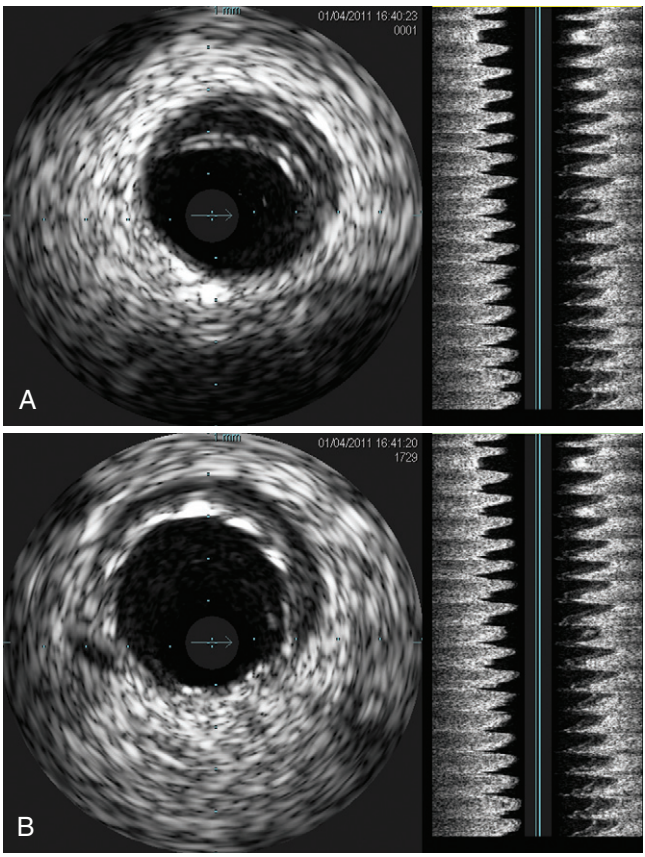


Figure 13-31 **A,** Intravascular ultrasound (IVUS) demonstration of intimal flap or dissection. **B,** IVUS showing stent in place.

"Vulnerable Plaque" or Atherosclerotic Lesions at High Risk for Rupture. IVUS studies suggest that lesion eccentricity and the presence of echolucent zones within the plaque (representing large necrotic lipid pools) are major determinants of plaque vulnerability and increased propensity for rupture (Fig. 13-32). The limited resolution of IVUS makes it unable to directly detect the thin (<65 μm) fibrous caps; hence the presence of a necrotic core in contact with the lumen (no IVUS evidence of a fibrous cap) has been used to identify vulnerable plaques. IVUS may reveal unstable lesions with demonstrated ulceration or thin mobile dissection flaps. In addition, the presence of

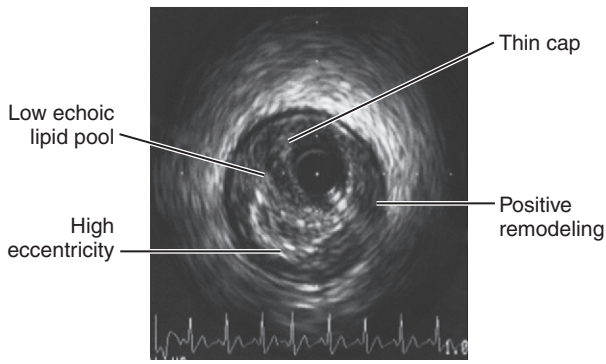


Figure 13-32 Intravascular ultrasound (IVUS) characteristics of vulnerable plaque.

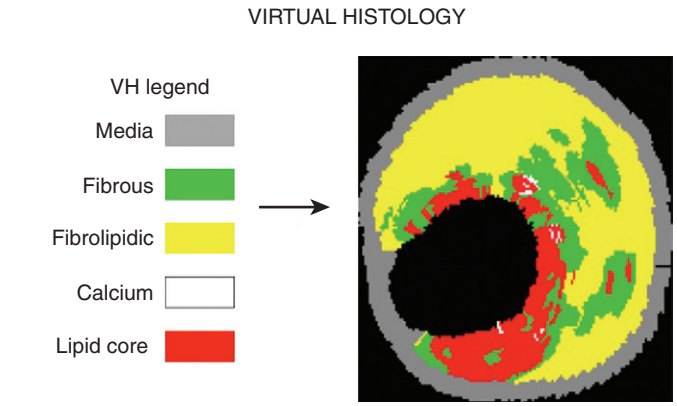


Figure 13-33 Virtual histology image representing tissue types. Media (*gray*), fibrous tissue (*green*), fibrolipidic tissue (*yellow*), calcium (*white*), and lipid core (*red*).

"positive remodeling," or compensatory enlargement of the vessel to accommodate plaque and maintain lumen, has also been found more commonly in unstable than in stable coronary lesions.

Recent advances have made possible automated gray-scale analysis of IVUS images and identification by color coding of four distinct plaque characteristics, namely fibrotic, fibrofatty, dense calcium, and necrotic core. This so-called virtual histology (VH) allows classification of lesions into fibrotic, fibrocalcific, pathologic intimal thickening, thick cap fibroatheroma, and VH-thin cap fibroatheroma based on their specific composition and morphology (Fig. 13-33). The prognostic impact of the various types of lesions was examined in the recently reported PROSPECT study, a trial evaluating the natural history of nonculprit stenoses in patients presenting with acute coronary syndrome. Lesion characteristics associated with a statistically significant increase in event rates included VH-thin cap fibroatheroma, plaque burden >70%, and minimal luminal area < 4.0 mm^2. However, overall event rates due to nonculprit stenoses were lower than expected (12% at 3–5 years) and generally less severe (no excess mortality or MI), suggesting that even plaques with vulnerable characteristics may not necessarily require invasive management.

Assessing Coronary Lesions Before PCI—Anatomy Is Not Always Equal to Physiology

IVUS parameters for predicting the clinical significance of intermediate coronary lesions have been compared with FFR and in one study to thallium stress imaging. In 70 patients the results of nuclear perfusion imaging were correlated to IVUS. A minimum lumen area (MLA) of <4.0 mm^2 had a sensitivity of 88% and specificity of 90% for predicting ischemia on the noninvasive nuclear test. Furthermore, in a large retrospective study of patients with intermediate lesions in whom PCI was deferred, Abizaid *et al.* found that an IVUS MLA of >4 mm^2 predicted freedom from adverse events.

When comparing IVUS to FFR, Takagi *et al.* demonstrated in 51 lesions that an IVUS MLA of <3.0 mm^2 had a sensitivity of 83% and a specificity of 92% for predicting an FFR of <0.75. An area stenosis of >0.6 had a sensitivity of 92% and specificity of 88% for predicting an FFR of <0.75. Kang *et al.* showed more recently in 236 lesions that FFR <0.80 was associated with IVUS MLA, plaque burden, lesion length of 3.1 mm with MLA <3.0 mm^2, and left anterior descending vessel location. In their study, the best IVUS cutoff value to predict an FFR <0.80 was an MLA of a little as <2.4 mm^2. Among 117 lesions with an MLA >2.4 mm^2, 96% had an FFR >0.80. Figure 13-34 compares IVUS with FFR.

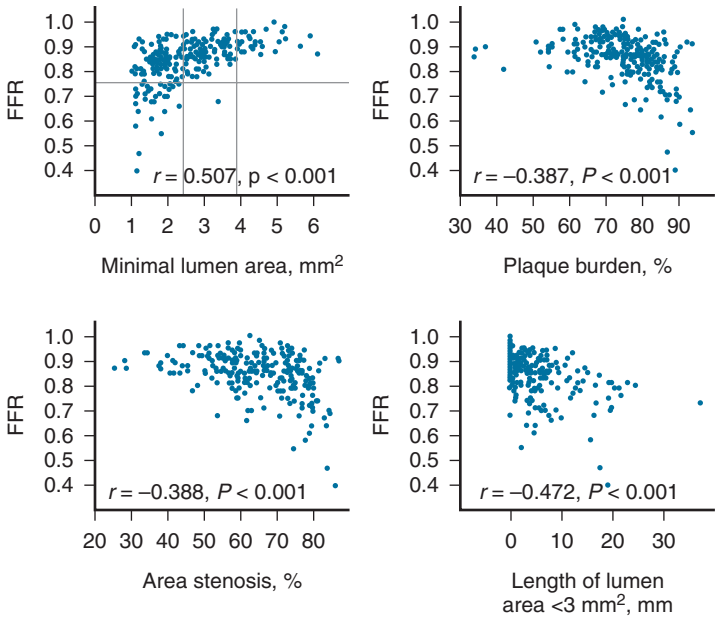


Figure 13-34 Relationship between fractional flow reserve (FFR) and intravascular ultrasound (IVUS) parameters. FFR significantly correlated with minimal lumen area (r = 0.507, P <0.001), plaque burden (r = – 0.387, P <0.001), area stenosis (r = – 0.388, P <0.001), and length with a lumen area <3.0 mm^2 (r = – 0.472, P <0.001). (Data from Kang S, *et al. Circ Cardiovasc Interv* 2011;4:65–71.)

IVUS and Left Main Stenosis

Interrogating intermediate left main coronary lesions is another area where IVUS is commonly employed. Unfortunately, there is no universal agreement on IVUS criteria for a significant left main coronary lesion. However, a lesion with an IVUS MLA <6.0 mm^2 and/or a percentage area stenosis >60% has been generally considered a significant stenosis. One study showed an increased 1-year event rate in patients with left main diameter <3.0 mm, especially in patients with diabetes. The most recent comparison of IVUS-derived parameters with FFR for assessing intermediate left main lesions found an MLA area of 5.9 mm^2 correlated best with an FFR <0.75.

In summary, the IVUS parameters for predicting ischemia have less clear absolute cutoff values than FFR parameters. Because of the complexity of any individual stenosis, including size of the reference vessel segment not accounted for in IVUS studies, lesion assessment for functional significance is best determined by FFR.

Assessing PCIs

IVUS has been studied extensively in the setting of assessing and optimizing PCI. It is a valuable tool for ensuring optimal stent expansion and strut apposition after stenting. IVUS allows a more thorough evaluation of arterial dissections, particularly involving the stent edges. After stenting, use of IVUS universally leads to improved stent expansion and larger final lumen dimensions, which in many studies, has translated into lower restenosis rates and better long-term outcomes. Both absolute and relative criteria have been put forth for gauging an optimal stent result. Complete stent apposition to the vessel wall, a minimum stent area of >90% of the average reference area, or 100% of the smallest reference area, and symmetric stent expansion with the minimum/maximum lumen diameter >0.7 are commonly cited relative criteria. An absolute minimum stent area that is >7 mm^2 is a useful absolute criterion.

There are data to suggest that an IVUS-guided PCI results in a lower target vessel revascularization rate during follow-up. This has been attributed to the improved stent expansion achieved with IVUS guidance compared with angiography alone. One randomized study documented cost savings over 2 years of follow-up. With the advent of drug-eluting stents, in which maximal expansion may not be as critical, although still important, IVUS guidance may appear less valuable. However, ensuring complete lesion coverage by accurate length measures, selection of the appropriate diameter stent, evaluating for calcium that may impair expansion or delivery, documenting appropriate apposition, and ensuring the absence of peri-stent dissection or hematoma remain important features associated with better clinical results.

Assessing Complications

Following coronary interventions, vessel stretching, plaque redistribution or shifting, plaque removal, plaque fissuring, and dissections can be clearly outlined by IVUS. IVUS studies have shown that dissections are dependent on differential plaque types, usually occurring at the edge of calcified segments.

Diagnosis of Allograft Vasculopathy

IVUS has been an excellent means of diagnosing and quantifying cardiac transplant vasculopathy. Routine annual angiographic studies often reveal "normal" vessels in the transplant patient, whereas IVUS studies of the same cohort reveal diffuse intimal hyperplasia. Serial assessments of the progression of intimal proliferation in cardiac transplant patients with angiography and IVUS have documented accelerated vasculopathy, occurring most actively within the first year following transplant.

Progression and Regression of Coronary Atherosclerosis

Because of the limitations of angiography in defining wall structure and pathology, IVUS has been useful in assessing the extent and progression or regression of atherosclerosis in trials of primary or secondary intervention for CAD. Several studies to assess atheroma progression after randomization to a lipid-lowering regimen or "regular care" have been completed and have documented slowing of lesion progression and enhanced echogenicity, possibly indicating reduced lipid content. The REVERSAL trial showed that intensive statin therapy could cause plaque regression using IVUS parameters.

OCT

Intracoronary OCT is a catheter-based optical imaging modality that is capable of providing high-resolution (about 7μm axial and 30μm transverse resolution), cross-sectional images of the coronary wall. OCT is an *interferometric* technique, typically employing *near-infrared* light. By analyzing the coherence of the light reflections, the OCT imaging catheter permits better structural imaging with tissue characterization to the 10- to 20-μm level of resolution.

The OCT catheter is nearly identical to an IVUS catheter except that the fiberoptic imaging core replaces the ultrasound imaging core. The catheter is introduced into the artery over a guidewire exactly like the IVUS catheter. A relatively recent modification of the signal acquisition method, called *frequency-domain* imaging, improves *signal-to-noise ratio*, permitting faster image acquisition. Images are acquired during rapid automated pullback after an injection of saline or contrast to displace blood and clear the viewing field. Compared with conventional imaging modalities, OCT has a superior resolution for evaluating certain

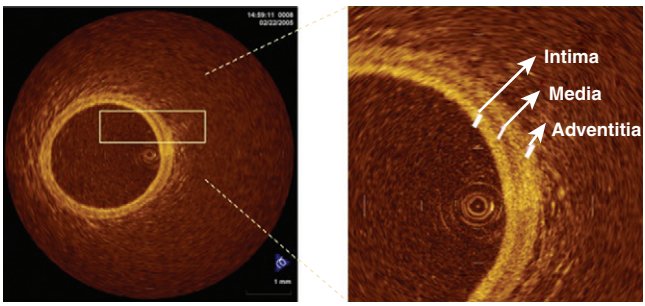


Figure 13-35 Optical coherence tomography (OCT) is a light-based imaging modality utilizing recently developed laser and fiber optic technologies to create real-time, high-resolution tomographic images most notably in medical applications. OCT's excellent resolution enables practitioners to distinguish the edges of the intima, media, and adventitia. Images show features of normal coronary artery in a male patient.

features of the vulnerable plaque, such as plaque rupture, IC thrombus, thin-capped fibroatheroma, and macrophages within the fibrous caps. Furthermore, OCT can provide visualization of stent malapposition and tissue protrusion after stenting and neointimal hyperplasia at late follow-up. One drawback of OCT in comparison with IVUS is its shallow depth of penetration (1–2 mm), limiting assessment of plaque composition. Figures 13-35, 13-36, 13-37, 13-38, and 13-39 show examples of OCT in coronary artery interventions.

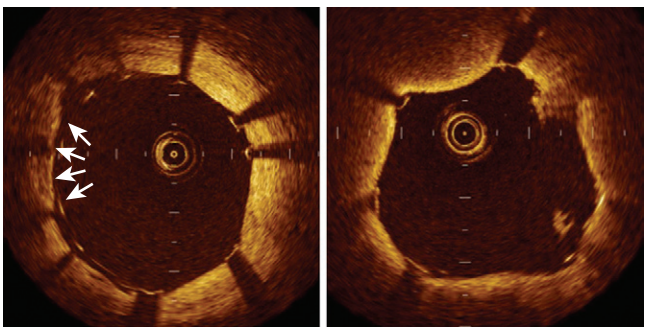


Figure 13-36 OCT images of stent strut incomplete apposition (left) and full implantation (right).

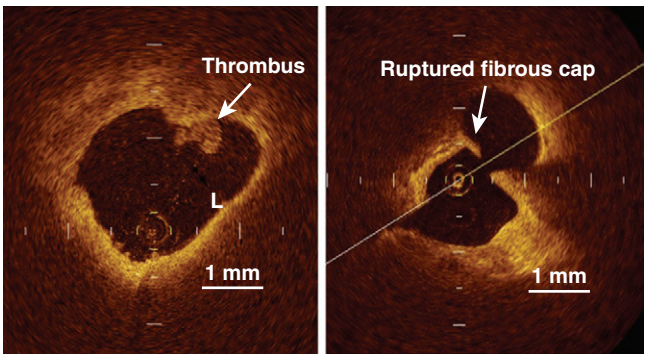


Figure 13-37 Culprit lesion of ST-segment elevation myocardial infarction (STEMI) by optical coherence tomography (OCT). Left panel shows thrombus on eroded plaque, right panel shows ruptured cap of the cultprit lesion. (Courtesy of Dr. Shigeo Takarada.)

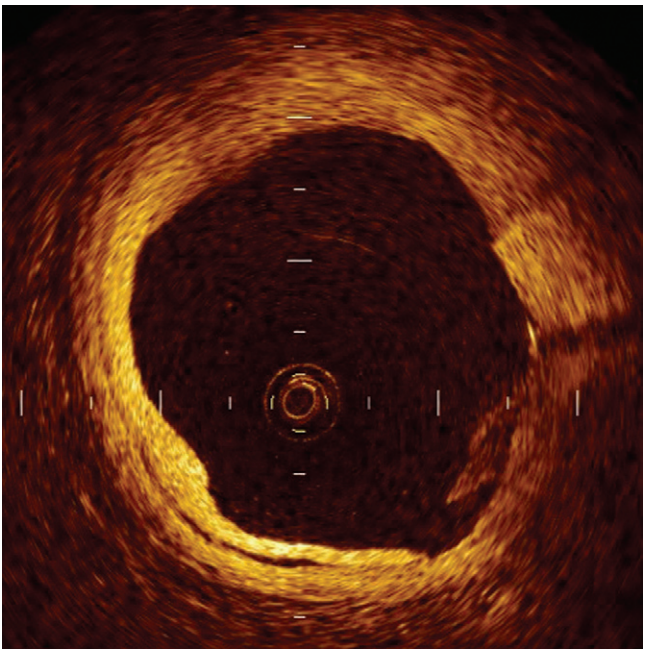


Figure 13-38 OCT image of coronary dissection with tissue flap at 4 o'clock. (Courtesy of Dr. Takarada).

The exact role of OCT in imaging coronary vessels remains to be determined. It may replace IVUS for certain applications, such as assessing stent deployment, but IVUS may remain the standard for assessing plaque composition. Combination coregistered OCT/IVUS catheters are in development.

Figure 13-40 compares coronary imaging modalities that can be used in the cath lab today.

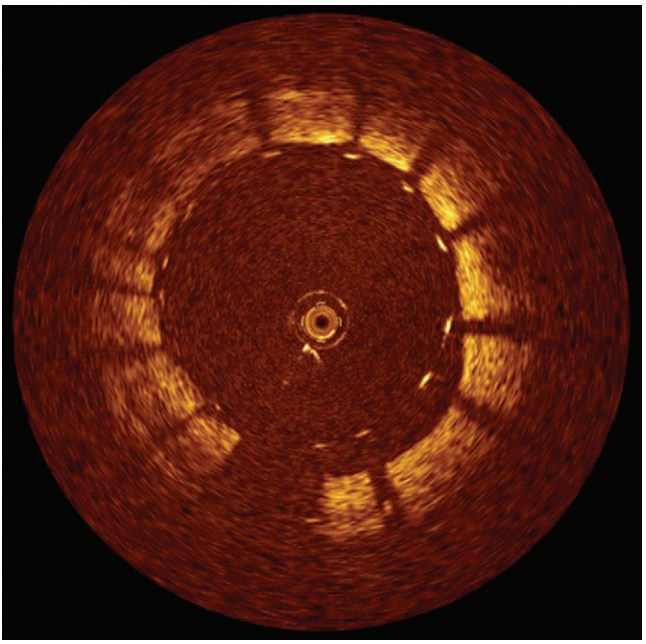


Figure 13-39 OCT image of incomplete stent strut apposition from 3 to 6 o'clock. (Courtesy of Dr. Takarada).

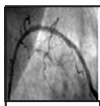
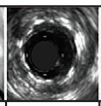
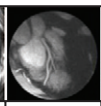
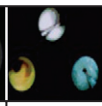
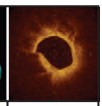
	CAG	IVUS	CT,MRI	Angioscopy	OCT
					
Resolution (μm)	100–200	80–120	80–300	<200	10–15
Probe size (μm)	N/A	700	1000	800	140
Contact	No	Yes	No	No	No
Ionizing radiation	Yes	No	No	No	No
Other	Flow only	N/A	N/A	Surface only	Plaque character

Figure 13-40 Comparison of coronary imaging devices in the cath lab. *CAG,* coronary angiography; *CT,* computed tomography; *IVUS,* intravascular ultrasound; *MRI,* magnetic resonance imaging; *OCT,* optical coherence tomography.

Coronary Doppler Flow

IC Doppler flow velocity measurements are most useful for research investigations into the status of the microcirculation with normal epicardial conduits. The Doppler flow wire can provide an objective, physiologic measurement of coronary blood flow and can measure flow velocity responses to pharmacologic or mechanical interventions. It is also useful in the study of collateral blood flow responses.

The Doppler angioplasty guidewire (Volcano Therapeutics, Rancho Cordova, CA) is a flexible, steerable guidewire 175 cm long and 0.014 inch in diameter with a piezoelectric ultrasound transducer integrated into the tip. The forward-directed ultrasound beam diverges in a 27-degree arc from the long axis (measured to the –6 dB roundtrip points of the ultrasound beam pattern). A pulse repetition frequency of more than 40 kHz, pulse duration of +0.83 msec, and sampling delay of 6.5 msec are standard for clinical usage. The system is coupled to a real-time spectrum analyzer, a videocassette recorder, and a video page printer. The quadrature/Doppler audio signals are processed by the spectrum analyzer using on-line fast-Fourier transformation to provide a scrolling gray-scale spectral display. The frequency response of the system calculates approximately 90 spectra/sec. Simultaneous electrocardiographic and arterial pressure is also input to the video display. The fundamentals and artifacts of flow velocity measurements have been described in detail elsewhere (see Suggested Readings).

Coronary Flow Velocity Signal Analysis

The velocity of red blood cells flowing past the ultrasound emitter/receiver on the end of a guidewire can be determined from the frequency shift, defined as the difference between the transmitted and returning frequency, where:

$$V = (F_1 - F_0) \times (C / 2F_0) \times \text{Cos}\emptyset,$$

where V = velocity of blood flow, F_0 = transmitting (transducer) frequency, F_1 = returning frequency, C = constant for the speed of sound in blood, Ø = angle of incidence. Volumetric flow is the product of the vessel area (cm^2) and the flow velocity (cm/sec), yielding a value in cm^3/sec.

The parameters of IC flow velocity, including maximal peak velocity (MPV) and mean or average peak velocity (APV) diastolic and systolic velocities, are displayed and recorded (Fig. 13-41).

CFVR is the ratio of the hyperemia APV to resting APV. CFR measures the summed response of both the epicardial artery and the microcirculation. For this reason, a patient without epicardial disease but with abnormal microcirculatory function can have an abnormal CFVR,

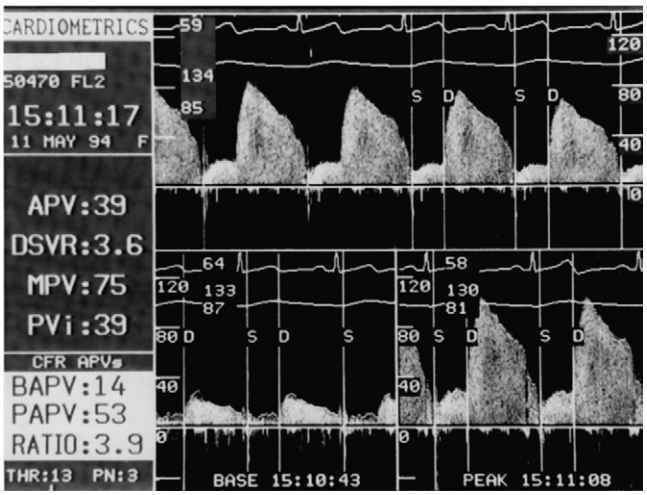


Figure 13-41 Panel of flow velocity signals for measurement of coronary vasodilatory flow reserve. Flow panel was divided into upper and lower parts. The upper panel is a continuous display in real time of the flow spectra. The normal phasic pattern is seen shortly after hyperemia. The electrocardiogram (ECG) and aortic pressure is displayed on top of the flow signals. The numbers in the upper left corner box are the heart rate, systolic pressure, and diastolic pressure. The lower panel is divided into left and right for storage of baseline and hyperemic signals respectively. The codes at the left are the values for the flow parameters of the top panel (*far right*). *APV,* average peak velocity; *BAPV,* base average peak velocity; *DSVR,* diastolic-systolic velocity ratio; *MPV,* maximal peak velocity; *PAPV,* peak (hyperemic) average peak velocity; APV; *PVI,* peak velocity interval; *Ratio,* coronary flow reserve.

limiting the utility of CFVR for assessment of intermediate epicardial stenoses in patients with microvascular disease.

Technique of Coronary Doppler Measurements

The technique of Doppler wire flow velocity signal acquisition is identical to that of the FFR pressure wire. Prior to introducing the sensor wire, heparin and IC nitroglycerin (200 μg) are given. Nitroglycerin blocks changes in epicardial lumen dimension during the measurements, which may alter the flow velocity down the vessel. Using standard angioplasty equipment, the wire is introduced through the guide catheter to the coronary artery. The tip of the wire should be positioned in a mid-vessel segment (approximately 3 mm diameter). Attempts should be made to position the wire in the middle of a major vessel and, by gentle torquing, maximize the velocity signal. The wire should not be moved between the resting velocity measurement and the hyperemic velocity measurement. Coronary hyperemia is induced exactly as done for determining FFR.

Although earlier studies report a coronary vasodilatory reserve ratio of 3.5 to 5 in normal patients, lower values are more commonly observed in patients with chest pain and angiographically normal arteries (normal 2.7 ± 0.6). Changes in cardiovascular hemodynamics (heart rate, contractility, blood pressure) can impact the CFVR (but not FFR), a limitation when performing follow-up or serial CFVR measurements.

Methodological Considerations

Doppler coronary velocity only measures relative changes in velocity. To measure absolute blood flow, APV × CSA is calculated. The following assumptions must be made:

- The cross-sectional area of the vessel being studied remains fixed during hyperemia.

- The velocity profile across the vessel is not distorted by arterial disease.
- The angle between the crystal and sample volume remains constant and <30 degrees from the horizontal flow stream.

Assessing Collateral Flow by IC Doppler

To quantify the presence and degree of collaterals, a Doppler collateral flow index (CFI) has been described. CFI is defined as the amount of flow via collaterals to a vascular region, divided by the amount of flow to the same region via the normally patent vessel. It is determined by summing the integral of systolic and diastolic flow velocities during balloon occlusion. In the case of temporally shifted bidirectional flow velocity signals, the antegrade and retrograde velocity integrals are added. The total velocity integral during balloon occlusion is then divided by the velocity integral after successful PCI, in order to calculate the CFI. A Doppler CFI >0.30 has been shown to accurately predict collateral circulation adequate enough to prevent myocardial ischemia during PCI. Moreover, the Doppler CFI is a more sensitive determinant of collateral flow than is angiographically visible collateral circulation. In another study, patients undergoing PCI who had a Doppler CFI of >0.25 had a fourfold decrease in the major adverse cardiac event rate at approximately 2 years compared with those with a CFI <0.25. The obvious limitation of this technique is that it requires performance of PCI (Fig. 13-42).

Safety of IC Sensor-Wire Measurements

Qian *et al.* examined the safety of IC Doppler wire measurements in 906 patients. Fifteen patients (1.7%) had severe transient bradycardia after IC adenosine, 14 in the right coronary artery and 1 in the left coronary artery. Nine patients (1%) had coronary spasm during passage of the Doppler guidewire (5 in the right coronary and 4 in the left anterior descending). Two patients (0.2%) had ventricular fibrillation during the procedure. Hypotension with bradycardia and ventricular asystole occurred in one patient. Transplant recipients had more of these complications than either diagnostic or interventional procedures. All complications could be managed medically. These data support the safety of using sensor wire measurements.

A summary of the characteristics of coronary vasodilatory reserve (CVR), relative CVR (rCVR), FFR, and IVUS is provided in Table 13-2.

Collateral flow reversal during balloon occlusion

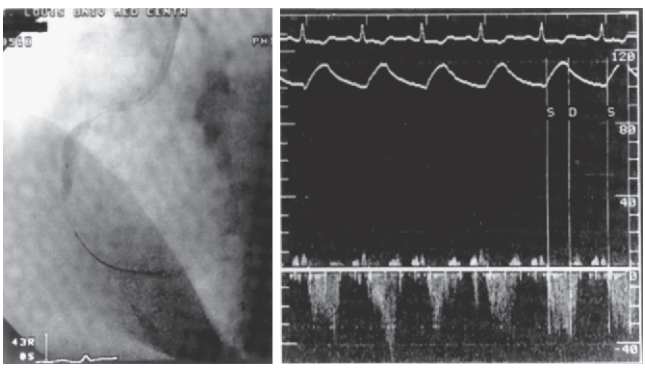


Figure 13-42 Flow velocity signal reversal characteristic of epicardial collateral flow.

Research in the Cath Lab: NIRS Coronary Imaging System

Invasive imaging of the coronary artery with IVUS provides a detailed anatomical quantitative description with some information relating to tissue composition (calcification, fibrosis, lipid, or soft plaque).

Using a catheter system similar to that of IVUS, near-infrared wavelength light can be used to detect cholesterol content in a vessel, another component intimately associated with vulnerable coronary plaques.

The NIRS LipiScan catheter uses the basic principle of spectroscopy, a technique used by chemists to identify molecules based on their distinct spectroscopic signature. Using this principle, an intravascular imaging catheter was equipped with a laser emitting a specific wavelength of light trained at linoleic acid, the major chemical constituent of cholesterol within plaques. The fiberoptic core transmits near-infrared light and is used in a manner analogous to an IVUS catheter. An automatic pullback device pulls the infrared catheter within the artery from distal to proximal during the scanning for cholesterol. As the spectrum of light goes through the blood and into the vessel wall, its reflection is collected and analyzed. Because the vessel wall absorbs some of the spectra, the spectroscopic signature is a function of the light sent out and the light returned (the difference is the absorbed light). Cholesterol signal is designated as yellow, nonlipid as red or black. No signal is white.

The LipiScan Console (Fig. 13-43) performs several functions. In brief, it provides (1) the near-infrared light source for spectroscopy, (2) a data-processing system that analyzes the signals returned from the pullback interface, (3) a user interface to the system, (4) a means of data storage, and (5) communication to the pullback interface that drives the automated scanning of the LipiScan Coronary Imaging Catheter core. The console consists of the following major components: laser and laser delivery system, computer system and software, and power module.

This technique provides a "chemographic" map of cholesterol deposits within the artery, displayed as if the artery had been laid open and spread out from distal to proximal. The "chemogram" is based on an algorithm that quantitates the likelihood of a lipid-core plaque in any particular 2-mm block of vessel. The chemogram is color-coded, with bright yellow indicating a >90% likelihood of a lipid-core plaque

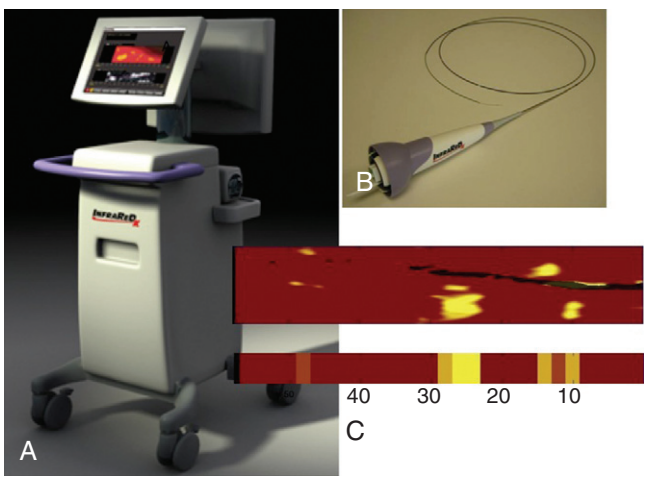


Figure 13-43 InfraReDx LipiScan system. LipiScan System. **A,** Console. **B,** 3.2 F catheter (Monorail, 0.014-inch compatible; no priming required; automated pullback; no occlusion blood flow). **C,** Validated lipid core plaque (LCP) detection algorithm.

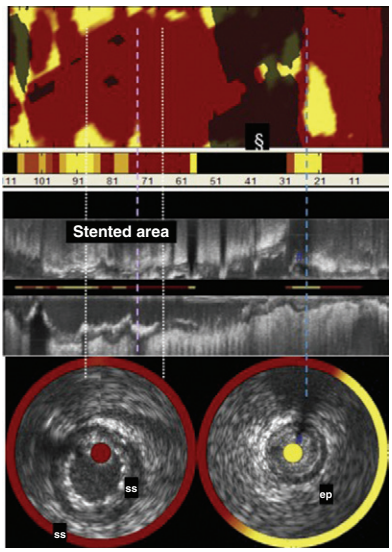


Figure 13-44 Near-infrared spectroscopy (NIRS) catheter combined with intravascular ultrasound (IVUS). (Courtesy of Dr. Patrick Serruys, Rotterdam.)

and red indicating no evidence of a lipid-core plaque. The chemogram approach was validated in an autopsy study (published in the *Journal of the American College of Cardiology,* 2009). The Food and Drug Administration (FDA) approved the LipiScan catheter for the detection of lipid core plaques. The risks and limitations of the LipiScan catheter are similar to the IVUS catheter, and a combined NIRS/IVUS device is currently available (Fig. 13-44).

Suggested Readings

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14

Peripheral Vascular Intervention

PRANAV M. PATEL

Peripheral arterial disease (PAD) refers to stenotic, occlusive, and aneurysmal diseases of the aorta and branch arteries that include the lower extremity, upper extremity, renal, mesenteric, and carotid arterial beds. PAD is a common manifestation of atherosclerosis, and its prevalence increases with age and concurrent cardiovascular risk factors such as diabetes and tobacco use. As with coronary artery disease (CAD), PAD has a natural history, progression pattern, and susceptibility for developing vulnerable and complex plaques with a strong positive correlation to cardiovascular events and mortality.

Cardiovascular disease is the major cause of death in patients with intermittent claudication. Patients with newly diagnosed PAD are six times more likely to die within the next 10 years when compared with patients without PAD.

In 2006 the American College of Cardiology and American Heart Association (ACC/AHA) developed guidelines to aid in the diagnosis and management of patients with PAD. These guidelines suggest that individuals with the following characteristics would be at risk from PAD:

- Age less than 50 years, with diabetes and one other atherosclerosis risk factor (smoking, dyslipidemia, hypertension, or hyperhomocysteinemia)
- Age 50 to 69 years and a history of smoking or diabetes
- Age 70 years or older
- Symptoms with exertion involving the lower extremities (suggestive of claudication) or ischemic rest pain
- Abnormal lower extremity pulse examination
- Known atherosclerotic coronary, carotid, or renal artery disease

Patient Selection for Peripheral Endovascular Intervention

When considering patients for peripheral endovascular intervention (PVI), an accurate history and physical exam are most important. Initial risk factor assessment and screening tests for cardiovascular disease, should be obtained. Patients should be medically optimized. The review of symptoms and family history is an essential component of the vascular history. The key component to the diagnosis of PAD is the presence of symptoms. However, <20% of PAD patients report the typical symptoms of intermittent claudication. Many patients present with atypical symptoms. These include:

- Any exertional limitation of the lower extremity muscles or any history of impaired ambulation. This limitation may be described as cramping, fatigue, aching, numbness, or pain. The primary site(s) of discomfort in the buttock, thigh, calf, or foot

Table 14-1

Questions Used to Distinguish PAD Symptoms From Non-PAD

Pain and location	Do you have pain or discomfort? Where is the discomfort?
Consistency	Is the pain the same every time?
Severity	How much can you do before the pain starts? Have your activities changed because of the pain?
Character and quality	What does the discomfort feel like? Can you describe it?
Exacerbation	What makes the pain worse? What relieves the pain?

PAD, peripheral arterial disease.

should be documented, along with the relation of such discomfort to rest or exertion.

- Any poorly healing or nonhealing wounds of the legs or feet.
- Any pain at rest localized to the lower leg or foot and its association with the upright or recumbent positions.
- Postprandial abdominal pain that is provoked by eating and associated with weight loss.
- Family history of a first-degree relative with an abdominal aortic aneurysm.

The patient history should include questions that try to distinguish PAD from diseases that have a non-PAD etiology (Table 14-1).

Intermittent claudication is the most classic manifestation of PAD. In 1962 epidemiologist Geoffrey Rose designed a questionnaire to assess the incidence and prevalence of intermittent claudication in large epidemiologic studies. The sensitivity of the Rose claudication questionnaire approaches approximately 10% to 30%; however, similar questions (and modifications to the Rose questionnaire) are still very helpful in diagnosing intermittent claudication (Table 14-2).

True vascular claudication must be distinguished from "pseudoclaudication" caused by severe venous obstructive disease, chronic compartment syndrome, lumbar disease and spinal stenosis, osteoarthritis, and inflammatory muscle diseases. The characteristic features of pseudoclaudication that distinguish it from claudication are summarized in Table 14-3.

Symptoms of intermittent claudication classically start distally within a muscle group (below the stenosis) and then ascend with continued activity. Rest pain that occurs with leg elevation and is relieved paradoxically by walking may suggest severe PAD (as the effects of gravity increase arterial perfusion of muscle groups). Critical PAD may present as tissue ulceration and gangrene. The ACC/AHA guidelines suggest that individuals with PAD present in clinical practice with distinct syndromes (Table 14-4).

The physical exam defines the location, severity, and etiology of PAD and its symptoms. Arterial pulse intensity should be assessed and should be recorded numerically, as shown in Table 14-5. Table 14-6 outlines some of the important findings on the physical exam of the legs.

Table 14-2

Rose Questionnaire: Symptoms of Classic Intermittent Claudication

Calf pain caused by exertion that:

1. Does not occur at rest
2. Does not resolve during walking
3. Stops the patient from continued walking
4. Resolves within 10 min of rest

Table 14-3

Distinguishing Characteristics Between Claudication and Pseudoclaudication

	Claudication	Pseudoclaudication
Characteristic of discomfort	Cramping, tightness, aching, fatigue	Same as claudication plus tingling, burning, numbness
Location of discomfort	Buttock, hip, thigh, calf, foot	Same as claudication
Induced by exercise	Yes	Variable
Reproducible with distance walked	Consistent	Variable
Occurs with standing	No	Yes
Actions that provide relief	Standing	Sitting, changing position
Time until relief	<5 min	<30 min

Table 14-4

Distinct syndromes of PAD

Individuals with peripheral arterial disease (PAD) present in clinical practice with a variety of distinct syndromes:

Asymptomatic: Without obvious symptomatic complaint (but usually with a functional impairment)

Classic claudication: Lower extremity symptoms confined to the muscles with a consistent (reproducible) onset with exercise and relief with rest

"Atypical" leg pain: Lower extremity discomfort that is exertional but that does not consistently resolve with rest, consistently limit exercise at a reproducible distance, or meet all Rose questionnaire criteria

Critical limb ischemia: Ischemic rest pain, nonhealing wound, or gangrene

Acute limb ischemia: The five "P"s, defined by the clinical symptoms and signs that suggest potential limb jeopardy: pain, pulselessness, pallor, paresthesias, paralysis (and polar, as a sixth "P")

Table 14-5

Gradation of Arterial Pulse

Numerical Gradation	Clinical Assessment
0	Absent
1	Diminished
2	Normal
3	Bounding

Table 14-6

Physical Exam Findings of Peripheral Arterial Disease

Limb examination (and comparison with the opposite limb) includes:

1. Absent or diminished femoral or pedal pulses (especially after exercising the limb)
2. Arterial bruits
3. Hair loss
4. Poor nail growth (brittle nails)
5. Dry, scaly, atrophic skin
6. Dependent rubor
7. Pallor with leg elevation after 1 min at 60 degrees (normal color should return in 10–15 sec; longer than 40 sec indicates severe ischemia)
8. Ischemic tissue ulceration (punched-out, painful, with little bleeding), gangrene

Diagnostic Testing

Ankle-Brachial Index

Performing ankle-brachial index (ABI) both at rest and after exercise is very useful, especially in individuals at risk of developing PAD. The toe-brachial index (TBI) should be used in individuals with noncompressible pedal pulses (e.g., the elderly). Exercise ABI may be even more useful than resting ABI, serving to unmask PAD when resting ABI is normal. Exercise ABI testing will also assess the functional severity of claudication and aid differentiation of intermittent claudication from pseudoclaudication. Performing segmental ABI and pulse volume recordings together with the ABI can indicate presence of multilevel occlusive lower extremity PAD.

Duplex Ultrasound

Arterial duplex ultrasound of the extremities identifies the anatomical location and degree of stenosis of PAD. Duplex ultrasound is recommended for routine surveillance after femoropopliteal or femoral-tibial-pedal bypass with a venous conduit. Minimum surveillance intervals are approximately 3, 6, and 12 months, and then yearly after graft placement as per ACC/AHA guidelines.

Magnetic Resonance Angiography

Magnetic resonance angiography (MRA) of the extremities is also useful to diagnose anatomical location and degree of stenosis of PAD. The MRA should be performed with gadolinium enhancement, although it must be noted that gadolinium use in individuals with an estimated glomerular filtration rate (eGFR) <60 mL/min has been associated with nephrogenic systemic fibrosis/nephrogenic fibrosing dermopathy. MRA of the extremities is useful in selecting patients with lower extremity PAD as candidates for endovascular intervention.

Computed Tomography Angiography

Computed tomography angiography (CTA) of the extremities also diagnoses the anatomical location and presence of significant stenosis in patients with lower extremity PAD. CTA may be considered as a substitute for MRA for those patients with contraindications to MRA (claustrophobia, presence of pacemaker/implantable cardioverter-defibrillator).

Peripheral Vascular or Endovascular Intervention

Endovascular procedures, or percutaneous catheter-based revascularization techniques, is the group name for techniques used to achieve the nonsurgical revascularization of PAD patients. Endovascular therapy offers several distinct advantages over surgical revascularization:

1. Performed using local anesthesia, enabling the treatment of patients who are at high risk for general anesthesia.
2. Lower morbidity and mortality compared to surgical revascularization.
3. Earlier ambulation on the day of treatment and earlier return to normal activity within 24 to 48 hours.
4. Endovascular therapies may be repeated if necessary, generally without increased difficulty or increased patient risk compared to the first procedure.
5. Prior angioplasty does not preclude surgery if required at a later date.

Problems secondary to endovascular intervention are generally related to bleeding and vascular access.

The evaluation prior to performing endovascular intervention is identical to that for a patient undergoing cardiac catheterization and includes a complete blood count, serum electrolytes, coagulation panel (activated partial thromboplastin time, prothrombin time, international normalized ratio), serum creatinine, glomerular filtration rate, stool guiac, fasting glucose, and an electrocardiogram.

Premedication

The standard premedication for endovascular intervention includes aspirin therapy (81–325 mg/day). Other antiplatelet agents (clopidogrel and ticlopidine) have been used prior to carotid artery and cerebrovascular intervention. There are no data to suggest that the use of these additional antiplatelet agents increases the procedural success rate or decreases the rate of complications. Their use is optional.

Vascular Access

Successful endovascular intervention requires appropriate choice of vascular access. In most cases, access is obtained using a 21-gauge needle and 0.18-inch wire (4F micropuncture set). The retrograde approach to the common femoral artery (CFA) is the most frequently used vascular access. The inguinal crease is highly variable in relation to the CFA bifurcation in up to 75% of patients. Identifying the femoral head under fluoroscopy is very helpful (Fig. 14-1), as this will help ensure puncture of the vessel above the CFA bifurcation and below the inguinal ligament. Vascular access with the use of ultrasound imaging is also safe and effective as this allows direct imaging of the vessel.

The majority of PVIs can be performed from several access sites (Table 14-7). On most occasions the location of the lesion (to be intervened upon) will determine the most appropriate access site.

Retrograde CFA access permits selective angiography and intervention of the contralateral pelvic and lower extremity vessels. After gaining retrograde access (Fig. 14-2) to the CFA, the contralateral iliofemoral system is reached by placing a diagnostic catheter with an acute bend at the tip (usually an internal mammary artery [IMA] or Simmons catheter) at the aortic bifurcation. The catheter is manipulated so that the

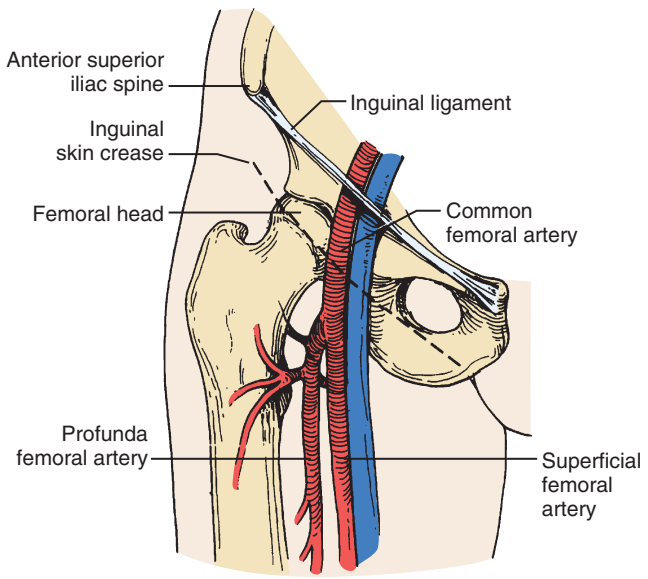

Figure 14-1 Schematic diagram showing vascular supply in right femoral area.

Table 14-7

Arterial Access for Different Vascular Territories	
Vascular Access	**Artery(ies) to Revascularize**
Retrograde CFA	Arch vessels, renal, & mesenteric
Contralateral CFA	Contralateral iliacs, CFA, PFA, SFA, popliteal
Antegrade CFA	Mid-distal femoral, popliteal, infrapopliteal
Brachial/radial artery	Renal (caudal takeoff), mesenteric, iliac arteries
Retrograde popliteal artery	SFA and iliac artery

CFA, common femoral artery; *PFA,* profunda femoris artery; *SFA,* superficial femoral artery.

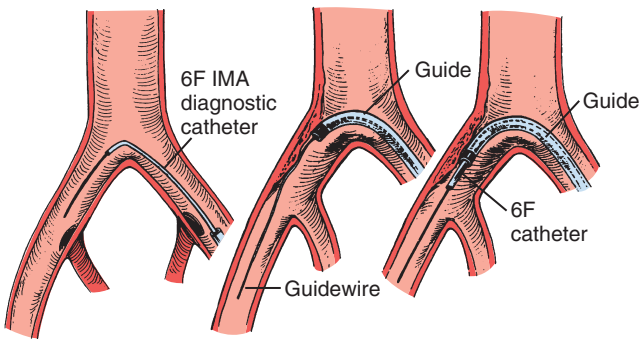

Figure 14-2 Schematic diagram of contralateral femoral access. *IMA,* internal mammary artery.

tip "engages" the ostium of the contralateral common iliac artery. A stiff-angled 0.035-inch Glidewire (Terumo Medical Corporation, Somerset, NJ) is then carefully steered to the femoral artery and the diagnostic catheter is advanced over the Glidewire into the CFA. The Glidewire is then exchanged through the diagnostic catheter for a stiff guidewire (Amplatz extra-stiff, Cook, Bloomington, IN), which is advanced into the distal femoral artery. The diagnostic catheter is then removed, leaving the extra-stiff wire in place. A crossover sheath (6F–8F) may then be advanced over the stiff guidewire and positioned in the contralateral CFA. This allows contrast injection during lesion dilation and backup support for crossing lesions. This type of sheath manipulation may be very difficult with individuals who have an acute angle between the origin of the common iliac arteries or those who have aortofemoral bypass grafts.

Antegrade CFA access allows for easier treatment of lesions located in the arterial tree just at or below the knee. It is more technically demanding than retrograde CFA access, particularly in obese patients. Antegrade CFA access may carry a higher complication rate than retrograde CFA access. When entering the CFA in an antegrade fashion, it is helpful to identify the femoral head under fluoroscopy. Depending on the amount of subcutaneous tissue, a skin incision is made 1 to 2 cm cephalad to the middle of the femoral head. After the CFA pulse is located at the middle of the femoral head, the percutaneous needle is introduced through the skin incision and directed obliquely and caudally toward the center of the femoral head. Once the CFA has been entered, a steerable guidewire (Wholey, Mallinckrodt, St. Louis, MO) is advanced under fluoroscopic guidance toward the superficial femoral artery (SFA) which runs medial to the profunda femoris artery (PFA). It is important to emphasize that, at their origin, the SFA and PFA overlap in the anteroposterior (AP) fluoroscopic view. To separate them, a lateral oblique view (20–40 degrees) is used. Relative contraindications for the use of this vascular access site include atherosclerotic disease of the CFA or proximal SFA, and extreme obesity.

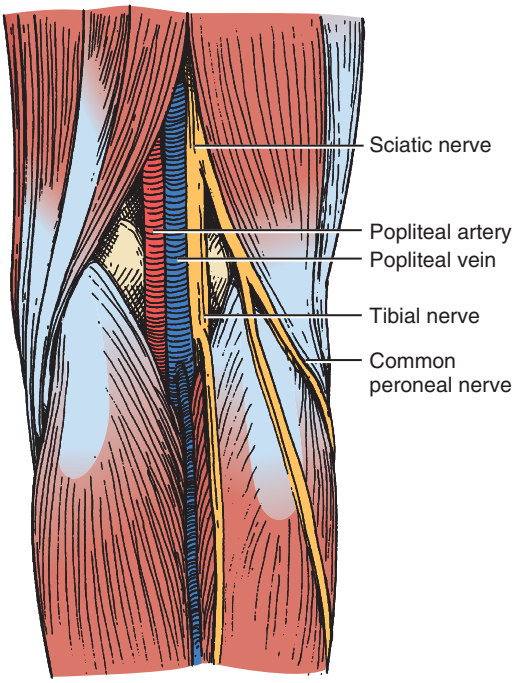

Figure 14-3 Schematic diagram of the popliteal fossa.

Retrograde popliteal artery access can be useful when trying to cross an occluded SFA. It is important to be aware of the anatomical relationship between the popliteal artery and vein. At the level of the joint space, the artery courses anterior to the vein, whereas, at approximately 6 cm cephalad to the joint space, the artery is medial to the vein (Fig. 14-3). For popliteal arterial puncture, the vessel should be free of significant disease and larger than 4 mm in diameter. Prior angiography and/or color-flow duplex imaging may provide useful information regarding puncture of this vessel. The first step is to gain contralateral CFA access in order to provide contrast injections to help visualize the target popliteal artery. The CFA sheath is secured in place and the patient is turned to the prone position. Contrast injections performed through the contralateral CFA sheath allow fluoroscopic visualization of the popliteal artery. In this way a micropuncture needle is directed obliquely from medial to lateral so that the artery is entered approximately 5 to 6 cm above the joint space. A 0.035-inch floppy guidewire is then advanced into the popliteal artery, and a 4F to 6F sheath is then inserted.

Nonselective Abdominal Angiography

Vascular access for initial aortoiliac intervention may be performed via brachial, axillary, or femoral artery access. After insertion of a 4 F to 6 F sheath, a pigtail or other "flush" angiographic catheter can be advanced to the level of the mesenteric or renal arteries (approximately lumbar level L1 at the spine) to perform nonselective angiography. The "flush" catheters have multiple side holes and include the tennis racket, straight, and universal (e.g., SOS Omni; AngioDynamics, Latham, NY) catheters. These catheters should generally be advanced over a 0.035-inch wire with a gentle, floppy tip such as a Wholey or other type of steerable wire. This type of 0.035-inch wire is more maneuverable and ultimately more forgiving in patients with severely stenotic or calcified vessels. If there is some difficulty navigating past severely stenotic lesions with these wires, then a 0.035-inch angled and tapered Glidewire may be

able to perform this task. Because angiographic contrast is delivered under force, using end-hole catheters during nonselective power injection may damage more fragile, smaller side branch arteries or atherosclerotic plaque, increasing the risk of vessel dissection and trauma. Operators should not inject into small branches of the aorta and should position their catheters safely (below T12), and not directly against the aortic wall. Positioning of catheters above T12 can result in accidental power injection into the artery of Adamkiewicz, which may cause paralysis. The operator should also be aware of the catheter's maximal flow tolerance, number of side holes, tapering of the tip, and internal diameter of the catheter.

Abdominal angiography is performed in order to evaluate the abdominal aorta, mesenteric vessels, renal arteries, and other visceral vessels. Digital subtraction angiography may be preferred over standard cineangiography. The angiogram can be performed in an AP projection. If there is a specific interest in the renal arteries and the aortorenal junction, then a left anterior oblique (LAO) projection of approximately 5 to 30 degrees may provide better visualization of the origin of both renal arteries. In this particular case the universal and tennis racket catheters may be preferred, as they deploy contrast dye in a caudal direction (rather than the cephalad direction of the pigtail catheter), and so prevent the dilution that may occur with illumination of the celiac trunk and superior mesenteric artery.

Nonselective angiography requires knowledge of image angulations and vascular anatomy to better define disease involving the aortovisceral vessel junction, and other ostial disease. Table 14-8 depicts some useful angiographic views for different vascular territories.

Selective Angiography

Selective angiography is the direct injection of contrast into a target vessel via a catheter. Prior to contrast injection, the catheter tip should be moving freely, and the fidelity of the hemodynamic waveform should be normal without any attenuation or "dampening" which may correlate with thrombus or atheroma within the catheter. The dampened waveform may suggest that the catheter tip is against the vessel wall or against an atherosclerotic plaque. Injection of contrast when the waveform is dampened may result in vessel dissection or embolus of the clot or atheroma.

Table 14-8

Most Useful Angiographic Views for Different Vascular Territories

Artery or Vascular Territory	Angiographic View
Aortic arch	30–60 degrees LAO (with slight cranial angulation)
Brachiocephalic vessels (origin)	30–60 degrees LAO
Subclavian	AP, ipsilateral oblique with caudal angulation
Vertebral origin	AP, ipsilateral oblique with cranial angulation
Carotid extracranial	Lateral, AP, ipsilateral oblique
Renal arteries (origin)	AP, 5–30 degrees ipsilateral oblique
Mesenteric arteries (origin)	Lateral or steep RAO
Iliac artery	Contralateral 20–45 degrees oblique and 20° caudal
CFA, SFA, and PFA arteries	Ipsilateral 30–60 degrees oblique
Femoropopliteal	AP
Infrapopliteal trifurcation and runoff	AP

AP, anteroposterior; *CFA,* common femoral artery; *LAO,* left anterior oblique; *PFA,* profunda femoris artery; *RAO,* right anterior oblique; *SFA,* superficial femoral artery.

Selective angiography also requires gentle torque movements of the catheter tip. Any type of aggressive catheter movement (without the use of guidewires) may also result in atheroemboli and vessel dissection. In some cases (especially cannulation of the renal and mesenteric vessels), a "no-touch" or minimal touch technique may be recommended. Catheters (in most cases) will be easier to manipulate than sheaths. The use of a braided catheter may be preferred for very torturous anatomy, as the metal braid within the catheter provides excellent catheter support, strength, and kink resistance. Many catheters used in selective angiography also have an outer hydrophilic layer that provides better tracking through torturous vessels, extra lubricity, and less thrombogenicity.

Aortoiliac Intervention

There are various types of aortoiliac occlusive disease and procedures to surgically treat them. The patency rate for these procedures is documented in Table 14-9. Most commonly, the lesions of greatest hemodynamic consequence are located in the iliac arteries. The most effective surgical procedure for the treatment for this type of atherosclerotic disease, and the resultant buttock and thigh claudication, is aortobifemoral bypass. If the aortoiliac lesions are confined to the area of the aortic bifurcation, localized aortoiliac endarterectomy may be considered. Less invasive approaches may be appropriate for patients with adequate aortic flow but stenosis or occlusion of both iliac vessels. Such patients may not be candidates for aortobifemoral bypass because of comorbid cardiovascular disease. If endovascular treatment of one iliac artery is possible and can achieve good results, then a subsequent endarterectomy, unilateral iliofemoral bypass, or femoral-femoral bypass can be considered. In the absence of an inflow stenosis within the iliac arteries, this procedure can provide flow to both lower extremities and eliminate the symptoms of claudication.

Table 14-9

Patency Rates for Specific Lower Extremity Bypass Surgery Procedures

Inflow Procedure	Operative Mortality (%)	Expected Patency Rates (%)	References
Aortobifemoral bypass	3.3	87.5 (5 yr)	de Vries SO, Hunink MG. 1997
Aortoiliac or aortofemoral bypass	1–2	85–90 (5 yr)	van der Vliet JA, Scharn DM, de Waard JW, et al. 1994 Ricco JB. 1992 Raptis S, Faris I, Miller J, et al. 1995
Iliac endarterectomy	0	79–90 (5 yr)	Oskam J, van den Dungen JJ, Boontje AH. 1996 Pretre R, Katchatourian G, Bednarkiewicz M, et al. 1992 Radoux JM, Maiza D, Coffin O. 2001
Femorofemoral bypass	6	71 (5 yr)	Mingoli A, Sapienza P, Feldhaus RJ, et al. 2001
Axillofemoral bypass	6	49–80 (3 yr)	Mohan CR, Sharp WJ, Hoballah JJ, et al. 1995 Harrington ME, Harrington EB, Haimov M, 1994
Axillofemoral-femoral	4.9	63–67.7 (5 yr)	Onohara T, Komori K, Kume M, et al. 2000 Martin D, Katz SG. 2000

Patients with severe distal aortic atherosclerosis who are at high cardiovascular or surgical risk for open aortobifemoral bypass may be treated with axillofemoral-femoral bypass. Because of lower patency rates, such bypasses are reserved for those who have no alternatives for revascularization. Unilateral iliac occlusions that cannot be effectively treated by angioplasty and stent placement can be treated by iliac artery endarterectomy, aortoiliac bypass, aortofemoral bypass, or iliofemoral bypass if the origin of the iliac artery is free of disease. Disadvantages of the surgical method include higher morbidity compared with endovascular therapy.

Endovascular reconstruction options include the following:

- Percutaneous transluminal angioplasty (PTA)
- Directional atherectomy, laser atherectomy, cutting balloon angioplasty, cryoplasty
- Stents

The advantages of using percutaneous interventional procedures over bypass surgery (especially to treat chronic limb ischemia) include:

- Avoiding complications of general anesthesia
- Avoiding surgical incision and subsequent wound healing complications
- Early recovery and ambulation
- Procedure may be repeated more readily than surgery

The efficacy of PTA versus stents for lower extremity arterial stenosis has not been demonstrated in randomized trials. PTA of distal abdominal lesions is effective; however, PTA followed by stenting offers greater advantages of larger vessel lumen gain, long-term patency (>70% at 5 years), high procedural success rates (90%), and less thromboembolism. Factors associated with a poor outcome with endovascular therapy include:

- Long area of segment occlusion
- Multiple and serial stenosis
- Eccentric calcification of lesions
- Poor distal vessel runoff

Iliac Artery Intervention

Iliac artery intervention is very important, not only for improving flow to the lower extremities but also for cardiovascular therapies such as coronary artery intervention, insertion of an intra-aortic balloon pump, other cardiac output assist devices, or for treatment of vascular access site complications. Retrograde CFA access is the most frequently used access for percutaneous angiography and intervention for both coronary and noncoronary vessels.

Indications

The indications to perform an intervention of the iliac arteries include vascular access and symptomatic lower extremity ischemia. Iliac intervention may also be appropriate in patients with severe stenosis or occlusion of the femoropopliteal or infrapopliteal arteries and concomitant moderate iliac artery disease, in whom revascularizing the moderately stenosed iliac artery may improve the arterial inflow and lead to symptomatic improvement or salvage of the limb. The following highlights some of the indications for revascularization in the patient with intermittent claudication:

- A predicted or observed lack of adequate response to exercise therapy and claudication pharmacotherapy

- Presence of a severe disability, either being unable to perform normal work or having very serious impairment of other activities important to the patient
- Absence of other disease that would limit exercise even if the claudication was improved (e.g., angina or chronic respiratory disease)
- The individual's anticipated natural history and prognosis
- The morphology of the lesion (must be such that the appropriate intervention would have low risk and a high probability of initial and long-term success)

Endovascular treatment of significant iliac artery stenosis with claudication is indicated as follows:

- Provisional stent placement is indicated for use in iliac arteries as salvage therapy for suboptimal or failed result from balloon dilation (e.g., persistent gradient, residual diameter stenosis >50%, or flow-limiting dissection).
- Stenting is effective as primary therapy for common iliac artery stenosis and occlusions.
- Stenting is effective as primary therapy in external iliac artery stenosis and occlusions.

Technique

The retrograde ipsilateral CFA access is the most commonly used vascular access for revascularization of the common and external iliac artery. Occasionally, the contralateral, axillary, or brachial access may be necessary when the distal portion of the external iliac and/or CFA artery is involved. Prior to the procedure, the patient should have had a trial of appropriate medical therapy for PAD including antiplatelet therapy with aspirin and/or clopidogrel. Conversely, these medications (especially clopidogrel) can be held when intervening on the iliac arteries in case of possible procedure complications such as vessel perforation or rupture.

After gaining vascular access, heparin is administered (and maintained to a therapeutic activated clotting time). In many cases direct thrombin inhibitors such as bivalirudin are also acceptable for anticoagulation (especially in patients with, or at risk for, heparin-induced thrombocytopenia [HIT] or HIT with thrombosis [HITT]).

After the target lesion has been identified, the reference vessel diameter (RVD) is determined. Peripheral balloon or stent over sizing may lead to tear or rupture of the external iliac artery, and so the use of quantitative angiography or intravascular ultrasound to measure vessel diameter is encouraged. Visual estimation of vessel diameter is discouraged.

Once the lesion has been crossed with a steerable wire such as a Wholey wire or Glidewire, a catheter such as a hydrophilic Glidecatheter (Terumo Medical Corporation, Somerset, NJ) is positioned immediately above the lesion. Universal or pigtail catheters may also be used, as distal abdominal aortograms will also provide excellent bilateral pelvic vessel angiograms. When the lesion is located in the distal common iliac or proximal external iliac artery, retrograde injections of contrast through the femoral sheath may also be used. One particular angiographic view, which separates the origin of the internal and external iliac arteries, is the contralateral caudal oblique view (20 degrees lateral oblique and 20 degrees caudal).

Next the soft-tip guidewire can exchanged for an extra-stiff guidewire (0.035-inch Amplatz wire, Cook, Bloomington, IN) to provide support and trackability for stent placement. The lesion is dilated with a balloon sized 1:1 with the RVD or using the lowest pressure that will fully expand the balloon. The balloon may also be sized smaller than the RVD. The results are assessed by reinserting the catheter above the lesion or using a hand injection of contrast through the sheath. Although

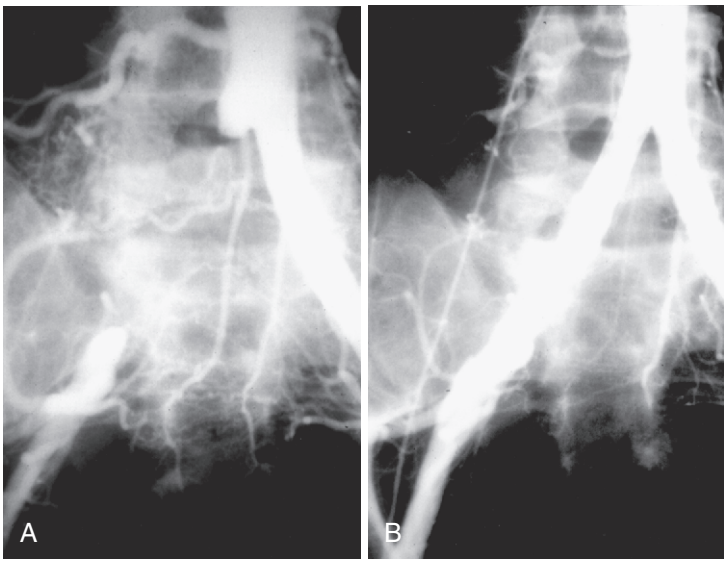

Figure 14-4 **A,** Baseline angiogram with occlusion of right common iliac artery. **B,** Angiogram following successful angioplasty and stent placement.

provisional stent placement is indicated for use in iliac arteries as salvage therapy for suboptimal or failed result from balloon dilation (e.g., persistent gradient, residual diameter stenosis >50%, or flow-limiting dissection), most experts believe that stenting is effective as primary therapy for common iliac and external artery stenosis and occlusions.

Balloon-expandable stents are preferred when a precise stent placement is required (ostial lesions), and self-expanding stents are preferred when precision is not a critical factor and the vessel tapers in size (Fig. 14-4). Balloon-expandable stents also offer greater radial force in heavily calcified vessels and bulky iliac vessels. The larger sized, covered VIABAHN (WL Gore & Associates, Flagstaff, AZ) stents are also used in iliac arteries. These stents feature a heparinized surface for a localized anticoagulation effect. They are reported to be durable and are reinforced with a polytetrafluoroethylene (ePTFE) liner attached to an external nitinol stent structure. For balloon-expandable stents, it is reasonable to use an arterial sheath long enough to cross the lesion to avoid having the undeployed stent strut catch on the lesion, risking embolization or dislodgement of the stent. With the sheath and stent across the lesion, the sheath is then withdrawn, and contrast is injected to confirm the correct position of the stent. The stent is then deployed using at least 6 to 8 atmospheres (atm) of pressure to ensure adequate stent expansion and apposition to the vascular wall. Repeat balloon inflation using higher atmosphere pressure can be performed if there are any questions regarding adequate stent expansion. Simultaneous pressures using a catheter proximal to the target lesion and the vascular sheath should be performed to ensure a final gradient (across the lesion) of ≤5 mm Hg. A perfect angiographic result is not mandatory, and residual stenosis of up to 30% may result in a translesional gradient of <5 mm Hg. This fact needs to be weighed against the greater risk of complications (vessel perforation) from aggressive postdilatation.

Clinical Outcome

There are certain groups of patients and lesions that will benefit from endovascular therapy compared to surgical therapy. The TransAtlantic Inter-Society Consensus (TASC) and TASC II divided patients and lesions into categories (Table 14-10) that would possibly have more

Table 14-10

TASC II Morphologic Stratification of Iliac Lesions

Type	Definition
A	• Unilateral or bilateral stenosis of CIA • Unilateral or bilateral single short (<3 cm) stenosis of EIA • Short (<3 cm) stenosis of infrarenal aorta
B	• Unilateral CIA occlusion • Single or multiple stenosis 3–10 cm involving the EIA not extending into the CFA • Unilateral EIA occlusion not involving the origins of internal iliac or CFA
C	• Bilateral CIA occlusions • Bilateral EIA stenosis 3–10 cm long not extending into the CFA • Unilateral EIA stenosis extending into the CFA • Unilateral EIA occlusion that involves the origins of internal iliac and/or CFA • Heavily calcified unilateral EIA occlusion with or without involvement of origins of internal iliac and/or CFA
D	• Infrarenal aortoiliac occlusion • Diffuse disease involving the aorta and both iliac arteries requiring treatment • Diffuse multiple stenosis involving the unilateral CIA, EIA, and CFA • Unilateral occlusions of both CIA and EIA • Bilateral occlusions of EIA • Iliac stenosis in patients with AAA requiring treatment and not amenable to endograft placement or other lesions requiring open aortic or iliac surgery

AAA, abdominal aortic aneurysm; *CFA,* common femoral; *CIA,* common iliac artery; *EIA,* external iliac artery; *TASC,* TransAtlantic Inter-Society Consensus.

success with iliac artery stenting (compared with surgery). The TASC study suggested that poor infrainguinal runoff was the main risk factor for decreased primary patency after surgical reconstruction and iliac stenting to treat TASC type B and type C iliac lesions. However, primary patency was less affected by poor runoff in patients undergoing surgical procedures. The presence of poor runoff, external iliac artery disease, and female gender were independent predictors of poor outcome after iliac stenting; therefore, these risk factors should determine the need for surgical reconstruction.

According to the TASC group, endovascular therapy is the treatment of choice for type A lesions and surgery is the treatment of choice for type D lesions. Endovascular treatment is the preferred treatment for type B lesions and surgery is the preferred treatment for good-risk patients with type C lesions. The patient's comorbidities, fully informed patient preference, and the local operator's long-term success rates must be considered when making treatment recommendations with regard to type B and type C lesions.

Traditional surgical therapies such as aortoiliac and aortofemoral bypass have a 74% to 95% 5-year patency rate, which is comparable with, but not superior to, percutaneous intervention. Ameli *et al.* reported a series of 105 consecutive patients undergoing aortofemoral bypass. The majority (58%) of patients had mild to moderate clinical symptoms and were treated for claudication. The operative mortality was 5.7%, the early graft failure rate was 5.7%, and the 2-year graft patency rate was 92.8%. PTA has shown clinical benefit with regard to relief of symptoms, improvement of walking distance, and patency of affected artery versus medical therapy in iliac lesions. The primary success rate of PTA for selected iliac artery stenosis is greater than 90%, with 5-year patency rates of 80% to 85%.

Other studies have suggested that the use of endovascular stents yields a higher procedural success rate and a lower restenosis rate than balloon angioplasty alone. In one meta-analysis comparing six balloon

angioplasty studies (1300 patients) with eight stent placement studies (816 patients), the technical success was higher for the stent group (96% vs. 91%; $P < 0.05$). The complication and mortality rates were similar for the two groups. The 4-year primary patency rate for restenotic lesions (77% vs. 65%) and occlusions (61% vs. 54%) in patients with claudication was statistically higher in the stent-treated group. The 4-year primary patency rate for stenosis (67% vs. 53%) and occlusions (53% vs. 44%) in patients with critical limb ischemia was also statistically higher in patients treated with stents.

Femoropopliteal Artery Intervention

Atherosclerotic occlusive disease is more common in the femoropopliteal arterial bed than in the iliac artery. When the femoropopliteal artery is involved in symptomatic lower extremity PAD, complete occlusions are three times more frequent than stenosis. This distribution is the opposite in the aortoiliac vessels. Table 14-11 demonstrates the morphologic stratification of femoropopliteal lesions according to the TASC group. According to the TASC recommendations, endovascular therapy is, once again, the treatment of choice for type A femoropopliteal lesions and surgery is the treatment of choice for type D lesions. Endovascular treatment is, once again, the preferred treatment for type B lesions and surgery is the preferred treatment for good-risk patients with type C lesions. The patient's comorbidities, fully informed patient preference, and the local operator's long-term success rates must again be considered when making these treatment recommendations for type B and type C lesions.

Endovascular interventions for TASC type A femoropopliteal arterial lesions have excellent procedural success and reported patency rates that vary from 30% to 80% at 1 year. The role of primary stenting for femoropopliteal disease remains incompletely defined. Stents (and other adjunctive techniques such as lasers, cutting balloons, atherectomy devices [Fig. 14-5], and thermal cryoplasty devices) can be use-

Table 14-11

Morphologic Stratification of Femoropopliteal Lesions

TASC Type A Femoropopliteal Lesions
• Single stenosis <10 cm in length • Single occlusion <5 cm in length
TASC Type B Femoropopliteal Lesions
• Multiple lesions (stenosis or occlusions), each <5 cm • Single stenosis or occlusion <15 cm not involving the infrageniculate popliteal artery • Single or multiple lesions in the absence of continuous tibial vessels to improve inflow for a distal bypass • Heavily calcified occlusion <5 cm in length • Single popliteal stenosis
TASC Type C Femoropopliteal Lesions
• Multiple stenosis or occlusions totaling >15 cm with or without heavy calcification • Recurrent stenosis or occlusions that need treatment after two endovascular interventions
TASC Type D Femoropopliteal Lesions
• Chronic total occlusions of CFA or SFA (>20 cm, involving the popliteal artery) • Chronic total occlusion of popliteal artery and proximal trifurcation vessels

CFA, common femoral artery; *SFA,* superficial femoral artery; *TASC,* TransAtlantic Inter-Society Consensus.

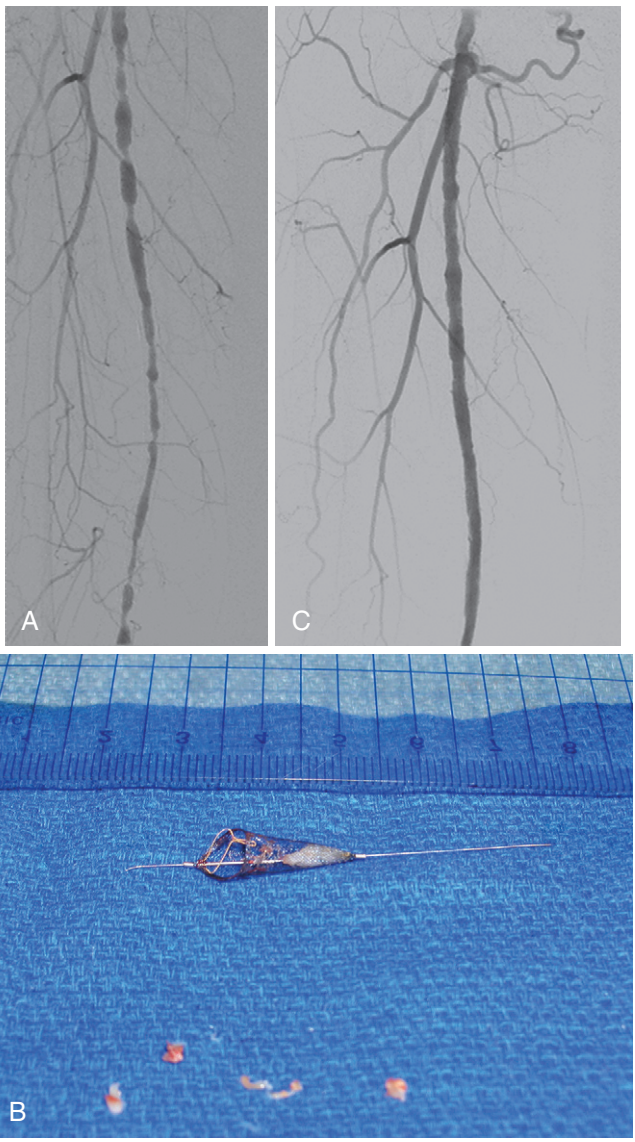

Figure 14-5 **A,** Angiogram of serial lesions in superficial femoral artery (SFA). **B,** Atherectomy of serial SFA lesions with subsequent collection of plaque (some in distal protection device/basket). **C,** Angiogram of SFA after successful atherectomy.

ful in the femoral, popliteal, and tibial arteries as salvage therapy for a suboptimal or failed result from balloon dilation (e.g., persistent translesional gradient, residual diameter stenosis >50%, or flow-limiting dissection). The effectiveness of stents, atherectomy, cutting balloons, thermal devices, and lasers for the treatment of femoropopliteal arterial lesions (except to salvage a suboptimal result from balloon dilation) is not well established.

Indications

Revascularization of the femoral or popliteal arteries is reserved for patients with lifestyle-limiting claudication, ischemic rest pain, and limb-threatening ischemia. Treatment of short (<5 cm) occlusions yields better results than treatment of long (>10 cm) occlusions or stenosis.

The presence of patent runoff vessels correlates with long-term benefits, reflected in the improved outcome in patients with milder symptoms. Significant residual stenosis after angioplasty correlates with a poor long-term outcome, whereas the absence of diabetes correlates with an improved patency rate.

Endovascular intervention is not indicated if there is no significant pressure gradient across a stenosis despite flow augmentation with vasodilators. Stenosis of 50% to 75% diameter by angiography may or may not be hemodynamically significant, and intravascular pressure measurements have been recommended to determine whether these lesions are significant and also to predict patient improvement if the lesion is treated. However, there is no consensus on a diagnostic trans-stenotic pressure criterion or on methods to measure these pressures. One criterion suggests a mean gradient of 10 mm Hg before or after vasodilators; another has suggested use of a mean gradient of 5 mm Hg, or 10, 15, or 20 mm Hg peak systolic. A third criterion uses a 15% peak systolic pressure gradient after administration of a vasodilator. Pressure measurements may be obtained with two separate pressure transducers or by obtaining pullback pressures with a single transducer. Pressures obtained with the catheter positioned across the stenosis may artifactually increase the pressure gradient by reducing the residual lumen with the catheter. No studies have been performed to assess the safety and efficacy of treating asymptomatic but hemodynamically significant lesions to prevent progression of disease. Primary stent placement is not recommended in the femoral, popliteal, or tibial arteries. Endovascular intervention is not indicated as prophylactic therapy in an asymptomatic patient with lower extremity PAD.

Technique

The most commonly used vascular access for the treatment of femoropopliteal arterial disease is the contralateral CFA access. The antegrade vascular access cannot be used for the treatment of CFA or ostial SFA disease. The brachial and retrograde popliteal access is occasionally used; in particular, the popliteal access may prove useful to recanalize SFA occlusions when antegrade approaches have failed. In cases of limb salvage, a retrograde posterior tibial approach can also be used.

As for iliac interventions, the operator obtains vascular access and administers antithrombin medications. All patients should be pretreated with 325 mg of aspirin at least 24 hours before the procedure (if there are no contraindications). For total occlusions, hydrophilic guidewires (Glidewire) are useful when other guidewires frequently fail to cross. On occasion, 0.014-inch to 0.018-inch wires can be used to cross subtotal occlusions. When a hydrophilic guidewire or 0.014-inch to 0.018-inch wires are used to cross a lesion, it is usually preferable to exchange these wires for a non-hydrophilic wire prior to intervention. This will provide better support and traction for the balloon catheters and stents. After the reference vessel diameter is measured with quantitative angiography, the lesion is dilated with a balloon sized 1:1 with the reference vessel, using the lowest pressure that will fully expand the balloon.

If the postprocedural angiogram shows a satisfactory angiographic result (a residual diameter stenosis of <30%) and no flow-limiting dissection, the procedure is terminated (Fig. 14-6). However, if there is significant residual stenosis, flow-limiting dissection, or abrupt occlusion, the operator should proceed with stent placement (Fig. 14-7). In general terms, balloon-expandable stents are not used outside the axial skeleton. Finally, when a stent is needed, we add to the pharmacologic regimen clopidogrel 75 mg for 1 to 3 months, after a loading dose of 300 to 600 mg.

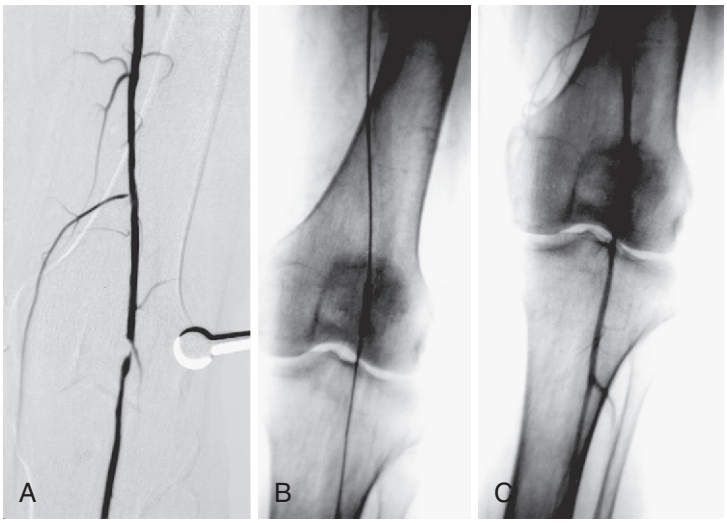

Figure 14-6 **A,** Baseline angiogram of lesion in popliteal artery. **B,** Balloon inflation. **C,** Post-balloon angiogram.

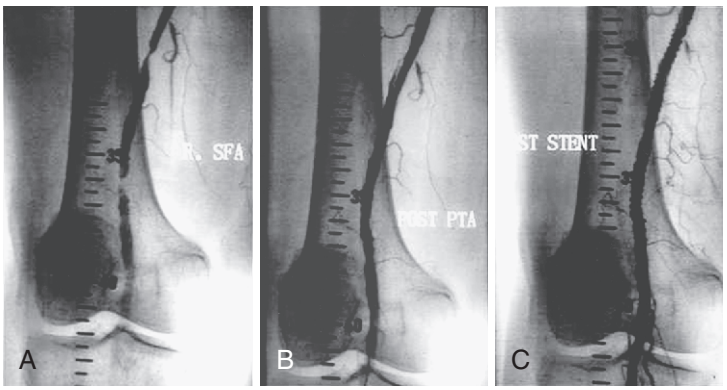

Figure 14-7 **A,** Right femoral and popliteal artery stenosis. **B,** Following balloon dilation with dissection present. **C,** Following stent placement.

Below-Knee Intervention

The traditional indications for infrapopliteal angioplasty have been limb salvage (ischemic rest pain and ischemic ulceration or gangrene). However, infrapopliteal angioplasty for severe claudication that prevents ambulation, and for patients with moderate to severe claudication to increase the durability and effectiveness of femoropopliteal angioplasty, has been advocated.

Technique

The preferred vascular access to perform percutaneous intervention of the infrapopliteal vessels is the ipsilateral antegrade CFA access, which enables an almost direct approach to the infrapopliteal vessels. The contralateral CFA access using a crossover approach is also useful, particularly when planning simultaneous revascularization of the iliac arteries, CFA, or proximal SFA. When using the contralateral crossover approach, the operator must bear in mind that catheter length is an issue and that long (150-cm) catheters are usually necessary to reach the infrapopliteal vessels. On occasion, a retrograde ipsilateral posterior tibial artery approach can be plausible, especially in the cases of

limb salvage. All patients are pretreated with aspirin (325 mg) at least 24 hours prior to the procedure. After contralateral CFA vascular access has been obtained, the patient is anticoagulated with heparin (50–60 U/kg) . Initially a soft-tipped 0.035-inch guidewire (e.g., Wholey wire) is advanced to the distal popliteal artery. A 6F multipurpose guiding catheter or 4F to 5F Glidecatheter is then advanced over the guidewire and positioned at the mid or distal popliteal artery. Baseline angiography of the infrapopliteal vessels is obtained using injection of contrast through the catheter or sheath. After the stenosis has been identified, the lesion is usually crossed with a 0.014-inch or 0.018-inch guidewire. After the lesion is crossed, online quantitative angiography is obtained for a more accurate measurement of the RVD. A balloon catheter is chosen for a 1:1 balloon to RVD ratio. The balloon is inflated usually at 6 to 8 atm of inflation pressure, or to allow complete expansion of the balloon. Multiple inflations are performed as necessary to attain a satisfactory angiographic result. In case of suboptimal angiographic result, more than 30% residual stenosis, dissection, or slow flow may require stent deployment. Poststenting angiography is obtained, and special attention must be paid to rule out dissection or perforation (Fig. 14-8).

When coronary stents are deployed in the infrapopliteal vessels, patients are treated with clopidogrel, with a loading dose of 300 to 600 mg given at the end of the procedure followed by 75 mg daily for at least 4 weeks. Glycoprotein IIb/IIIa inhibitors may have some benefit in selected cases of infrapopliteal intervention. The postprocedural sheath management is similar to revascularization in other vascular territories. However, gentle manual compression for hemostasis is likely superior to other techniques in the setting of calcified, stenotic, and small lumen arterial vessels.

Clinical Outcome

Below-knee angioplasty has led to a dramatic decrease in the amputation rate. Dorros *et al.* reported their results of below-knee angioplasty in 111 patients and 168 tibioperoneal vessels. The indications were claudication (42%), nonhealing ulcer/gangrene (27%), and rest pain (26%). The procedural success was 90% (99% in stenoses and 65% in occlusions). Significant complications (death, emergent bypass surgery, or distal embolization) occurred in 3%. At discharge, 95% of the patients were clinically improved. At a mean follow-up of 9 +/– 6 months, 40% needed a second PTA; however, only a third of those who required a second PTA showed lesion recurrence, with the rest showing progression of disease. In another study, Feiring *et al.* investigated the safety and efficacy of primary below-knee stent-supported angioplasty for restoring straight inline arterial flow in patients with critical limb ischemia (CLI) or lifestyle-limiting claudication (LLC). The mean age of patients was 74 ± 17 years. In 86 limbs, straight inline flow was

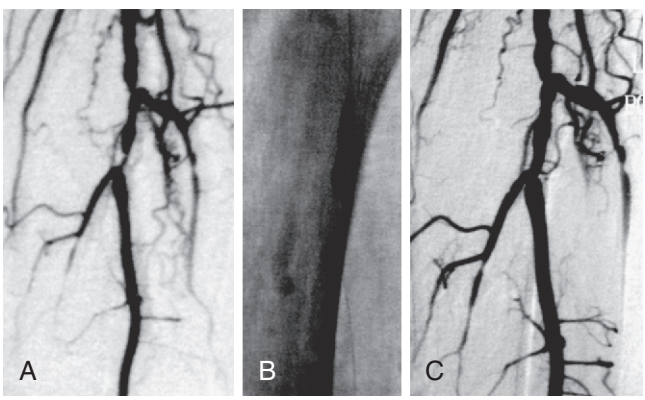

Figure 14-8 **A,** Baseline below-knee popliteal stenosis. **B,** 3.5-mm coronary balloon inflation. **C,** Postangioplasty result.

restored to at least one tibial vessel. Technical success was 94% for de novo lesions and there were no major adverse events. ABIs increased for all groups (CLI = 0.32 ± 0.13 to 0.9 ± 0.14 and LLC = 0.65 ± 0.09 to 0.95 ± 0.12; $P = 0.0001$, preprocedure vs. postprocedure). Relief of rest pain and healing of ulcerations and amputations were seen in 96% (47 of 49) of patients with CLI who underwent successful intervention. In a prospective series of 284 critically ischemic limbs, tibioperoneal angioplasty was successful in 95% of the limbs. Clinical success (relief of rest pain or improvement of lower extremity blood flow) was successful in 95% of the limbs. At 5-year follow-up, 91% of the limbs were salvaged and 8% required surgery. Balloon angioplasty of the infrapopliteal vessels is an effective technique for treating patients with distal atherosclerotic occlusive disease. It has been employed mainly in patients with limb-threatening ischemia and multisegment disease. Appropriate anatomical selection is a key factor in maximizing the benefit of this technique. In specific cases, below-knee stent-supported angioplasty is also possible.

Brachiocephalic Vessels

When performing endovascular intervention on the subclavian and innominate artery, one must be very familiar with the aortic arch and great vessels. The aortic arch typically gives rise to the brachiocephalic trunk, the left common carotid artery, and the left subclavian artery. The brachiocephalic trunk usually bifurcates into the right subclavian artery and right common carotid artery. In 20% to 30% of the population, the brachiocephalic trunk and left common carotid artery share a common origin. Upper extremity occlusive disease accounts for approximately 5% to 6% of all cases of limb ischemia and thus is less prevalent than lower extremity ischemia.

Aortic arch angiography and the origin of the great vessels are usually best visualized in the LAO projection (with some cranial angulation). It is usually performed with a 5F or 6F pigtail catheter (placed above the aortic sinotubular junction) using mechanical injection of contrast dye. In most cases the selective angiography of the great vessels should not be performed until first performing nonselective aortic arch angiography. In this way the anatomical variations of the arch and subsequent arthrosclerosis can be identified.

Patients with upper extremity ischemia may report symptoms such as arm or hand claudication or paresthesias. In patients with coronary-subclavian steal syndrome, blood is diverted from the coronary circulation to the arm via the IMA graft during arm exercise. This can lead to symptoms of angina. In vertebral-subclavian steal syndrome, upper extremity exertion leads to retrograde vertebral flow and neurologic symptoms and arm claudication. Subclavian artery stenosis is considered significant if the pressure difference between arms is more than 20 mm Hg.

Segmental arm pressures, Doppler waveforms, and digital plethysmography can also be very helpful. CTA, MRA, or invasive angiography of the aortic arch can be used to initially determine the extent of upper extremity arterial stenosis. The LAO view is useful for delineating the left subclavian artery, while the RAO view with caudal angulation will allow separation of the innominate artery bifurcation.

Technique

The most commonly used vascular access is retrograde CFA access. The LAO view is useful for delineating the left subclavian artery, while the RAO view with caudal angulation will allow separation of the innominate artery bifurcation. Occasionally, the ipsilateral brachial access may be necessary, particularly when the subclavian artery is totally occluded close to its origin from the aorta.

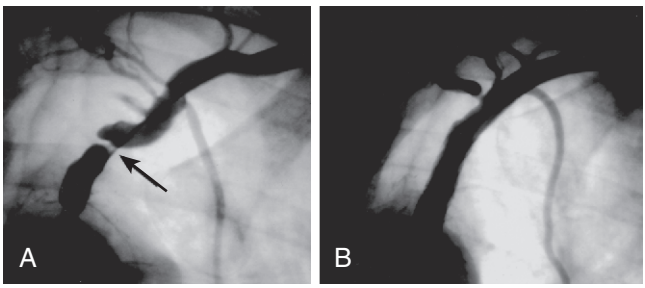

Figure 14-9 **A,** Baseline angiogram of discrete (*arrow*) left subclavian artery stenosis. **B,** Angiogram following balloon-expandable stent placement with resolution of stenosis and pressure gradient. Note that antegrade vertebral flow is now present.

The intervention is performed in an identical manner as for other PVIs. After vascular access has been obtained, heparin is given (50–60 U/kg). Alternatively, bivalirudin can be used. The areas of stenosis and runoff vessels are imaged. A steerable angioplasty guidewire may be advanced across the lesion and the diagnostic catheter used to measure a translesional pressure gradient. If the brachial approach is used, the guidewire can be advanced into the abdominal aorta, snared, and then externalized via the groin sheath.

When using the CFA access, the guidewire is left across the lesion and the diagnostic catheter is exchanged for either a 6F or 7F sheath or an 8F guiding catheter (multipurpose or hockey-stick-shaped) positioned proximal to the subclavian artery stenosis. Using the diagnostic catheter or other external scaling object, the reference vessel diameter is measured using quantitative angiography. The lesion is dilated with a balloon sized 1:1 with the RVD, using the low pressure that will fully expand it (Fig. 14-9). The angiographic results are assessed with hand injection of contrast through the guiding catheter or sheath. Provisional stenting, stent placement for suboptimal results (<30% residual stenosis or translesional gradient >5 mm Hg), is possible, although most experts believe that primary stenting (stent placement regardless of the balloon dilation result) is more appropriate for subclavian lesions to minimize restenosis. Balloon-expandable stents are preferred when precise stent placement is required (aorto-ostial lesion or when trying to avoid "jailing" a branch artery) and self-expanding stents are used when the vessel tapers in diameter or for lesions distal to the vertebral artery where stent compression is possible.

When primary stent placement with a balloon-expandable stent is planned, the sheath or guiding catheter is carefully advanced across the lesion while the predilation balloon is deflating. The balloon catheter is then removed. A stent is then positioned at the lesion site, while the sheath or the guiding catheter is still across it. This maneuver helps to prevent the undeployed stent from catching on the lesion and so reduce the risk of distal embolization. Additionally, this maneuver is not as necessary with today's stents, which are well crimped onto balloon catheters. When the stent is across the lesion (but still within the sheath or guiding catheter), the sheath or catheter is withdrawn and contrast is injected to confirm the correct position of the stent. The stent is then deployed with balloon inflation to ensure adequate stent expansion and apposition of the struts to the vessel wall. Repeat balloon inflation using a higher inflation pressure or the use of a bigger balloon is acceptable if it appears that there is unacceptable stent expansion (Fig. 14-9).

Clinical Outcome

PVI has largely replaced surgical revascularization for treating symptomatic subclavian artery stenosis. Commonly used extrathoracic methods for subclavian artery revascularization include

carotid-axillary, carotid subclavian, or axillo-axillary bypass. The surgical repair can produce excellent long-term patency with low mortality and morbidity. Endovascular procedures can be carried out with a high technical success and are sometimes preferred over surgery. Literature review demonstrates equivalent patency and complications in the other published series of stenting. Subclavian or brachiocephalic artery obstruction can be effectively treated by primary stenting or surgery. Comparison of stenting and the surgical experience demonstrated equal effectiveness but fewer complications and suggested that stenting could be considered as first-line therapy for subclavian or brachiocephalic obstruction.

The Visceral Vessels

Peripheral artery disease of the intestines can include atherosclerosis, arteritis, aneurysms, arterial infections, fibromuscular dysplasia (FMD), mechanical damage, and arterial thromboemboli. Mesenteric PAD can be acute or chronic in nature. Acute mesenteric ischemia is a medical emergency and is almost always fatal if not treated. Thromboembolism is one of the most common causes of this disease entity. Occlusive and non-occlusive mesenteric ischemia is difficult to diagnose, and arteriography is the first choice for diagnosis. Approximately two thirds of patients with acute intestinal ischemia are women, with a median age of 70 years. Most patients have a history of preexisting cardiovascular disease. Abdominal pain is always present and, most commonly, the pain is anterior and periumbilical in location.

Surgical treatment of acute obstructive intestinal ischemia includes revascularization, resection of necrotic bowel, and, when appropriate, a "second look" operation 24 to 48 hours after the revascularization. Percutaneous interventions (including transcatheter thrombolytic therapy, balloon angioplasty, and stenting) can also be performed in patients with acute intestinal ischemia caused by arterial obstructions. Patients treated in an endovascular fashion may still require laparotomy.

Non-occlusive intestinal ischemia should be suspected in patients with low output states, especially cardiogenic shock, who also develop abdominal pain. It should also be suspected in patients with abdominal pain and receiving vasoconstrictor substances and medications (e.g., cocaine, ergots, vasopressin, or norepinephrine). Non-occlusive ischemia can also develop in patients after repair of aortic coarctation. Treatment of the underlying shock state is the most important initial step in treatment. Surgical therapy includes laparotomy and resection of nonviable bowel. Endovascular therapy consists of transcatheter administration of vasodilator medications into the area of vasospasm.

Chronic intestinal ischemia is usually caused by atherosclerosis. Other causes include vasculitis and FMD. Clinical history is very important for diagnosis, and typical symptoms include abdominal pain after eating, and weight loss. Diagnosis is aided by duplex ultrasound, CTA, MRA, and catheter-based angiography. Endovascular treatment of chronic ischemia is possible with a high success rate and few complications. Several reports of concurrent series treated by angioplasty/stenting or surgery indicate that recurrences after percutaneous procedures have been more frequent than after open surgery, but many of the recurrences can be managed by percutaneous interventions. At this time there have been no prospective randomized therapeutic trials, and so data are limited.

Technique

After vascular access is obtained, a nonselective abdominal aortogram is performed using a universal, flush, or pigtail catheter. Next, various diagnostic catheters can be used to selectively engage the visceral

arteries. These include the Shepard crook, renal double curve, cobra (C1, C2, C3), Judkins right size 4 (JR4), hockey stick, multipurpose, or SOS Omni and IMA catheter. The celiac and superior mesenteric arteries are engaged in the lateral view. Many times brachial artery access allows for easier engagement into the mesenteric vessels.

After appropriate anticoagulation, a 0.014-inch or 0.018-inch wire is used to cross the lesion and is positioned distal to the lesion. The diagnostic catheter is then exchanged for a 7F or 8F guiding catheter, which is positioned in contact with the ostium. In most cases a 5F diagnostic catheter has been initially inserted into the guide catheter. Otherwise a 6F or 7F sheath (Shuttle, Raabe, Balkan, or Ansel sheath, Cook, Bloomington, IN) is used instead of the guiding catheter, and in the same way a 5F or 6F diagnostic catheter is inserted through the sheath. The sheath is then positioned at the origin of the mesenteric vessels prior to angioplasty and stenting. After the RVD is measured with quantitative angiography, a peripheral angioplasty balloon (4–7 mm in diameter) is advanced over the guidewire and positioned at the lesion. The lesion is then dilated with a balloon sized 1:1 with the RVD, using the lowest pressure that will fully expand the balloon. Stenting with balloon-expandable stents can then be performed if angioplasty is not sufficient and significant vessel recoil or stenosis persists.

Renal Arteries

Renal artery stenosis (RAS) is a common and progressive disease in patients with atherosclerosis and is a relatively uncommon cause of hypertension. Atherosclerosis accounts for approximately 90% of cases of stenosis within the renal arterial bed. Atherosclerotic lesions usually involve the origin and proximal third of the main renal artery and also the peri-renal aorta. FMD accounts for <10% of cases of RAS and usually involves the distal two thirds of the main renal artery or its branches.

Renal arterial disease has been documented to be present in 30% of patients undergoing screening renal artery angiography at the time of cardiac catheterization. In these populations, significant obstructive RAS (i.e., >50%) has been reported in 11% to 18% of patients. Prevalence studies have also demonstrated significant RAS in 22% to 59% of patients with PAD.

Atherosclerotic RAS is a progressive disease. Progression to occlusion is more common in renal arteries with more severe stenosis. Patients with atherosclerotic RAS who progress to end-stage renal disease, and require dialysis, have high mortality rates. This is probably due to the systemic atherosclerotic and higher rates of cardiovascular ischemic events in those individuals with atherosclerotic RAS.

Several clinical features provide relative indications for application of more specific diagnostic testing strategies for RAS (Table 14-12). One such indication is the presence of an atrophic kidney (<7–8 cm)

Table 14-12

Clinical Clues to the Diagnosis of Renal Artery Stenosis
1. Accelerated, resistant, or malignant hypertension
2. Hypertension at early onset (<30 yr) or severe hypertension at late onset (>55 yr)
3. Development of new azotemia or worsening renal function after administration of angiotensin-converting enzyme inhibitor or angiotensin receptor blocking agent
4. Sudden unexplained pulmonary edema
5. Unexplained renal dysfunction
6. Multivessel coronary artery disease
7. Refractory angina
8. Unexplained congestive heart failure

or discrepancy in renal sizes (>1.5 cm). If the renal atrophy is unexplained by a prior history of pyelonephritis, reflux nephropathy, and trauma, then this is an indication for additional renal diagnostic tests to define RAS.

The blood pressure in patients with RAS may be associated with sustained or labile hypertension. Fluid retention and history of flash pulmonary edema, unexplained congestive heart failure, and refractory angina are also useful markers. The patient should also have an evaluation for evidence of atherosclerosis in other vascular territories. The physical exam should include checking for a renal abdominal bruit.

Patients at high risk for RAS should undergo a noninvasive screening using renal duplex ultrasound, MRA, or CTA (Table 14-13). Captopril renal artery scintigraphy is a relatively specific but insensitive test to demonstrate unilateral RAS; however, the incidence of false negatives is substantial. Measurement of plasma renin levels is discouraged, because it is neither a specific nor a sensitive indicator of renovascular hypertension.

Angiography

Catheter-based renal angiography remains the gold standard for imaging renal arteries, although the noninvasive testing mentioned above has superseded this particular test. Angiography is required to establish the diagnosis of RAS in the case of ambiguous noninvasive imaging. Catheter-based angiography has a low rate of complications; however, care must still be taken to reduce the risks of atheroembolization, contrast-related nephropathy, vascular complications/damage, bleeding, and contrast allergy. To avoid these complications, the following are recommended:

- Prehydrate with intravenous fluids prior to administrating the contrast.
- Consider administering acetylcysteine (600 mg twice a day) before and after the procedure.
- Consider hydration with intravenous sodium bicarbonate prior to the procedure.
- Use iso-osmolar, non-ionic contrast agents.
- Obtain as much information from noninvasive studies prior to performing the catheter-based study.

Table 14-13

Screening Tests for Renal Artery Stenosis

Test	Advantage(s)	Disadvantage(s)
Duplex ultrasound	High sensitivity Operator/experience-dependent	Difficult specificity in obese patients
Magnetic resonance angiogram	Good sensitivity and specificity Operator/experience-dependent	Increased false positives Not useful if stents are present
Computed tomographic angiography	Good sensitivity and specificity; useful for visualizing stents	Ionizing radiation Iodinated contrast
Captopril renal artery scintigraphy	Good specificity	Poor sensitivity (approximately 10%–25% false negative)
Renal vein renin	Lateralizing renin predicts treatment response	Poor sensitivity/specificity Invasive
Renal catheter-based angiography	High sensitivity and specificity	Invasive

Indications

The most important indications for revascularization of the renal arteries include the following:

1. Blood pressure control. Stenting for RAS has been shown to have a beneficial immediate and long-term impact for controlling hypertension.
2. Preservation of renal function, reversal of end-stage renal failure in selected patients, or decrease in progression of renal failure.
3. Improved functional class in patients with unstable angina and congestive heart failure. This probably occurs through a mechanism of better blood pressure control and by favorably affecting the renin-angiotensin system.

Technique

All steps to perform PVI are begun as noted earlier. Aspirin (325 mg) is started at least 1 day prior to the procedure. Although in the majority of the cases the retrograde femoral access is used (when the takeoff of the renal artery is horizontal, caudal, or mildly cephalad), in some cases the brachial access is necessary (when the takeoff of the renal artery is downward angulated) to ensure a successful procedure. The choice of access is important because of the high rate of PAD in these patients. Downward angulation of the renal arteries, detected by MRA or CTA, may be more readily approached from the left arm. Access from the right arm is sometimes avoided to minimize complications arising from crossing the origin of the great vessels in the neck.

Nonselective angiography using a pigtail or universal catheter is performed. Careful catheter manipulation is used to define the status of the aorta and exact locations of the renal ostia to facilitate selective cannulation. To reduce contrast exposure, use diluted contrast and digital subtraction angiography. Alternative angiographic techniques include the use of carbon dioxide angiography or gadolinium as the contrast agent. It is important to make certain that there are no anomalous renal arteries and that the arterial supply to all portions of the nephrogram is visualized.

The choice of catheters for selective renal artery angiography is dependent on the anatomy of the renal artery. Soft-tipped atraumatic catheters and guidewires are recommended for these procedures. Commonly used catheters include the IMA, JR4, cobra, renal double curve, hockey stick, multipurpose, or SOS Omni.

When the brachial access is used for a downward angulated renal artery, a 6F to 7F, 90-cm long vascular sheath (Shuttle, Raabe, Balkan, or Ansel sheath, Cook, Bloomington, IN) is advanced over the guidewire and positioned in the suprarenal abdominal aorta. A 5F to 6 F IMA, JR4, or multipurpose catheter is then advanced through the long sheath and is used to engage the renal artery. A 0.014-inch or 0.018-inch wire is then advanced into the renal artery. Alternatively, a soft-tip exchanged-length 0.035-inch steerable guidewire (Wholey wire, Mallinckrodt, St. Louis, MO) is advanced into the renal artery. Keeping the diagnostic catheter engaged in the renal artery and the guidewire in a distal branch of the renal artery, the sheath is advanced over the multipurpose catheter and positioned in contact with the ostium of the renal artery. The diagnostic catheter is then removed, leaving the guidewire in the renal artery and the sheath in contact with the ostium of the renal artery.

When retrograde CFA access is chosen, a short 7F or 8F sheath is inserted into the CFA. Otherwise a 6F or 7F 55-cm sheath (Ansel, Raabe, or Shuttle) can be used. Next a 5F or 6F diagnostic catheter (IMA, cobra, or JR configuration) is advanced to engage the ostium of the renal artery. It is recommended that these diagnostic catheters be inserted through a 7F or 8F guiding catheter or 55-cm sheath prior to vessel engagement. This will enable easy exchange and manipulation of the catheters once the wires are in place. Then a 0.014-inch, 0.018-inch wire

or a soft-tip exchange-length 0.035-inch soft-tipped Wholey guidewire is used to cross the lesion and is positioned in a renal artery branch. The guiding catheter or 55-cm sheath is then positioned in contact with the renal artery ostium. In this way the diagnostic catheter can then be removed without losing access to the renal vessel.

The use of a Glidewire should be *avoided* because this may cause inadvertent vessel perforation and/or dissection. The use of 5F or 6F diagnostic catheters is recommended to locate the ostium of the renal arteries to avoid trauma and potential cholesterol embolization from scraping the aorta that may occur with larger angioplasty guiding catheters. Cholesterol embolization is also prevented by using the "no-touch" technique. Using this technique, a 0.035-inch J-tipped guidewire is manipulated to hold the distal tip of guide catheter away from the wall of the aorta, and a 0.014-inch or 0.018-inch coronary wire is advanced across the lesion into the distal renal artery. In this way we minimize the unnecessary scraping of the luminal atherosclerotic aortic plaque from guiding catheter manipulations during cannulation of the renal artery ostium.

After the RVD is measured with quantitative angiography, a peripheral angioplasty balloon (4–8 mm in diameter) is advanced over the guidewire and positioned at the lesion. The lesion is then dilated with a balloon sized 1:1 with the RVD, using the lowest pressure that will fully expand the balloon. Before removal, the balloon is reinflated at a low pressure (1–2 atm) and, while the balloon is deflating, the catheter is advanced across the lesion over the balloon. This maneuver enables the stent to be positioned at the lesion site (within the sheath) without risking its edges catching on the plaque and reducing the risk of stent embolization. The use of distal vessel protection devices during balloon angioplasty and stenting can reduce and prevent the chance of distal vessel atheroembolism.

Distal protection devices come in variety of assortments and are thought to be useful in preventing renal atheroembolism. A distal occlusion balloon (GuardWire; PercuSurge Inc., Sunnyvale, CA) embolic protection device, which is used off-label for renal protection during stent deployment, has been described in several studies. Distal filter embolic protection devices have been used in other studies where there has been documentation of visible captured embolic material. The use of intravenous glycoprotein IIb/IIIa platelet receptor inhibitors could also have a role in improving outcomes after renal stent placement. Embolic protection devices and glycoprotein IIb/IIIa inhibitors used together could protect the renal microcirculation from atheroembolization and platelet aggregation.

Balloon angioplasty is much less effective than stent placement for treating atherosclerotic aorto-ostial plaque. Renal stents have been shown to lower the translesional pressure gradient significantly when compared with balloon dilation alone, and they are superior to balloon angioplasty alone. Balloon-expandable stents are used to scaffold the lesion and maximize the angiographic result. When treating ostial lesions, it is important to allow approximately 1 mm of the stent to protrude into the aorta to ensure complete coverage of the ostium of the artery. The stent is deployed at 6 to 8 atm, and then the balloon is withdrawn into the sheath or the guiding catheter. Angiography is then performed and, if inadequate expansion of the stent is observed, the operator should repeat dilation of the stent at a higher inflation pressure or with a larger balloon (Fig. 14-10).

The Szabo technique is another safe and reproducible technique to exactly deploy stents at the aortorenal artery junction. This technique was initially used in coronary artery ostial lesions and can also be used in guiding and deploying renal stents into position at the aortorenal junction. Here, for the exact deployment, two 0.014-inch wires (with the second wire inserted through the last cell of a stent) are used for stent deployment. This stent tail wire or anchor technique facilitates precise aorto-ostial stent deployment in cases of atherosclerotic

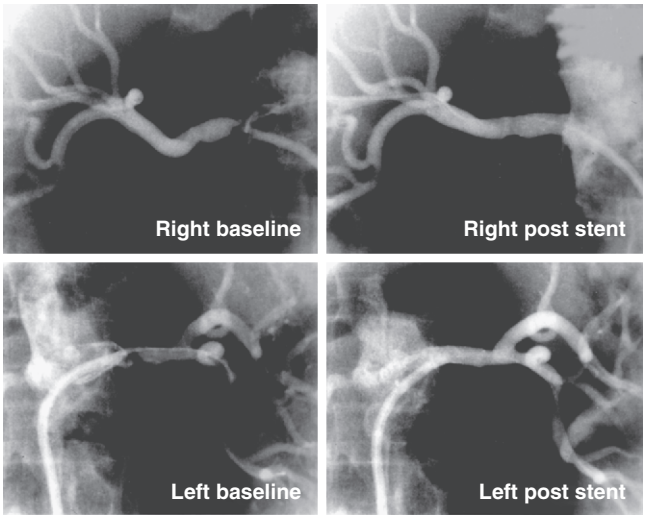

Figure 14-10 Bilateral renal artery stenosis (RAS). Top left panel, baseline angiogram of ostial RAS. Top right panel, angiogram after stent placement. Bottom left panel, baseline angiogram of ostial RAS. Bottom right panel, angiogram after stent placement.

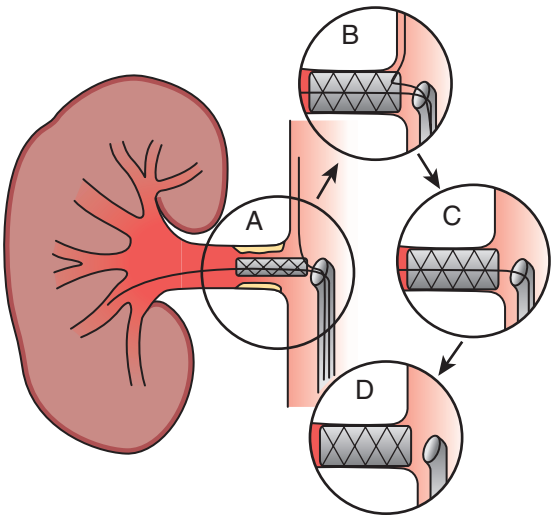

Figure 14-11 Schematic diagram showing Szabo technique applied to renal artery stenting. **A,** The stent is guided to the lesion with the aid of two wires. **B,** The tail wire properly engages the stent at the aorto-ostial junction and the stent is partially deployed. **C,** The wire is then removed and the stent is fully deployed. **D,** Finally, the guidewire is removed and the stent remains in an optimal position.

RAS. It also helps to eliminate errors of improper stent positioning at this aortorenal junction, and may possibly minimize patient exposure to ionizing radiation and contrast dye (Fig. 14-11).

Clinical Outcome

Renal artery stenting for symptomatic (hypertension, ischemic nephropathy, "flash" pulmonary edema, uncontrolled heart failure, or uncontrolled angina pectoris), hemodynamically significant,

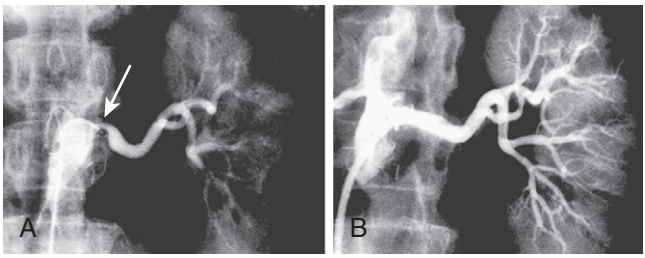

Figure 14-12 **A,** Baseline right renal artery ostial stenosis. **B,** Angiogram after stent placement.

atherosclerotic RAS is the preferred method of revascularization (Fig. 14-12). Balloon angioplasty remains the treatment of choice for FMD and is an accepted treatment for selected patients with RAS causing renovascular hypertension and/or renal insufficiency. However, atherosclerotic aorto-ostial renal artery lesions are particularly difficult to treat with balloon angioplasty alone because they are prone to significant vascular recoil, leading to a restenosis rate of approximately 50% over 6 months. Balloon angioplasty alone may have negligible long-term benefit for controlling blood pressure, probably because of a high restenosis rate. The current long-term patency rates for renal stenting are excellent, with restenosis rates approaching 10%. Stent placement is favored over balloon angioplasty and carries ACC/AHA class I recommendation for treatment of atherosclerotic RAS.

Some data suggest discordance between the high procedural success and the moderate clinical response after stenting. Researchers for the Angioplasty and Stenting for Renal Artery Lesions (ASTRAL) trial enrolled 806 patients with atherosclerotic renovascular disease in the study and randomly assigned them to undergo revascularization with medical therapy (n = 403) or to receive medical therapy alone (n = 403). The primary outcome measure was renal function as measured by the reciprocal of the serum creatinine level. They followed patients to 5 years. Revascularization was not associated with a significant improvement in kidney function in patients with atherosclerotic renovascular disease. This study, however, included patients without severe lesions and, of the 403 patients randomized to the interventional group, only 83% actually got the stent. Critics of the study have suggested that mild lesions should not be treated with stenting and that there is still a role for endovascular therapy in patients with severe and critical RAS. Therefore, further prospective randomized studies are needed to establish the clinical viability of these strategies.

Aortic Arch Angiography

Aortic arch angiography is very important when considering carotid and vertebral artery intervention (Fig. 14-13). The origin of the great vessel is best visualized in the LAO position. In most cases selective angiography of the great vessels should not be completed without first performing nonselective angiogram of the aortic arch. Arch angiography is usually performed with a pigtail catheter. The image intensifier is positioned in an LAO position until no foreshortening of the catheter is visible. This occurs when the intensifier is perpendicular to the arch. The arch angiogram can then be followed by selective vertebral and carotid artery angiograms.

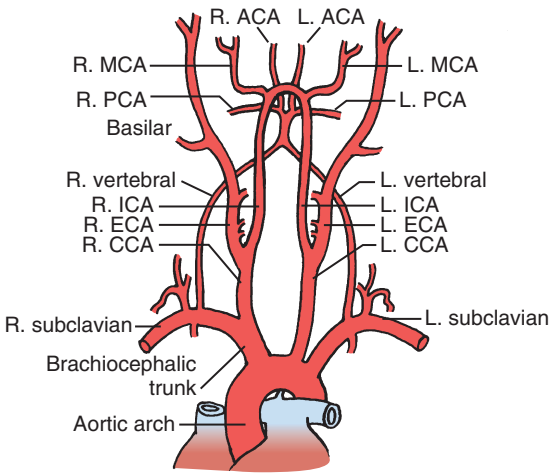

Figure 14-13 Normal aortic arch vessels. *ACA,* anterior carotid artery; *CCA,* common carotid artery; *ECA,* external carotid artery; *ICA,* internal carotid artery; *MCA,* middle cerebral artery; *PCA,* posterior cerebral artery.

Carotid and Vertebral Artery Angiography

Various shaped catheters are available for carotid artery and vertebral angiography. The catheters can be divided into three groups: passive, intermediate, and active catheters. Use of a particular category of catheter will depend on the shape of the aortic arch and takeoff of the great vessels. Elongation of aorta with aging and atherosclerosis, along with different anatomy of the chest cavity, gives rise to tortuosity of the arch vessels. This may also alter the relationship of their origins to descending aorta. It is important to recognize these changes as they determine accessibility of these vessels for percutaneous interventions. The aortic arch can be classified into three types based on the distance of the origin of the great vessels from the top of the arch. The widest diameter of the left common carotid is used as a reference vessel. In a type I arch, all great vessels originate within one diameter length (diameter length of the widest portion of the left common carotid) from the top of the arch; in a type II arch, all great vessels originate within two diameter lengths from the top of the arch; and in a type III arch, the great vessels originate more than two diameter lengths from the top of the arch (Fig. 14-14). In addition, a segment of the population has the left carotid artery originating from the innominate artery (Fig. 14-15). This is known as a "bovine arch."

Passive catheters such as headhunter, multipurpose, and vertebral are used to access the great vessels in patients with type I aortic arch. Intermediate catheters include the Vitek (Cook, Bloomington, IN), and Bentson (JB 1-3; Cordis Corporation, Miami, Florida). These catheters

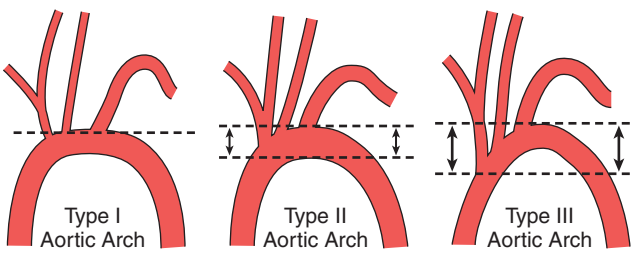

Figure 14-14 Schematic diagram showing classification of aortic arch.

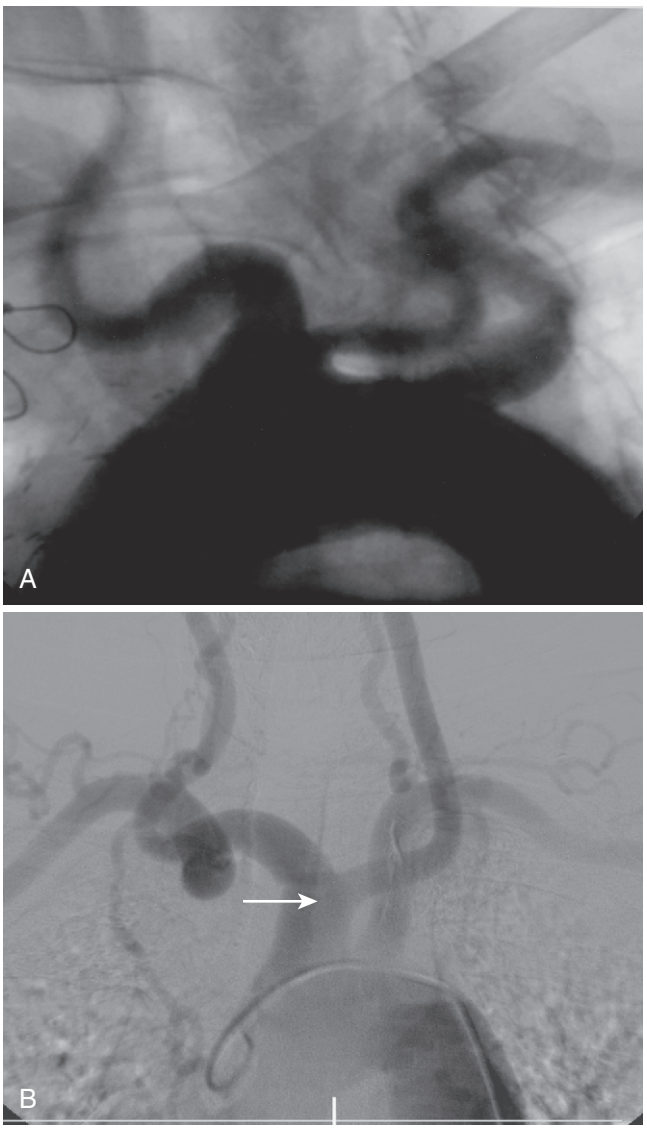

Figure 14-15 **A,** Bovine arch angiogram demonstrating the left common carotid arising from the innominate artery (*arrow*). **B,** Another Bovine arch angiogram demonstrating the left common carotid arising from the innominate artery (dipicted by arrow).

will require more manipulation than the passive catheters, and they are ideal for type II aortic arches. Active catheters such as the Simmons sidewinder (Cook, Bloomington, IN) and Newton (Cordis Corporation, Miami, FL) may require more maneuvers to get into the preformed shape in order to facilitate access into type II or type III arches.

Active catheters must be shaped in the ascending aorta and therefore can be a source of atheroemboli. The best way of shaping these catheters requires advancing them into the aortic arch over a wire (angled Glidewire is recommended). With removal of the wire, the catheter is then flushed. The catheter can then be retracted and the tip positioned in the left subclavian artery. The wire is once again advanced into the catheter and, subsequently, into the left subclavian artery. Further advancing of the catheter (over the wire) will allow the secondary curve of the catheter to climb to the origin of the subclavian. If the wire is removed and the catheter rotated (so that the secondary curve points

to the right side of the arch), this allows the catheter to prolapse into the ascending aorta. The catheter can then be manipulated into each specific great vessel. The great vessels can usually be viewed in a lateral or ipsilateral oblique view. The RAO view allows visualization of the origins of the right common carotid, right subclavian, and right and left vertebral arteries. The LAO view allows visualization of the left common carotid and left subclavian and innominate arteries.

Vertebral Artery Intervention

Approximately 25% of ischemic strokes involve the posterior or vertebrobasilar circulation. Stenosis of the vertebral artery may account for up to 20% of posterior circulation ischemic strokes. In an angiographic study of 4748 patients with ischemic stroke, extracranial vertebral artery stenosis was seen in 18% of cases on the right and 22.3% on the left. This was the second most common site of stenosis after internal carotid artery stenosis at the carotid bifurcation. Such stenotic lesions are potentially treatable by endovascular techniques. In marked contrast with carotid artery stenosis, the optimal management of vertebral artery stenosis has limited surgical treatment options. Vertebral artery angioplasty, however, has opened up new opportunities for intervention in this disease.

The vertebral artery arises from the supra-posterior aspect of the first part of the subclavian artery. In 6% of cases, the left vertebral artery arises directly from the aortic arch. Anatomically, the vertebral artery can be divided into three extracranial parts and one intracranial portion (Fig. 14-16). The first part of the artery originates from the subclavian artery until it enters the transverse foramina of either the fifth or

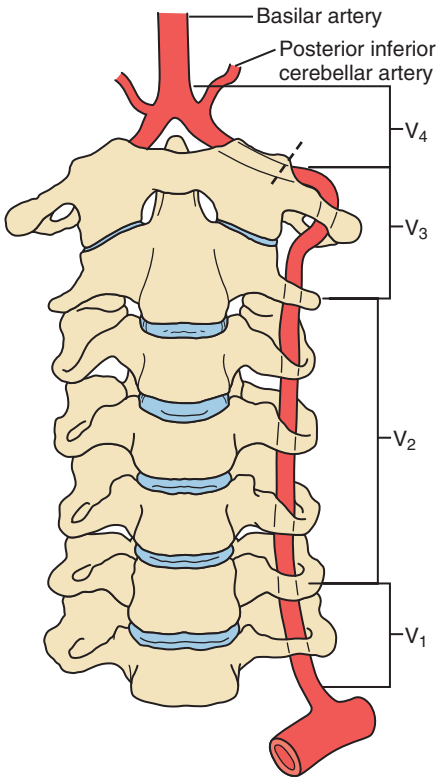

Figure 14-16 Schematic drawing of the vertebral artery, showing branches and vessel segments.

sixth cervical vertebra. The second part travels within the intervertebral foramina. The third portion exits behind the atlas and travels toward the foramen magnum. The final intracranial portion pierces the dura and arachnoid mater at the base of the skull and ends as it meets its opposite vertebral artery to form the basilar artery at the level of the medullopontine junction.

The gold standard for diagnosing vertebral artery stenosis remains digital subtraction angiography (DSA), although this has a small morbidity and associated mortality. Stenosis at the vertebral artery origin can still be missed with standard arch views, because of superimposition of the subclavian artery over the first segment of the vertebral artery, and additional oblique views are required.

Noninvasive test of choice to investigate for extracranial vertebral artery disease is Doppler ultrasound. Recent studies have shown that a combination of Doppler with color flow techniques have a high sensitivity for detecting significant stenosis, which approaches 100% in some studies. Transcranial Doppler ultrasound can be used to detect intracranial vertebral artery stenosis with a sensitivity of as high as 80% and a specificity of 80% to 97% when compared with DSA. Helical or spiral CTA is able to image the extracranial vertebral artery without the risks associated with catheter angiography, but its use has not been fully validated against DSA. Magnetic resonance imaging used alone can detect intracranial vertebral artery disease, but it is best used in combination with MRA to assess both extra and intracranial vertebral arteries. However, an important pitfall with MRA is an overreporting of occlusion in cases of high-grade stenosis.

Medical treatment alone has been the standard treatment for posterior circulation stroke. To date, there have been no randomized trials of the use of different antiplatelet therapies or anticoagulation against antiplatelet therapy in known cases of extracranial vertebral artery atherosclerotic stenosis. Surgery for vertebral artery stenosis can be performed either by endarterectomy or reconstruction. Endarterectomy has variable success rates. The procedure is technically difficult and complications such as lymphoceles, fistulas, vocal cord paralysis, and pneumothorax have been reported. Endovascular intervention, with PTA and stenting, is a safe and effective treatment for extracranial vertebral artery atherosclerotic stenosis. The best treatment for intracranial vertebral artery stenosis remains controversial because of uncertainty about benefits of PTA and the lack of acceptable surgical alternatives. In practice, such intervention is only being recommended for surgery after optimal medical treatment has failed (Table 14-14).

Technique

Preprocedural management is essential and begins with aspirin (325 mg daily) and clopidogrel (75 mg daily) administration starting 3 to 5 days before the procedure. If clopidogrel cannot be initiated 3 to 5 days before the procedure, a loading dose of 300 mg is administered.

A complete neurologic examination is also documented before the procedure. After arterial access through the femoral is established, a 70 U/kg bolus of heparin is administered intravenously to achieve an activated coagulation time of approximately 300 seconds. A 6 F guide catheter (hockey stick, JR4) is placed in the ipsilateral subclavian artery. If necessary, the guide catheter is stabilized by coaxial placement of a 0.018-inch wire (V-18 control wire; Boston Scientific Corporation, Natick, MA) into the distal subclavian artery. A distal protection device (FilterWire EX; Boston Scientific Corporation, Natick, MA) is introduced through the lesion and deployed into the distal cervical segment of the vertebral artery. Bare-metal (balloon-expandable) or drug-eluting coronary stents are used for lesion treatment. Additionally, angioplasty (before or after stent deployment) is performed in selected situations to provide the most optimal results (Fig. 14-17). In each case the stenosis

Table 14-14

Pharmacologic Management of Elective Carotid Stenting

Preprocedure	Intraprocedure	Postprocedure
	Antiplatelet Agents	**Antiplatelet Agents**
1. Aspirin 325 mg PO at least 24 hr before procedure 2. Clopidogrel 75 mg PO 5 days or 300 mg 6 hr prior to procedure	1. Heparin 70–100 U/kg keep ACT ≥ 300 sec 2. Heparin 70 U/kg and keep ACT at 200–250 sec if abciximab used 3. Abciximab (optional) 0.25 mg/kg bolus, then 0.125 µg/kg/min	1. Aspirin 325 mg indefinitely 2. Clopidogrel 75 mg PO for at least 4 wk
No sedation	**Bradycardia**	**Hypotension**
	1. Atropine 0.6–1 mg IV	1. Neo-Synephrine infusion to keep SBP ≤130 mm Hg
	Hypotension	**Persistent Hypotension**
	1. Normal saline IV infusion 2. Neo-Synephrine 100 µg IV boluses to keep SBP <130 mm Hg	1. Midodrine hydrochloride 2.5–5 mg PO 2–3 times daily

ACT, activated clotting time; *SBP,* systolic blood pressure.
(Modified from Silva JA, White CJ. Adjunctive pharmacologic treatment for elective stenting of the extracranial carotic arteries. *Int J Cardiovasc Interv* 2001;4:141–144.)

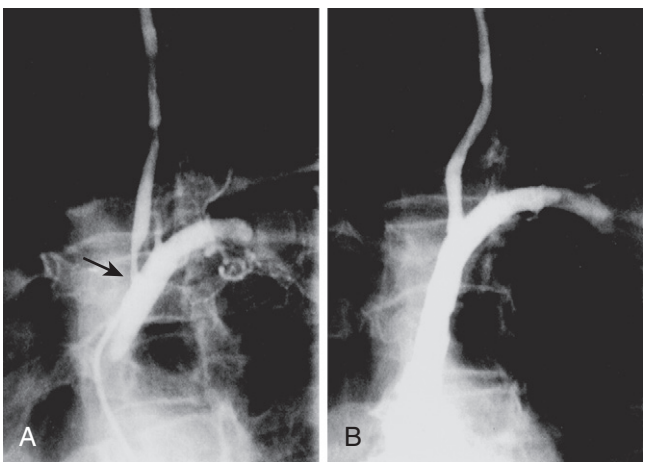

Figure 14-17 **A,** Baseline angiogram of left vertebral ostial stenosis (*arrow*). **B,** Angiogram following balloon-expandable stent placement.

is pre- and postdilated using a balloon with a diameter ratio of 1:1 or less to the RVD, using the minimum inflation pressure necessary to completely expand the balloon. After treatment of the stenosis, the distal protection device is retrieved using the retriever catheter provided by the manufacturer. A complete neurologic examination is performed immediately after and 24 hours after the procedure. Aspirin (325 mg daily) and clopidogrel (75 mg daily) are prescribed at discharge. Clopidogrel is discontinued after 3 to 6 months for drug-eluting stents, but aspirin is continued indefinitely.

Clinical Outcome

Vertebral artery stenosis is an important cause of posterior circulation stroke. However, surgical procedures are associated with significant morbidity. Endovascular intervention (especially with primary stenting) for extracranial vertebral artery stenosis is a promising potential treatment. Patients with symptomatic vertebral artery stenosis who have failed medical treatment should be considered for percutaneous revascularization. Percutaneous revascularization procedures with balloon angioplasty and stent placement offer a less invasive alternative to surgery and produce durable results, excellent clinical success, and low complication rates.

Carotid Artery Intervention

Chapter 15 reviews the percutaneous interventional approach to carotid artery stenting.

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15

Carotid Artery Stenting

JONATHAN A. RAPP · PRANAV M. PATEL · CHRISTOPHER J. WHITE

Nearly 800,000 strokes occur each year in the United States, and more than 130,000 Americans die annually from stroke. Stroke is the third leading cause of mortality in the United States, and among survivors, 15% to 30% are permanently disabled. Warning symptoms, such as a transient ischemic attack (TIA), historically defined as a neurologic event lasting <24 hours, precede a minority (15%) of all strokes. A new, tissue-based definition of TIA has been formalized, but most of the studies referred to in this chapter predate its publication. Following a TIA, the 90-day risk of stroke is 15%, and the 6-month risk of a stroke, TIA, or death is as high as 30%. Therefore, TIAs should be treated as medical emergencies.

Approximately half of all strokes occur in the distribution of the carotid artery, and carotid artery disease (CAD) amenable to revascularization accounts for as high as 12% of new strokes. Although occlusion of the carotid artery due to plaque burden can cause a stroke, the more common scenario is for carotid plaque to rupture resulting in distal embolization and cerebral infarction. Because more than 80% of strokes have no warning symptoms, stroke prevention with management of asymptomatic carotid atherosclerosis and carotid revascularization for high-risk patients is important.

Roughly 5% to 10% of patients over age 65 have a carotid stenosis >50%, and only 1% have a stenosis ≥75%. The natural history of carotid artery disease depends on the patient's symptomatic status and lesion severity. In the Asymptomatic Carotid Atherosclerosis Study (ACAS), among medically treated asymptomatic patients with stenosis ≥60%, the 5-year risk of ipsilateral stroke or any stroke or death within 30 days of randomization was 11%.

Symptomatic patients with carotid atherosclerosis have a much worse prognosis than asymptomatic patients. In the North American Symptomatic Carotid Endarterectomy Trial (NASCET) trial of symptomatic carotid lesions, the 5-year risk of ipsilateral stroke in those medically managed was 18.7% among those with lesions <50% in severity. Results were similar in the European Carotid Surgery Trial (ECST). The risk of stroke increased with severity of stenosis, with the 3-year risk of ipsilateral stroke in those with stenosis >80% being 26.5%.

Medical therapy for carotid atherosclerosis should focus on preventing stroke and stabilizing atherosclerotic lesions to prevent plaque rupture and atheroembolization. Blood pressure control with angiotensin-converting enzyme inhibitors and angiotensin receptor blockers are of particular benefit in stroke prevention. In addition, a review of more than 70,000 patients with, or at high risk for, cardiovascular disease found that statins significantly lower the risk of stroke. Current American Heart Association/American Stroke Association (AHA/ASA) stroke guidelines endorse the National Cholesterol Educational Program (NCEP III) recommendations for the use of statins. The Justification for the Use of Statins in Prevention: An Intervention Trial Evaluating Rosuvastatin (JUPITER) study showed that rosuvastatin treatment in

patients with normal cholesterol levels but elevated levels of C-reactive protein is effective in reducing the rate of stroke and is indicated for patients with carotid artery disease.

Antiplatelet medications are a critical component of primary stroke prevention. In secondary prevention, aspirin reduces the risk of future strokes by 15% to 25%. High-dose aspirin provides no more benefit than lower doses (160–325 mg daily) but is associated with more side effects. The Clopidogrel for High Atherothrombotic Risk and Ischemic Stabilization, Management, and Avoidance (CHARISMA) trial included more than 4300 patients with a prior TIA or stroke and found that aspirin 75 to 162 mg daily was as effective as aspirin plus clopidogrel in preventing future myocardial infarction (MI), stroke, or cardiovascular death. AHA/ASA guidelines recommend that all patients with carotid atherosclerosis be placed on antiplatelet medications. Aspirin 50 to 325 mg daily, aspirin-dipyridamole, or clopidogrel should be initiated for secondary prevention of stroke. The combination of aspirin and dipyridamole is recommended over aspirin alone, however. The combination of aspirin and clopidogrel is not recommended.

Clinical Presentation

Patients with carotid artery stenosis may be asymptomatic or exhibit ischemia in one of three vascular territories: retinal, hemispheric, or global. In symptomatic patients, the history, neurologic exam, and imaging studies can often localize a lesion to a particular vascular territory. The National Institutes of Health Stroke Scale (NIHSS) should be performed in all symptomatic patients to quantify the neurologic deficit and predict outcome.

Diagnosis of Carotid Artery Disease: Anatomical Imaging

Duplex ultrasonography is most often the initial test used to assess the severity of carotid artery stenosis. Carotid ultrasound also has a high accuracy for carotid restenosis after endarterectomy. Numerous criteria have been proposed to diagnose severe carotid stenosis. In most cases >80% stenosis correlates with systolic velocity >300–400 cm/sec, diastolic velocity >100–135 cm/sec, and ratio of internal carotid artery/common carotid artery (ICA/CCA) systolic velocity of >3.5. Factors such as contralateral occlusion, diminished cardiac output from severe left ventricular dysfunction, aortic stenosis, and common carotid artery stenosis may make these measurements less reliable. Magnetic resonance angiography and computed tomography angiography are the other noninvasive imaging studies that are helpful in identifying carotid artery stenosis. Duplex imaging is often the test of choice given its safety profile, low cost, and wide availability. Imaging that can define the aortic arch and the circle of Willis is useful in planning endovascular procedures. The particular noninvasive method used should reflect local availability and expertise.

Digital subtraction angiography (DSA) is the gold standard for defining carotid anatomy with the NASCET method of stenosis measurement the most widely used (Fig. 15-1). Cerebral catheter-based angiography carries a risk of cerebral infarction of 0.5% to 1.2%; therefore, noninvasive imaging should be the initial strategy for evaluation.

Surgical Therapy

Current AHA/ASA guidelines give a class I indication for CEA in symptomatic patients with stenosis of 50% to 99% if the risk of perioperative stroke or death is <6%. In asymptomatic patients, AHA/ASA

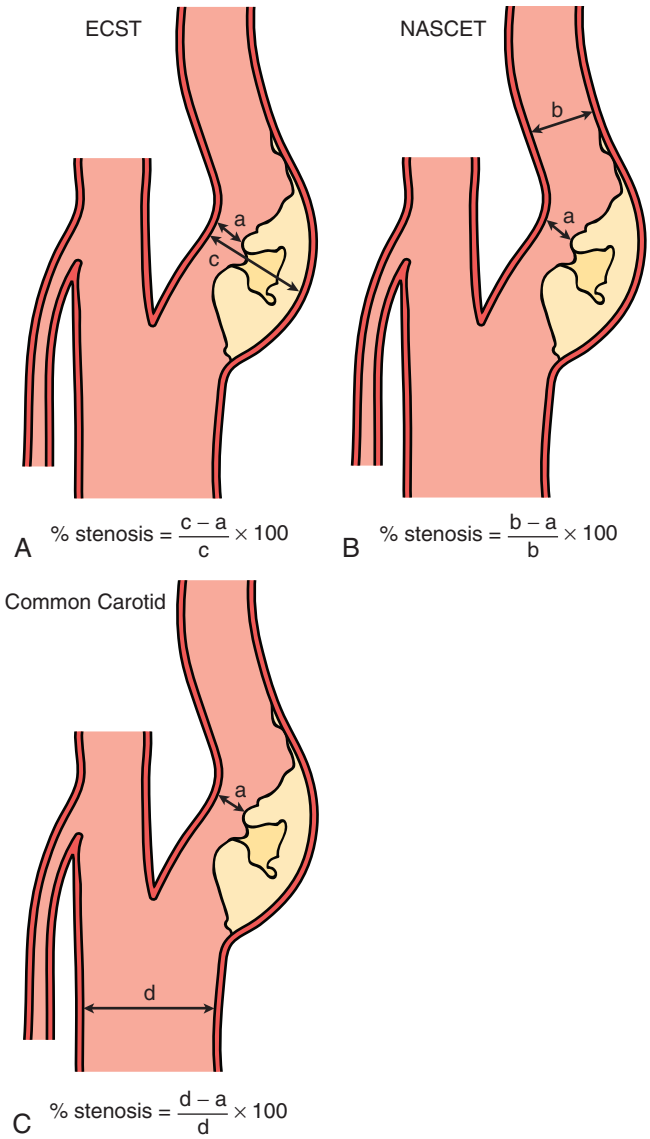

Figure 15-1 Methods of carotid stenosis assessment. The NASCET method is the most widely used.

guidelines give a class IIa indication to CEA in patients with stenosis of >70% if the risk of perioperative stroke, death, or MI is low, historically defined as <3%. Patients considered especially high risk for CEA include those with:

- Carotid artery stenosis after prior radical neck surgery
- High cervical carotid artery lesions that are surgically inaccessible
- Sequential lesions of the proximal to distal ICA
- Lesions of the common carotid artery and associated ICA lesions
- Recurrent stenosis of the carotid artery after CEA
- Non-atherosclerotic cause of carotid artery stenosis (e.g., fibromuscular dysplasia, Takayasu's arteritis)
- Ipsilateral stenosis due to prior radiation therapy to the neck

- Increased operative risk due to concomitant illnesses such as CAD requiring coronary artery bypass surgery
- Contralateral occlusion and concurrent high-grade ipsilateral stenosis

Carotid Artery Stenting

Carotid artery stenting (CAS) was developed as a less invasive alternative for carotid revascularization. The interventionalist should be part of a multidisciplinary team that includes neurologists and/or vascular medicine specialists that can provide valuable pre- and postprocedure care. Additionally, it is necessary for the operator to possess the ability, or have access to an on-site expert, to perform neurovascular rescue procedures in the event of a complication, a standard of care not met by CEA.

Medications

Aspirin (81–325 mg daily) is begun at least 24 hours prior to the procedure and is continued indefinitely. Clopidogrel 75 mg daily (or alternatively ticlopidine 250 mg twice daily) should be given for 5 consecutive days preceding stent placement and continued for at least 1 month after stent deployment. Minimal, if any, sedation is used during the procedure because the patient requires neurologic assessments during the procedure. Because of potential hypotension during angioplasty or stenting, antihypertensive medications should be held the morning of the procedure.

Intravenous unfractionated heparin should be given such that the activated clotting time (ACT) is ≥ 250–300 seconds. Additional boluses of heparin may be required during the procedure. Unless another indication exists for it, anticoagulation is not used following the procedure.

Procedural Techniques

Baseline Aortography and Cerebral Angiography

Vascular access is most commonly obtained from the femoral artery although brachial or radial access may be used. Prior to selective angiography, an arch aortogram is performed with a pigtail catheter placed in the proximal ascending aorta to define the anatomy of the aortic arch, which is critical to the success of the stent procedure. This is done in the 45° left anterior oblique position with a large-format image intensifier (12-inch to 16-inch) using DSA (15 mL/sec for 3 sec) and a power injector.

Once the morphology of the aortic arch is determined (Fig. 15-2), catheters are chosen for selective angiography of the cervical arteries supplying the brain (right and left carotid and vertebral arteries) and the cerebral vasculature. In a type I arch, Berenstein or Judkins right (JR) catheters are often used. In type II or III arch morphologies, shepherd's crook–shaped catheters (i.e., Simmons or Vitek catheters) may be best (Fig. 15-3).

Angiograms are obtained to delineate the anterior and posterior circulation supplying the brain. The intracranial and extracranial portions of each vessel are studied. Generally, two views of each are obtained, one in the anteroposterior projection and one in the lateral projection. Alternatively, some operators use rotational angiography. It is important to demonstrate the circle of Willis to define any baseline abnormalities. DSA may be performed with a 50/50 mix of saline and contrast. An external reference object is used with carotid angiograms in order to accurately measure the diameter of the artery.

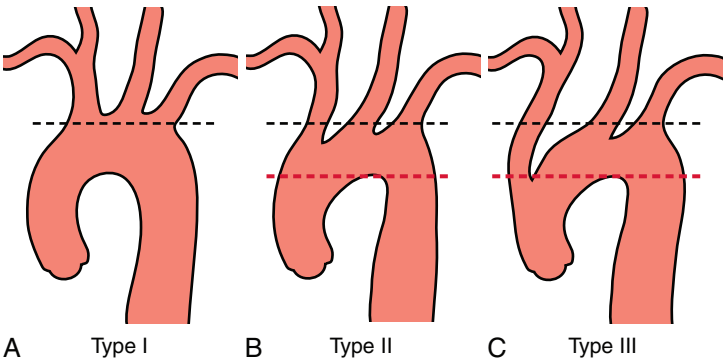

Figure 15-2 Aortic arch morphologies. Arch morphology is defined based on the origin of the great vessels. **A,** Type I arch: all vessels originate at the superior margin of the arch. **B,** Type II arch: at least one vessel originates between the superior and inferior margins of the aortic arch. **C,** Type III arch: at least one vessel originates below the inferior margin of the aortic arch.

Internal Carotid Intervention

A diagnostic catheter is used to engage the common carotid artery (CCA), and a roadmap angiogram is made of the carotid bifurcation. A 0.035-inch stiff-angled hydrophilic wire is advanced into the external carotid artery, and the diagnostic catheter is advanced over the wire. The hydrophilic wire is exchanged for a 0.035-inch stiff Amplatz wire over which an 8F guiding catheter or a 6F sheath may be advanced to the target vessel CCA. Care must be taken to avoid plaque disruption with wires and catheters, and at this point in the procedure, the plaque in the ICA should remain untouched.

For procedures performed with a filter-type distal embolic protection device (EPD), the target lesion is crossed with the EPD. Although there are no randomized trials comparing stenting with EPDs to stenting alone, one study found that 57% of EPDs contained debris upon retrieval. EPDs are standard of care in the United States, and several types exist (Fig. 15-4). If the distal EPD will not cross the lesion, the stenosis may be crossed with a conventional 0.014-inch guidewire and subsequently predilated with a small (2.5 mm) balloon. Then the EPD should be placed. After distal EPD deployment, the lesion is often predilated with an undersized coronary balloon, typically 3 to 4 mm in diameter. A self-expanding stent is then placed across the lesion. The stent is sized to fit the CCA, and as a general rule, self-expanding stents are typically

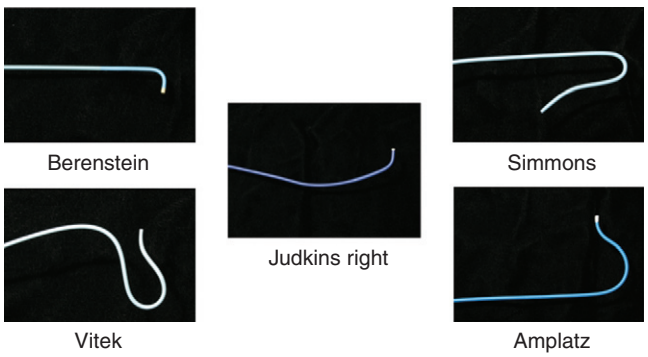

Figure 15-3 Catheters for accessing the carotid artery. Berenstein or JR4 catheters are usually best for a type I arch. Shepherd's crook catheters may be best for type II or type III arches.

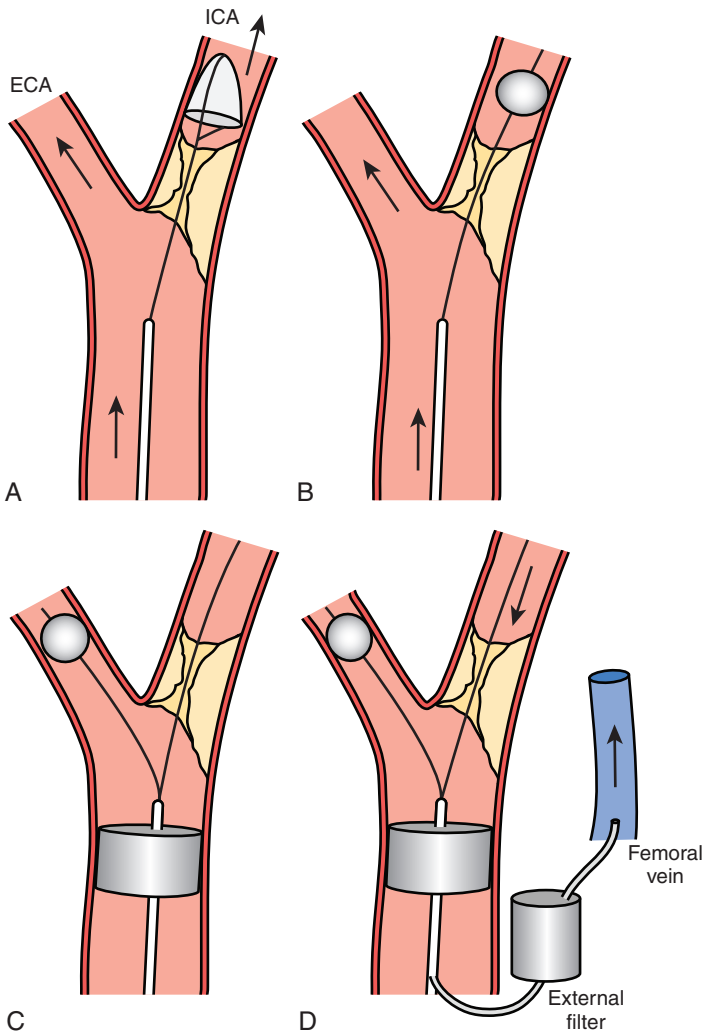

Figure 15-4 Embolic protection devices (EPDs). **A,** Filter-type device. **B,** Balloon occlusion of internal carotid artery (ICA). **C,D,** Proximal protection with flow reversal. See text. *ECA,* external carotid artery.

sized at least 1 mm larger than the reference diameter. There is no demonstrated benefit for using tapered stents. It is common practice, when treating an internal carotid bifurcation lesion, to place the stent across the ostium of the external carotid artery (Fig. 15-5).

An alternative to distal embolic protection is proximal protection. Two devices are available: the Gore flow reversal system (WL Gore & Associates, Flagstaff, AZ) and the Mo.Ma system (Medtronic, Minneapolis, MN). Both are positioned in a similar fashion. With the Gore device, the external carotid artery is accessed as described earlier and a balloon-tipped sheath is advanced over the 0.035-inch Amplatz wire into the CCA. This sheath has a port for an occlusion balloon to be placed in the external carotid artery. The external and common carotid balloons are inflated, arresting antegrade flow. The Mo.Ma system is similar but consists of a single sheath with two balloons: a proximal balloon in the CCA and a distal balloon in the external carotid artery. When the balloons are inflated, blood flow is arrested. In either system, once patient tolerance of balloon occlusion is confirmed, the internal carotid lesion is crossed with a 0.014-inch wire, dilated, and stented as described earlier. With the Mo.Ma system, blood is manually aspirated after the

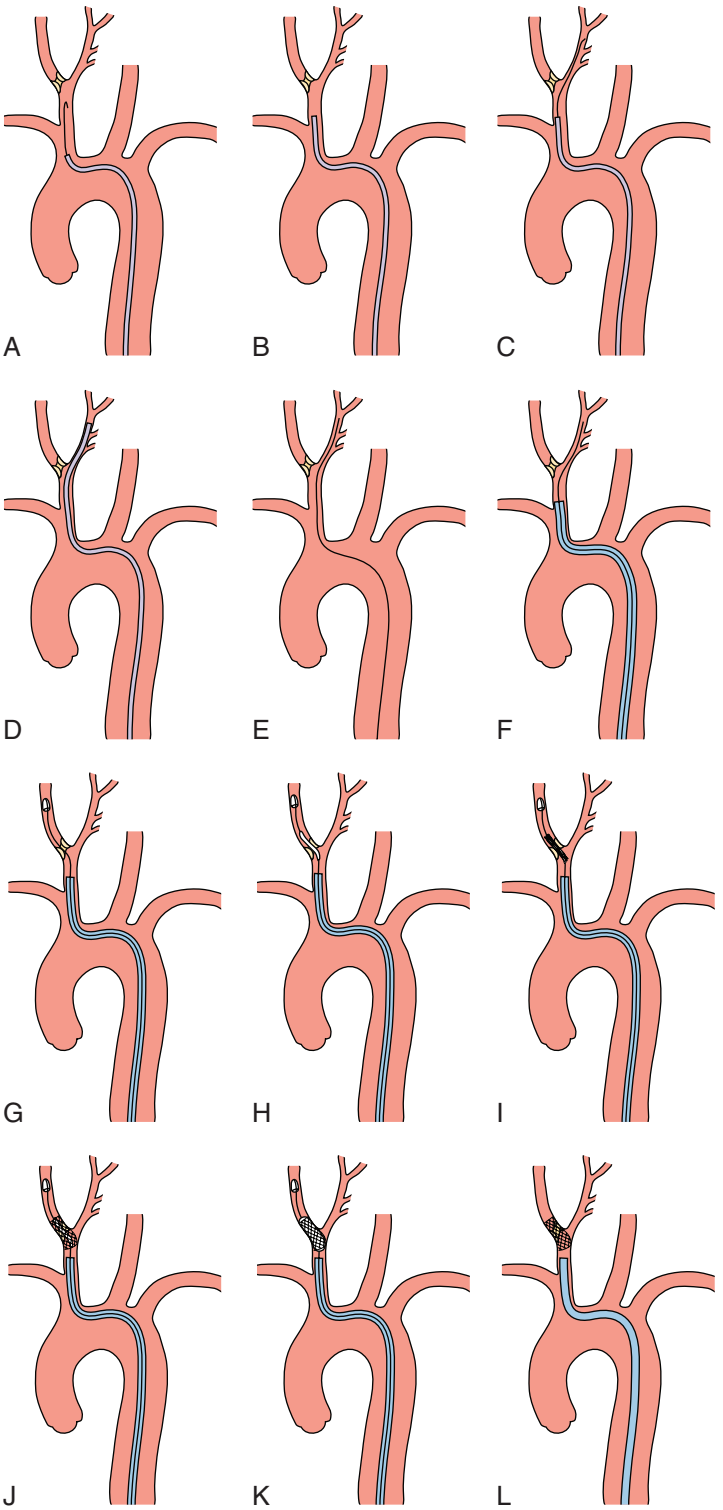

Figure 15-5 Stenting of the internal carotid artery (ICA). **A,** The common carotid artery (CCA) is accessed with a diagnostic catheter and standard 0.035-inch J wire. **B,** The catheter is advanced over the J wire but remains in the CCA. **C,** The J wire is exchanged for a hydrophilic stiff-angled 0.035" wire. **D,** The catheter is advanced to the ECA and the hydrophilic wire is removed. **E,** A stiff Amplatz wire is advanced to the ECA and the c atheter is removed. **F,** A long 6F sheath is advanced over a dilator to the CCA. **G,** After removing the Amplatz wire and dilator, the lesion is crossed with a wire/filter device. **H,** Predilation. **I,** Stent placement. **J,** Stent deployment. The ostium of the ECA is often "jailed." **K,** Postdilation. **L,** Final result.

stenting procedure to clear the debris distal to the common carotid balloon. The Gore system, however, provides continuous flow reversal by having the arterial sheath connected to a venous sheath (Fig. 15-4). Although experience with these devices is limited, data indicate that they can provide excellent results.

Stents

There are two types of self-expanding stents: closed-cell and open-cell (Fig. 15-6). Open-cell stents are more flexible and may better navigate tortuous vessels. Closed-cell stents are more rigid but may better "cover" atherosclerotic plaque. Whereas some evidence suggests that the frequency of embolic complications in symptomatic patients is lower with closed-cell stents, others have found no significant correlation between stent design and outcomes. Typical stent sizes are 6 to 10 mm in diameter and 2 to 4 cm in length. Gentle postdilation with a ≤5-mm balloon is often performed to improve stent apposition with the vessel wall. There is no benefit to aggressive postdilation since

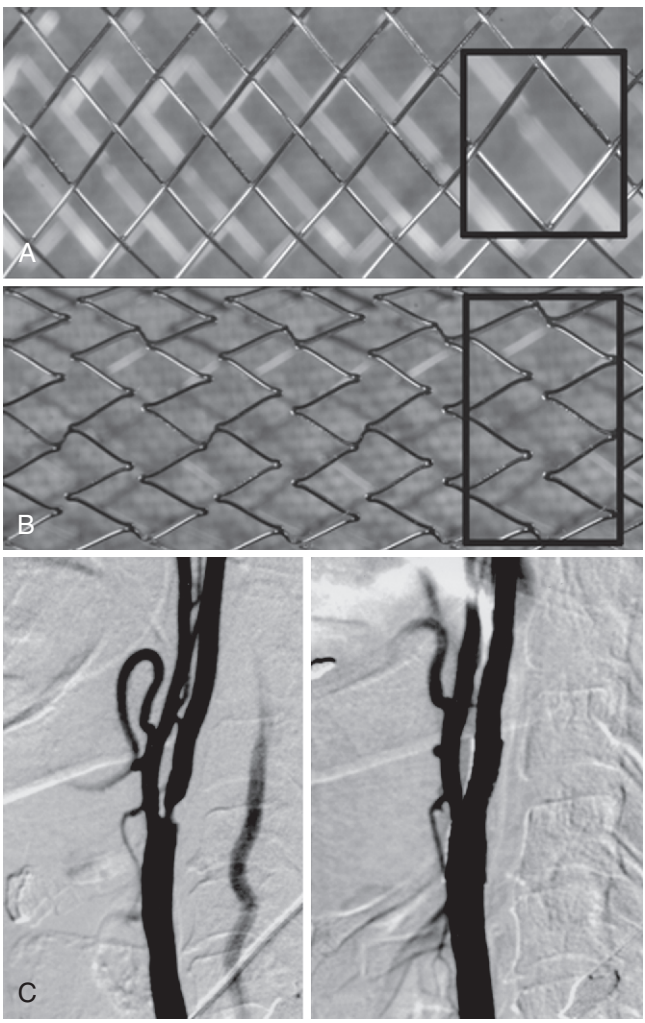

Figure 15-6 Closed- and open-cell stents. **A,** Closed-cell stents are less maneuverable but may better "cover" plaque. **B,** Open-cell stents have more "open" space and are more flexible. **C,** Baseline angiogram of right internal carotid artery stenosis (*left*); angiogram after self-expanding stent placement (*right*).

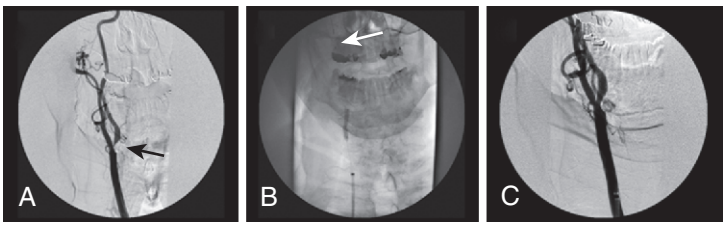

Figure 15-7 Internal carotid artery (ICA) stenting. **A,** Baseline carotid angiography demonstrating ostial internal carotid artery (ICA) stenosis (*arrow*). **B,** Predilation with filter-type Embolic protection device (EPD) in place (*arrow*). **C,** Final angiography. The stent is placed across the ostium of the external carotid artery (ECA); ≤50% residual stenosis is an acceptable result.

the rates of restenosis and late loss are very low in the carotid artery. Balloons are conservatively sized (≤1:1) to minimize vessel trauma/dissection, plaque embolization, and stimulation of the carotid sinus. A poststent carotid diameter stenosis of ≤50% is an acceptable result. Figure 15-6*C* shows a carotid bifurcation lesion after self-expanding stent placement.

Following the procedure, if a filter-type EPD is used, the EPD is retrieved and final carotid and cerebral angiography is performed (Fig. 15-7). If a proximal protection device is used, the balloons are deflated and final angiography is performed. It is important to confirm that the carotid artery is free of dissection and that the cerebral vasculature is intact. Prior to removal of equipment, a neurologic exam assessing speech, movement, and mental status should be performed. If a neurologic deficit is found, a culprit lesion is sought and neurovascular rescue attempted.

Aorto-Ostial Interventions

Femoral access is obtained with a 6F to 9F sheath depending on the diameter of the balloon and stent that will be used. After anticoagulation (ACT ≥ 250 sec) and appropriate diagnostic imaging of the target lesion, a 5F diagnostic catheter is advanced through a guide catheter (i.e., JR4 or multipurpose guide) to the ostium of the target CCA. The ostial lesion is crossed with a steerable 0.035-inch hydrophilic wire. The diagnostic catheter is then advanced across the lesion into the distal vessel. The hydrophilic wire is exchanged for a stiff 0.035-inch Amplatz wire, and the guide catheter is carefully advanced over the diagnostic catheter until it engages the ostium of the CCA. The diagnostic catheter is then slowly removed.

The lesion is predilated with a balloon sized 1:1 with the CCA. As the balloon deflates, the guide is gently advanced or "telescoped" over the balloon and across the lesion. This will protect the stent as it is delivered to the lesion. The predilation balloon is removed, and a balloon-expandable stent is placed (in arteries protected by the axial skeleton, balloon-expandable stents are more often used). After positioning the stent at the target lesion, the guide catheter is withdrawn, uncovering the stent and placing it in contact with the target lesion. The proximal stent should protrude slightly into the aorta (≤1 mm) to ensure adequate lesion coverage. After verifying adequate placement with contrast injections through the guide catheter, the stent is deployed at nominal pressure (Fig. 15-8). As the balloon deflates, the guide is again gently telescoped over the balloon to allow further stents to be delivered distally if needed. Final angiography and neurologic assessment are performed. The access site is managed similarly to other interventional procedures. Sheath removal is performed when the ACT is ≤170 seconds if a closure device is not used.

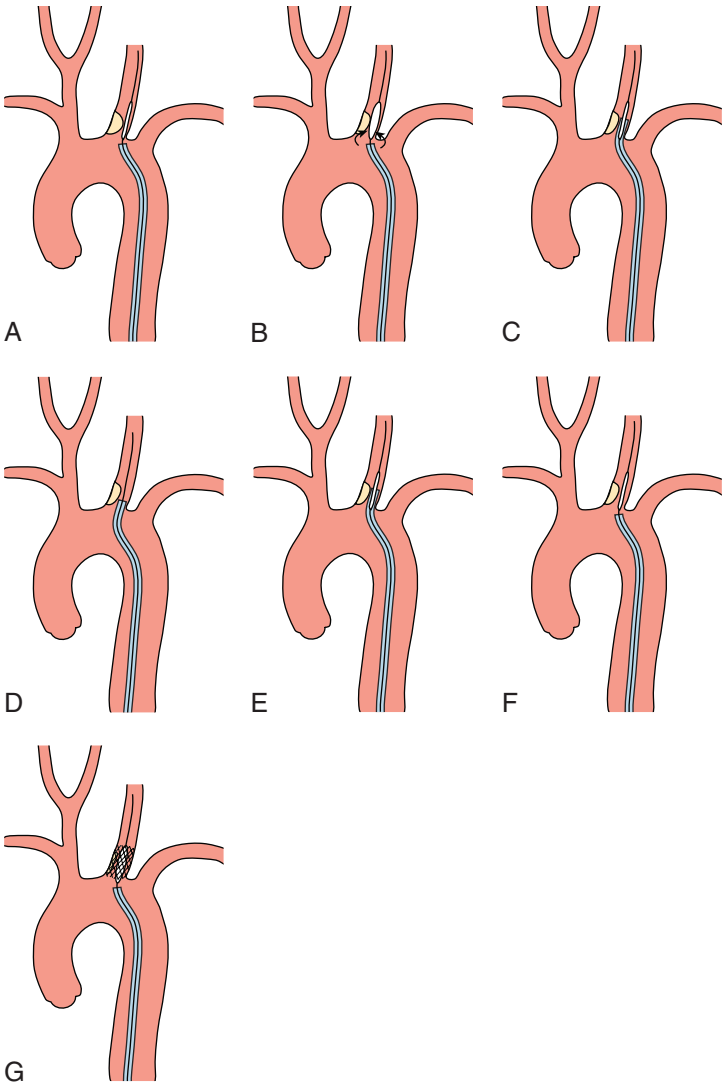

Figure 15-8 Dilating and stenting aorto-ostial lesions. **A,** The lesion is crossed with a 0.035-inch wire and a predilation balloon is placed. **B,** The lesion is predilated, and as the balloon deflates, the guide catheter is advanced, thus "swallowing" the balloon. **C,** The guide is now distal to the lesion. **D,** The balloon is removed. **E,** A balloon-expandable stent is placed, although a portion of it remains within the guide. **F,** The guide is withdrawn, uncovering the stent and leaving it in contact with the lesion. **G,** The stent is deployed. If a stent is required distally, the stent balloon is "swallowed."

Complications and Troubleshooting

Stroke

In a review of more than 54,000 patients, the 30-day risk of stroke during or after CAS was 3.9%. Symptomatic patients were twice as likely to have an adverse event as asymptomatic patients. While providing a good general idea of the stroke risk, this review found significant heterogeneity between studies, and stroke risk differs among patients depending on lesion severity, symptomatic status, and other factors such as renal function.

Most events occur within 24 hours of the procedure. If the patient develops a focal neurologic deficit *during* the procedure, an embolic

event is assumed. Immediate cerebral angiography should be performed, and rescue intervention should be attempted. Typically these emboli are plaque elements and not amenable to thrombolytic agents. Attempts at revascularization with angioplasty and stenting and/or thrombectomy are recommended. Mental status changes *after* the procedure warrant evaluation by means of computed tomography to rule out intracranial bleeding or hyperperfusion syndrome (see the following section below).

Hemodynamic Instability

Stimulation of the carotid sinus baroreceptor is common during carotid interventions and can cause hypotension and bradycardia. Typically, patients who are most sensitive will react negatively to predilation of their lesion. Acute hypotension can lead to brain hypoperfusion and neurologic symptoms due to impaired cerebral autoregulation.

Atropine (0.4–1 mg) is used to treat acute bradycardia. A prophylactic dose may be considered before stent deployment if the patient was sensitive to predilation, but there is a risk of urinary retention in men. The dose may be repeated if necessary. Aggressive fluid administration is important in treating hypotension, but vasopressor medications are often needed to maintain a systolic blood pressure of 120 mm Hg. We use IV phenylephrine in repeated boluses of 50 to 100 mcg as needed. A continuous infusion may be required if hypotension persists. In most patients, however, phenylephrine can be weaned within several hours of the procedure, and the patient can ambulate in preparation for discharge the next day. Midodrine 2.5 to 10 mg three times daily can be useful to support blood pressure in the setting of prolonged hypotension. Adjusting the patient's antihypertensive regimen will be necessary over the short term. Keep in mind that as in any interventional cardiovascular procedure, access site bleeding is a common cause of hypotension and should be ruled out in these patients.

Hyperperfusion Syndrome and Intracranial Hemorrhage

The opening of a stenotic carotid artery can lead to significant increases in cerebral blood flow, sometimes to levels more than twice the preprocedure flow. Hyperperfusion syndrome occurs in <1% of carotid stent patients and is defined clinically by the presence of an ipsilateral throbbing headache, a seizure, or a focal neurologic deficit. A chronically stenotic carotid artery can cause the cerebral vasculature to remain in a state of constant, maximal vasodilation. When the stenosis is suddenly alleviated, cerebral autoregulatory mechanisms fail to control blood flow, a problem exacerbated by hypertension. The resulting elevated cerebral perfusion pressure can lead to cerebral edema or, worse, intracranial hemorrhage.

Neurologic symptoms from cerebral edema are usually transient but must be addressed. A neurology consultation and head CT should be obtained if this diagnosis is entertained. When diagnosed, strict control of blood pressure is critical, and consideration of mannitol, diuretics, or antiepileptic medications (depending on presentation) is warranted. Medications that cause cerebral arterial vasodilation (i.e., hydralazine) should theoretically be avoided. Intracranial bleeding is life threatening. If it occurs, antiplatelet medications should be stopped and a neurosurgical team consulted. Strict blood pressure control (goal systolic pressure of 120–140 mm Hg) may decrease the risk of hyperperfusion syndrome and intracranial bleeding.

Carotid Stenting: Clinical Outcomes

When interpreting data on carotid stenting, it is important to realize that a patient who is high risk for surgery is not necessarily high risk for stenting (and vice versa). Features that place a patient at increased risk for complications from CEA and CAS are summarized in Table 15-1.

Table 15-1

High-Risk Features of CAS and CEA

High-Risk Features for CAS		High-Risk Features for CEA	
Clinical Features	**Angiographic Features**	**Comorbidities**	**Anatomical Features**
Age ≥75/80	≥2 acute (90°) bends	Age ≥80	Lesion C2 or higher; below clavicle
Dementia	Circumferential calcification	Class III/IV CHF or angina	Prior neck surgery (including ipsilateral CEA) or radiation
Bleeding disorder	Intracranial microangiopathy	Left main or ≥2 vessel CAD	Contralateral carotid occlusion
Multiple lacunar strokes	Evidence of thrombus	Urgent heart surgery	Tracheostoma
Renal failure	Poor vascular access	LVEF ≤30% MI within 30 days Severe chronic lung disease Severe renal disease	Contralateral laryngeal nerve palsy

CAD, coronary artery disease; *CAS,* carotid artery stenting; *CEA,* carotid endarterectomy; *LVEF,* left ventricular ejection fraction; *MI,* myocardial infarction.
Adapted from Bates ER, Babb JD, Casey Jr DE, *et al.* ACCF/SCAI/SVMB/SIR/ASITN 2007 clinical expert consensus document on carotid stenting: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents (ACCF/SCAI/SVMB/SIR/ASITN Clinical Expert Consensus Document Committee on Carotid Stenting). *J Am Coll Cardiol* 2007;49:126–170; Roubin GS, Iyer S, Halkin A, *et al.* Realizing the potential of carotid artery stenting: proposed paradigms for patient selection and procedural technique. *Circulation* 2006;113:2021–2030.

High Surgical Risk Patients

The Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy (SAPPHIRE) trial is the only randomized trial comparing high surgical risk (HSR) patients treated with CEA to those treated with CAS. Patients (N = 334) with a symptomatic stenosis of ≥50% or an asymptomatic stenosis ≥80% (~30% were symptomatic) were randomized to either CEA or CAS. The primary end point of death, stroke, or MI at 30 days plus ipsilateral stroke or death from neurologic cause between day 31 and 1 year occurred in 12.2% of patients in the stenting group and 20.1% in the CEA group (P = 0.004 for noninferiority; Fig. 15-9). The 30-day stroke and death rate among the asymptomatic patients was 4.6% for the CAS group and 5.4% for the CEA group. At 3 years, there were no differences between the groups.

Most of the contemporary registry data focuses on HSR patients, and data from more than 10,000 HSR patients have been published. These registries generally include symptomatic patients with ≥50% stenosis and asymptomatic patients with ≥70–80% stenosis. Data from some of these studies are summarized in Figure 15-10.

Usual Surgical Risk Patients

Four large randomized studies in average or usual surgical risk patients compared CAS to CEA. The Endarterectomy Versus Angioplasty in Patients with Symptomatic Severe Carotid Stenosis (EVA-3S) trial found that the 30-day incidence of stroke or death was 9.6% in the CAS group and 3.9% in the CEA group. The Stent-Supported Percutaneous Angioplasty of the Carotid Artery versus Endarterectomy (SPACE) trial noted that the 30-day rate of ipsilateral stroke or death was not different between the two groups (6.8% in the CAS group and 6.3% in the CEA

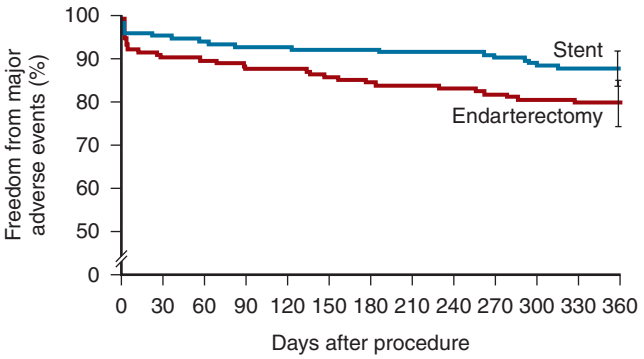

Figure 15-9 Freedom from major adverse events at 1 year in the SAPPHIRE trial. (From Yadav JS, Wholey MH, Kuntz RE, et al. Protected carotid-artery stenting versus endarterectomy in high-risk patients. *N Engl J Med* 2004;351:1493–1501. Reprinted with permission.)

group, $P = 0.09$ for noninferiority). However, the 2-year outcomes for this trial demonstrated a statistically significant benefit for CAS over CEA in patients <68 years of age (Fig. 15-11). The International Carotid Stenting Study (ICSS) published only their interim safety analysis, which demonstrated that the 30-day rate of death, stroke, or MI was 7.4% in the CAS group and 4% in the CEA group ($P = 0.003$). The rate of death and stroke alone also favored CEA (7.4% vs. 3.4%, $P = 0.0004$).

The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) is the largest randomized trial published comparing CAS with EPD to CEA (Fig. 15-12). The primary outcome of periprocedural stroke, death, or MI or follow-up ipsilateral stroke was not significantly different between the two groups (7.2% for CAS and 6.8% for CEA). The 30-day risk of stroke was higher for CAS (4.1% vs. 2.3%, $P = 0.01$), whereas CEA was associated with a higher 30-day risk of MI (2.3% vs. 1.1%, $P = 0.03$). CAS appeared safer than CEA for patients ≤ 69 years of age while CEA yielded better outcomes in those >70 years of age.

CREST differed from the previous three trials in three significant ways. Most importantly, the European trials, EVA-3S, SPACE, and ICSS, allowed inexperienced operators to treat patients. All allowed stent operators, but not surgery operators, to be "tutored" during the randomized trial. CREST requirements were more stringent. In fact, many of the "experienced" CAS

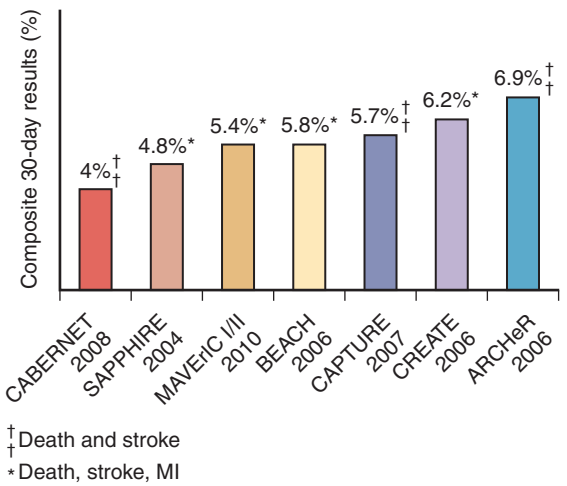

Figure 15-10 Thirty-day outcomes from U.S. carotid artery stenting (CAS) studies/registries of high surgical risk patients.

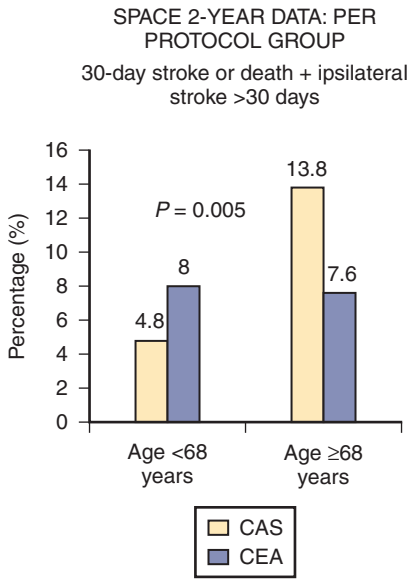

Figure 15-11 Two-year outcomes from SPACE. Age <68 years had better outcomes with carotid artery stenting (CAS) compared to carotid endarterectomy (CEA). Age ≥68 years appeared to have better outcomes with CEA.

operators in the first three trials were not very experienced. The fact that so many neurologic events involve the nonculprit carotid circulation is testament to the importance of catheter skills, and the value of experience cannot be overstated. Second, CREST mandated the use of EPDs, whereas the other trials did not. Lastly, just over 50% of the patients in CREST were symptomatic, whereas the other trials were specifically for symptomatic patients. When taken together, the message from these four trials is that CAS with embolic protection is a legitimate alternative to CEA for average surgical risk patients but only when performed by experienced operators. The Asymptomatic Carotid Trial (ACT-1) will further help evaluate CEA vs. CAS in asymptomatic, usual surgical risk patients. Preliminary data have been reported (Table 15-2).

The 2011 AHA guidelines on the treatment for extracranial carotid and vertebral artery disease give carotid stenting a class I indication in patients with symptomatic carotid stenosis of >70% by noninvasive imaging or >50% by catheter-based angiography if the periprocedural rate of stroke or death is <6%. This recommendation is independent of surgical risk. CAS in asymptomatic patients is given a class IIb indication

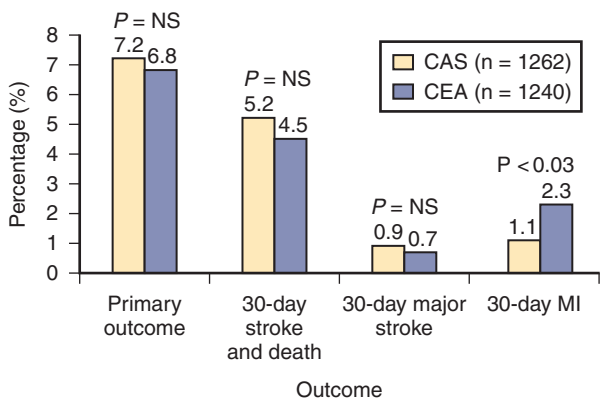

Figure 15-12 Results from CREST. *CAS,* carotid artery stenting; *CEA,* carotid endarterectomy; *MI,* myocardial infarction.

Table 15-2

Preliminary Data From ACT-1	
Event	**30 Days, *N* = 135**
Death, stroke, and MI*	1.4%
All stroke and death*	1.4%
Major stroke/death*	0%
Death	0%
All stroke	1.4%
Major stroke	0%
Minor stroke	1.4%
MI	0%
Ipsilateral stroke, days 31–365	0%

*Hierarchical: only the most serious event is counted.
ACT-1, Asymptomatic Carotid Trial; *MI,* myocardial infarction.

if the degree of stenosis is >70% by catheter angiography. Carotid revascularization is contraindicated in those with a total occlusion of the target carotid artery and those with severely disabling strokes.

Summary

Multiple studies have shown the benefits of aggressive medical therapy and carotid revascularization in patients with carotid stenoses, particularly those with a prior TIA or stroke. Several studies have proven the safety of CAS in HSR patients. The CREST trial has demonstrated that, among average surgical risk patients, CAS performed by experienced operators is a legitimate alternative to CEA. As reflected in the AHA guidelines, procedure selection should be individualized to best suit a patient's clinical and anatomical features as well as the patient's personal preference. As technology progresses, event rates should continue to decrease.

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16

Percutaneous Mitral Commissurotomy and Balloon Aortic Valvuloplasty

TED FELDMAN · MICHAEL H. SALINGER

Percutaneous Mitral Commissurotomy

Inoue reported a single balloon technique for mitral commissurotomy in 1984. Although a number of other techniques have subsequently been described, the Inoue balloon technique and the double balloon technique have been used most commonly. The Inoue technique is the most frequently used in practice internationally and is at present the only approved mitral dilatation balloon in the United States.

Hemodynamic results have been well characterized by the Inoue Multi-Center Registry. On average there is more than 80% increase in mitral valve area. Balloon inflation results in splitting of the fused commissures with reductions in the transmitral pressure gradient, the mean left atrial pressure, and the pulmonary artery pressure. The cardiac output and mitral valve area increase (Table 16-1).

The most important complication of the procedure is mitral regurgitation. Mitral valve replacement is needed during the initial hospitalization in about 2% of patients. An additional 3% to 4% have resultant 3+ or greater mitral regurgitation without the need for immediate valve replacement. Other complications are shown in Table 16-2.

The durability of the results is excellent. Figure 16-1 shows the stability of the achieved valve area over a period of years. The 5-year actuarial freedom from death with mitral valve replacement or repeat balloon commissurotomy for the Inoue Registry population was 71%. More than 80% of the patients remained symptomatically improved at 5 years.

Table 16-1

Hemodynamic Results of Balloon Mitral Valvotomy

Parameter	Pre	Post	*P*
Left atrium (mm Hg)	24 ± 8	19 ± 12	<0.001
Pulmonary artery (mm Hg)	34 ± 14	29 ± 12	<0.001
Mitral gradient (mm Hg)	13 ± 6	6 ± 3	<0.001
Cardiac output (L/min)	4.1 ± 1.1	4.4 ± 1.3	<0.001
Mitral area (cm^2)	1.0 ± 0.3	1.7 ± 0.6	<0.001

Table 16-2

Complications of Percutaneous Transvenous Mitral Commissurotomy

Complication	%
Hospital mitral valve replacement (MVR)	1.0
Hospital death	1.4
Transient ischemic attack	0.6
Stroke	0
Cardiac perforation	1.4
Pericardiocentesis	1.0
Myocardial infarction	0.3
Cardioversion shock for atrial or ventricular fibrillation	<1
Vascular repair	0.6
Transfusion	0.3
Temporary pacer	0
Mitral regurgitation 3+ or more (no MVR)	3.8
Atrial septal defect >1.5	3.1
Failure to cross mitral valve	1.7

Technique

The Inoue Balloon

The Inoue device differs substantially from conventional balloons. It is constructed of two layers of latex with a nylon mesh sandwiched in between them. The latex is compliant, whereas the nylon mesh limits the maximum inflated diameter of the balloon and gives it a unique shape and three-stage inflation characteristics (Fig. 16-2).

The front half of the balloon inflates first, giving the appearance of a balloon flotation catheter. The proximal half of the balloon inflates next, creating a dumbbell or hourglass shape. When it is passed across the mitral valve, this shape facilitates self-positioning of the balloon device in the valve orifice. Finally, the center portion of the balloon inflates, resulting in splitting of the fused mitral valve leaflet commissures. The distensibility of the latex material allows each balloon to be inflated over a 4-mm range of diameter sizes (i.e., between 26 and 30 mm diameter for the largest available model). A single balloon can thus be used to cause sequential dilatation of the valve by inflating it to serially larger diameters without removing it from the patient. This procedure is thus analogous to coronary angioplasty, during which the result of the balloon inflations is evaluated and additional balloon inflations are performed if necessary.

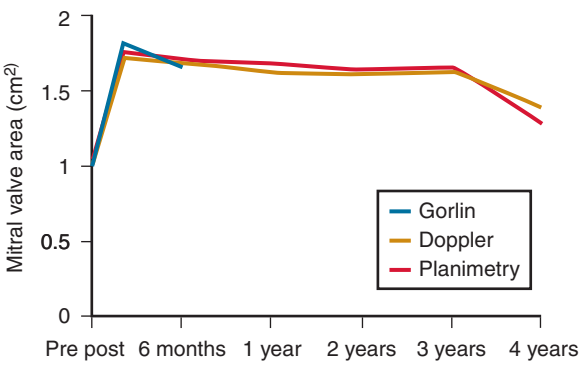

Figure 16-1 Mitral valve area before percutaneous transvenous mitral commissurotomy (PTMC), immediately after and 4 years following PTMC. Gorlin-calculated valve areas were obtained in 86 patients at repeat catheterization. Doppler and planimetry areas remained relatively constant for 3 years and then fell off slightly in the fourth year.

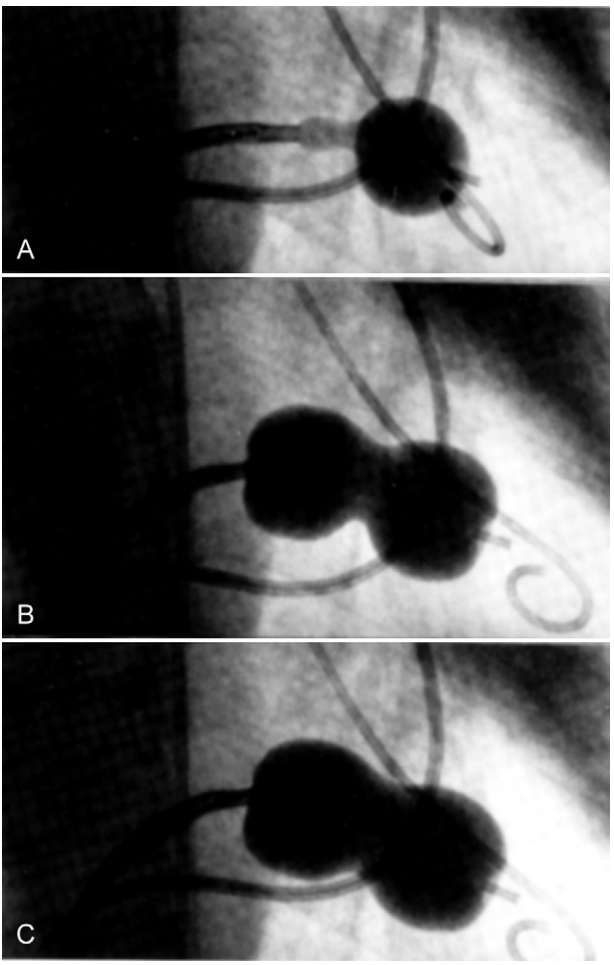

Figure 16-2 **A,** Front half of balloon inflated and passed across the mitral valve orifice. This is analogous to the manner in which a balloon flotation catheter is maneuvered from the right atrium to the right ventricle during right heart catheterization. The partially inflated balloon is pulled back until it engages the mitral valve. **B,** Front and back portions of balloon inflated, creating a "dog-bone" shape that self-positions the balloon in the mitral orifice. **C,** Almost fully inflated balloon opening the commissures. Note that the inferior indentation in the balloon is more pronounced than the superior indentation, signifying incomplete commissural separation.

Patient Evaluation

Evaluation by two-dimensional transthoracic and transesophageal echocardiography is essential before mitral valvotomy. Patients with thin, pliable mitral leaflets and minimally diseased subvalvular apparatus have the best long-term outcome from surgical commissurotomy (Fig. 16-3). This is no less true when using percutaneous methods to achieve commissurotomy. Although the immediate results of percutaneous transvenous mitral commissurotomy (PTMC) are acceptable in patients with significant valve deformity, the restenosis rate and the need for rate mitral valve replacement remains higher in these patients. The goal of therapy and the long-term prospects for event-free survival must be appropriate for patients with significant valve deformity and echocardiographic scores greater than 10 to 12.

Transesophageal echocardiography before PTMC is useful for the detection of atrial thrombi. Even when PTMC was performed in patients before the widespread use of transesophageal echocardiography,

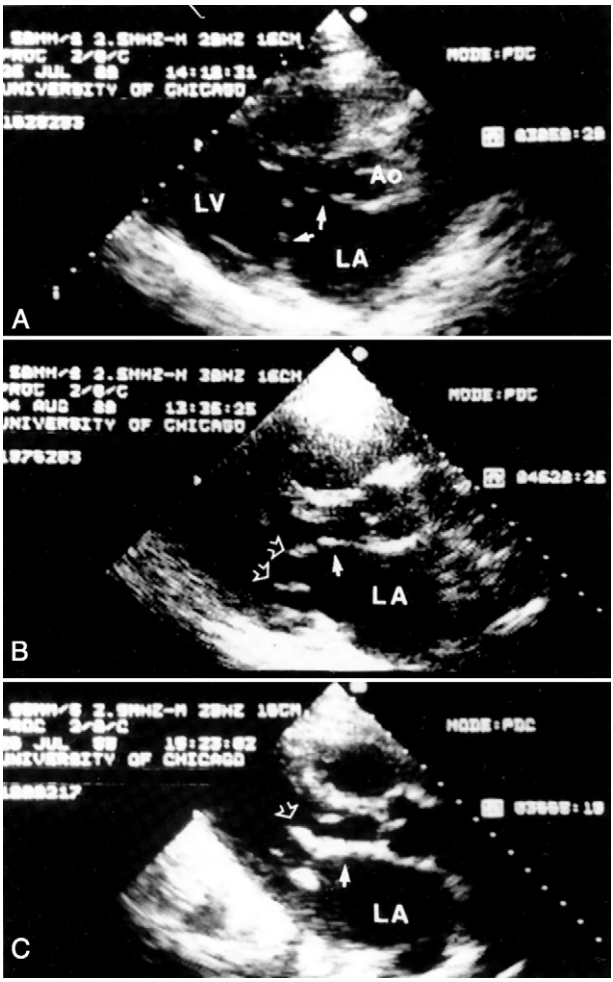

Figure 16-3 **A,** Long-axis two-dimensional echocardiographic image from an ideal candidate for mitral commissurotomy. The solid arrows show the thin, domed leaflets. The mitral apparatus is not visible in the left ventricle, signifying its freedom from significant thickening. **B,** Typical valve replacement candidate. The solid arrow points at a thickened and calcified anterior mitral leaflet. The open arrows show the thickened submitral apparatus. These patients have echocardiographic scores between 8 and 12 and are reasonable candidates for percutaneous transvenous mitral commissurotomy, although they may have poorer long-term freedom from mitral valve replacement. **C,** Elderly patient, not a likely candidate for surgical therapy of any kind. This patient was an 88-year-old woman. The solid arrow shows a densely calcified, thickened, and rigid anterior mitral leaflet. The open arrow points to the similarly thickened and calcified mitral apparatus. Balloon dilatation may be accomplished successfully in these patients but with acute results that are not as good as those in patients with less deformed valves. The long-term event-free outcome for these patients is poor. (From Feldman T, Carroll JD. Cardiac catheterization, balloon angioplasty, and percutaneous valvuloplasty. In Hall JB, Schmidt GA, Wood LDH, eds. *Principles of critical care.* New York: McGraw-Hill, 1992:343–360.)

embolic events were infrequent. Experience since the routine use of transesophageal echo screening has virtually eliminated the chance of this devastating complication.

Atrial thrombi are a strong relative contraindication to the performance of both transseptal puncture and balloon mitral valvotomy. Atrial thrombi are found in 15% to 25% of patients with mitral stenosis being considered for PTMC, many of whom have been on long-term

warfarin anticoagulation therapy even when sinus rhythm is present. In many cases when atrial thrombi are noted, it is possible to either institute or intensify anticoagulation for 3 to 12 months and achieve resolution of thrombi. PTMC may then be undertaken without unnecessary risk. In some cases, small, densely organized thrombi in the atrial appendage may be present. These thrombi are not as likely to contain fresh clots or to be mobile. It is possible to do PTMC in these cases without complications, although this must be done with extreme care and recognition of the serious risk of stroke. Operator experience with the handling characteristics of the Inoue balloon steering stylette is essential in this setting. An option for patients with atrial thrombi, when the risk of PTMC seems justified for other clinical reasons, is to cross the mitral valve with a 7F balloon-tipped catheter, pass the Inoue exchange wire through the balloon catheter into the left ventricle, and then pass the Inoue balloon over this wire. This avoids manipulation of the valvuloplasty device in the left atrium. Some patients in atrial fibrillation without prior anticoagulation therapy are found not to have atrial thrombi upon transesophageal echocardiographic examination. In these cases balloon dilatation may proceed without a prior course of anticoagulation.

Cardiac Catheterization Technique

1. The left femoral arterial and venous sheaths are placed. Because a pigtail catheter will be left in place in the left ventricle for a relatively long period of time, we prefer to use 5F or 6F arterial catheters.
2. A multilumen pulmonary artery balloon catheter with thermodilution cardiac output capability is used for right heart catheterization. Left femoral access is preferred for these catheters, leaving the right side for insertion of the dilatation balloon catheter. Pulmonary artery catheters with oximetric monitoring simplify the evaluation of venous saturations for the detection of atrial shunting following the procedure, although these catheters are more difficult to place than are conventional pulmonary artery catheters. Passage of the pulmonary artery catheter is facilitated by the use of an extra-stiff 0.025-inch guidewire.
3. Left ventriculography and coronary arteriography are performed when indicated. The AHA/ACC guidelines for valvular heart disease recommend arteriography for men over age 35 years, or women over age 35 years who also have risk factors.
4. Right heart pressures and cardiac output are measured.
5. Right femoral venous puncture is performed for placement of an 8F Mullins sheath. Placement of a 14F sheath at this stage makes passage and removal of the balloon much easier. An extra-stiff 0.035-inch wire should be used for insertion of the large venous sheath. If a 14F sheath is not used, free movement of the balloon can be impaired by binding in the subcutaneous tissues at the groin puncture site. In very heavy patients the catheter may make a severe angle between the skin and the femoral vein. An ipsilateral pulmonary artery catheter does not interfere with the performance of the transseptal catheterization.
6. Following transseptal puncture, heparin is administered. The transmitral pressure gradient is measured using the Mullins sheath for the left atrial and the pigtail for left ventricular pressures. If the Mullins sheath can be passed into the left ventricle with a gentle counterclockwise rotation, a transaortic gradient is measured with the Mullins and pigtail to exclude aortic valve disease.

A simplified procedure with no arterial access and no pulmonary artery catheterization is not recommended. The safety of the procedure and the evaluation of the resultant possible complications mandate continuous arterial pressure monitoring, a full right heart catheterization before and after the procedure, and accurate cardiac output determination.

Selection of Balloon Size

Balloon sizing has not been rigorously defined by any study; rather a combination of experience in the first decade of mitral valvotomy, common sense, and data from a few studies has established the approach to balloon sizing.

The maximum expected inflated balloon diameter may be selected based on the patient's height (Table 16-3). This value provides a guideline for balloon selection with a stepwise technique. A first inflation is always performed at a diameter smaller than the maximum possible for the selected balloon. An initial inflation of 2 to 4 mm less than the maximum is usually chosen. An alternative method for selecting balloon size is to calculate the ratio of inflated dilating balloon area to the body surface area, called the effective balloon dilating area (EBDA).

This method results in somewhat different values for maximal balloon size in a given patient compared to the recommendations originally made by Inoue based on his empiric observations. When the Inoue balloon is inflated to an EBDA of 4.0 using a single inflation without the stepwise technique, results similar to those reported for the stepwise technique have been achieved. EBDA may not be equally useful in all patient populations. For overweight or obese patients, in particular, a better estimate of largest expected balloon inflation balloon diameter may be based on height alone.

For patients with pliable valves, the first balloon inflation can be made with a balloon inflation 2 or 3 mm smaller than the reference size and then increased in increments of 1 mm until either a maximal diminution of gradient has occurred or mitral regurgitation has begun to worsen significantly. For patients with more deformed valves, the first inflation can be performed at 4 mm less than the reference size with increments of 1 mm in size while the balloon is in the shallow or low-pressure portion of the pressure-volume cure. Increments of 0.5 mm may then be used over the last couple of millimeters of balloon diameter when the balloon reaches the high- pressure portion of its pressure-volume curve.

Special Considerations

There are a number of special considerations in balloon size selection. Smaller balloons than initially estimated may be useful in patients with advanced age, patients with subvalvular disease, or those in whom persistence with marked constriction during full inflation indicates that balloon pressure may be insufficient. In this last situation, the use of a smaller balloon inflated to the same diameter as a previous larger balloon will result in a greater inflation pressure.

The Stepwise Technique

The stepwise balloon expansion technique obviates the need for precise determination of maximum inflated balloon diameter. Because the Inoue device may be inflated over a range of sizes, balloon size selection need only be accurate enough to address this range. Although patient and balloon characteristics may be evaluated in a consistent

Table 16-3

Selection of Balloon Size for Percutaneous Transvenous Mitral Commissurotomy

Balloon diameter (range, mm)	Balloon dilating area (cm^2)	Patient height, cm (inches)
26 to 30	7.07	>180 (70.9)
24 to 28	6.16	>160 (62.9)
22 to 26	5.13	<160

manner, the inhomogeneity of the valve pathology and the limitations of our ability to predict ultimately what balloon sizes and pressures will produce commissural splitting make the stepwise approach more practical than preprocedure predictions of expected balloon size.

Balloon Preparation

Once the diagnosis of mitral stenosis is confirmed after successful transseptal puncture, the balloon catheter can be prepared. The balloon catheter comes packaged with all the components necessary for the dilatation procedure (Fig. 16-4). These include:

- A balloon-stretching metal tube
- A calibrated inflation syringe specifically matched to each balloon
- A rigid 12F to 14F plastic dilator
- A 0.025-inch spring-tipped exchange guidewire
- A stylet for manipulating the balloon across the mitral valve after it has been placed in the left atrium
- The Inoue balloon catheter
- Calipers for measuring the balloon diameter and confirming its inflated size

The balloon catheter lumen is flushed with saline. Dilute contrast (saline:contrast 2:1 or 3:1) is injected through the vent lumen to purge air from the inflate/deflate channel to the balloon and the stopcock is closed on that lumen.

The precalibrated balloon inflation syringe is filled to the calibration corresponding to the smallest inflated diameter. After connecting the inflation syringe to the inflation port and checking that all connections are secure, the balloon is slowly inflated over a period of 5 seconds so that the nylon mesh may be slowly stretched without risking mesh rupture.

The balloon is allowed to deflate passively in a bath of flush solution. Small bubbles will escape from within the mesh layer of the balloon. The balloon is then inflated rapidly and the inflated diameter is measured using calipers to verify the precalibrated inflation syringe. If the balloon does not inflate to the desired diameter, small amounts of contrast are added or subtracted to achieve proper calibration.

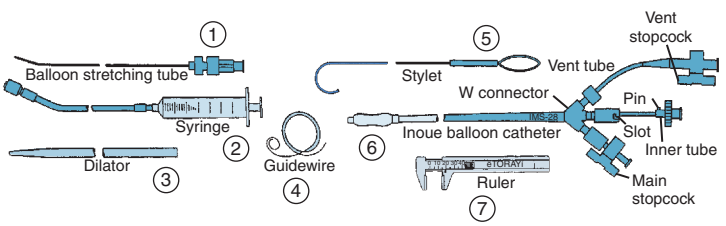

Figure 16-4 The components of the equipment box supplied by Toray include (*1*) a long metal hypotube, the balloon-stretching tube, used to pass through the inner tube of the Inoue balloon catheter to elongate and slenderize the balloon; (*2*) a calibrated syringe used for inflation of the balloon. The syringe provides calibration marks so that predetermined diameters of the balloon can be achieved driven by the volume rather than pressure; (*3*) a dilator used to dilate the subcutaneous tissue at the femoral venous puncture site and to dilate the septum as well; (*4*) a 0.025-inch stainless steel spring guidewire; (*5*) a steering stylet that is introduced through the inner tube after the balloon is in the left atrium to help guide it across the mitral valve; (*6*) the balloon catheter itself, which has a W connector from which arise a vent tube, an inner tube used for introduction of the balloon-stretching tube and stylet, and for stretching the balloon, and a main stopcock for balloon inflation via the syringe; (*7*) a ruler or caliper, which is used to confirm that the graduations on the syringe used to inflate the balloon result in the desired inflation diameters.

The syringe is then filled to the calibration corresponding to the maximum nominal inflated size. The balloon may be tested to ensure that the maximum size calibration is also correct. In practice, this calibration step is often omitted. The next step in balloon preparation is to elongate the balloon catheter along its long axis, causing it to become more slender. A metal tube (balloon-stretching tube) is inserted into the center lumen of the balloon over the guidewire and advanced until it locks into the metal hub at the proximal end of the balloon catheter. The balloon and stretching tube are then advanced into the balloon catheter shaft until they engage the plastic slot on the balloon catheter Luer lock. This leaves the balloon in its elongated, slenderized form to ease not only percutaneous insertion but also delivery across the interatrial septum.

Balloon Valvotomy

The major steps in valvotomy are illustrated diagrammatically in Figure 16-5. The 0.025-inch spring guidewire is advanced through the Mullins sheath into the left atrium with the fully coiled distal portion out of the sheath and positioned in the roof of the atrium. The Mullins sheath is withdrawn over the guidewire with the guidewire remaining

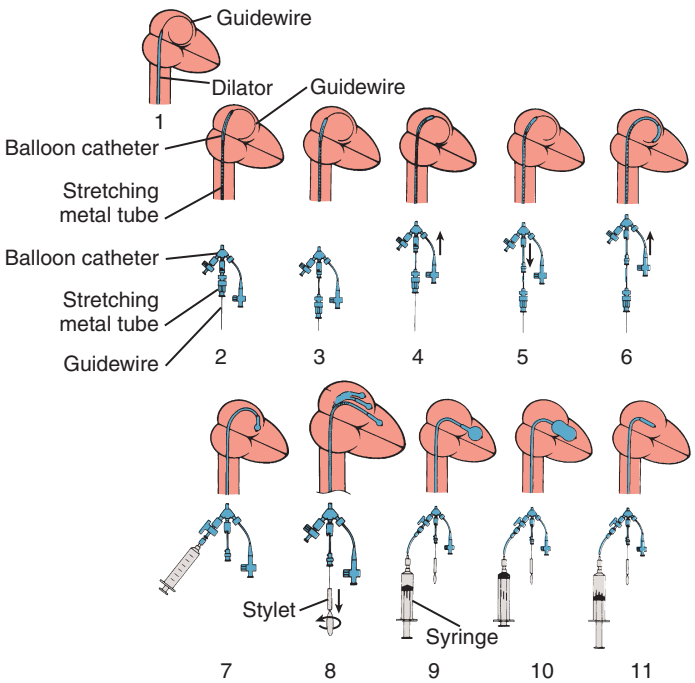

Figure 16-5 Schematic illustration of the Inoue balloon mitral valvotomy procedure. (*1*) After a spring guidewire is introduced via a Mullins sheath into the left atrium, the interatrial septum is dilated using a rigid 14F plastic dilator. (*2*) The elongated balloon catheter is advanced over the wire through the interatrial septum. (*3*) The stretching metal tube is partially withdrawn, allowing the balloon to shorten and curl within the left atrium. (*4*) The balloon is advanced through the interatrial septum. (*5*) The stretching metal tube and balloon straightening device are withdrawn further. (*6*) The balloon is advanced beyond the mitral orifice. (*7*) The distal portion of the balloon is partially inflated with a contrast-saline mixture. (*8*) With counterclockwise rotation of the stylet, slight advancement of the catheter shaft, and withdrawal of the stylet, the balloon is directed through the mitral orifice and left ventricle. (*9*) The partially inflated balloon is withdrawn against the mitral orifice. (*10*) The balloon is fully and rapidly inflated and allowed to deflate. (*11*) After deflation, in most instances, the balloon passively returns to the left atrium from the left ventricle. (Courtesy of Toray, Inc., Tokyo, Japan.)

in the left atrium. The dilator is advanced through the skin and then into the atrial septum, where it may be passed through the septal puncture as shown in Figure 16-5. The dilator is left sitting in the septal puncture for several seconds to stretch the septal tissue. The dilator is removed and the balloon catheter is passed over the guidewire via the 14F sheath and then across the atrial septum.

After the balloon is passed through the atrial septum, it must be allowed to resume its unstretched conformation to prevent the very stiff slenderizing tube from puncturing the roof of the left atrium. In some cases the blunt tip of the balloon will catch on the right atrial side of the septal puncture. Rotating the catheter slowly with gentle probing pressure will allow it to find its way through the septal puncture into the left atrium. Rarely, a 10- to 12-mm peripheral angioplasty balloon must be used to dilate the atrial septum. After the tip of the balloon has passed across the atrial septum, the stretching metal tube is then disengaged from the catheter metal hub and withdrawn as the balloon catheter is advanced. The tip of the balloon will then begin to track around the coiled spring guidewire. As the balloon reaches the roof of the left atrium, the gold metal Luer lock is disconnected and pulled back, allowing the balloon to shorten. The balloon catheter is then advanced further over the spring-tipped guidewire. The balloon-stretching tube and spring guidewire are removed from the patient and cleaned and prepared for later use to remove the balloon. It is important to track the balloon around over the wire until it reaches the inferior portion of the left atrium so it overlies the mitral orifice before removing the wire.

The balloon catheter can be flushed and connected to a pressure transducer. The transmitral pressure gradient can be remeasured through the balloon catheter to verify that the pressure wave form is similar to that obtained through the Mullins sheath. The wave form appears slightly damped through the lumen of the Inoue balloon.

Before crossing the mitral valve with the balloon, it is useful to change the x-ray projection from straight anteroposterior to shallow right anterior oblique.

The distal half of the balloon is partially inflated and, once positioned in the left ventricle, the balloon is gently withdrawn until the mitral valve is engaged. The proximal half of the balloon is inflated. When the position of the balloon appears correct, full inflation is achieved. The balloon is allowed to deflate passively. This ensures a constant amount of dead space fluid for subsequent balloon inflations. The entire cycle of inflation and deflation takes 5 seconds or less and it is unusual for patients to sense the inflation, as frequent ventricular ectopy does not usually occur and hypotension persists for no more than a few cardiac cycles.

To cross the mitral valve, the tip of the balloon is inflated and the steering stylet is passed into the catheter for its full length. It is important to completely advance the steering stylet within the shaft of the catheter. The stylet is then rotated in a counterclockwise direction as the balloon catheter is advanced and withdrawn over a 2- to 5-cm range, allowing the tip of the balloon to find its way across the mitral valve in a manner similar to that in which a pulmonary artery flotation catheter crosses from the right atrium through the tricuspid orifice into the right ventricle. As the balloon passes across the mitral orifice, the stylet is withdrawn about 5 to 10 cm. The balloon must be advanced gently and moved forward and backward to make sure it is free of entanglements in the subvalvular apparatus. The stylet may be gently bent to accentuate its curve to facilitate passage of the balloon across the mitral valve if initially crossing the valve is very difficult (Fig. 16-6). A useful observation during balloon inflation is the "popping sign" denoting splitting of one or both commissures. During the final portion of the inflation, one observes the inferior or superior margin of the mid section of the balloon suddenly popping outward. This is a welcome sign, which shows a clear decrease in gradient due to the commissurotomy.

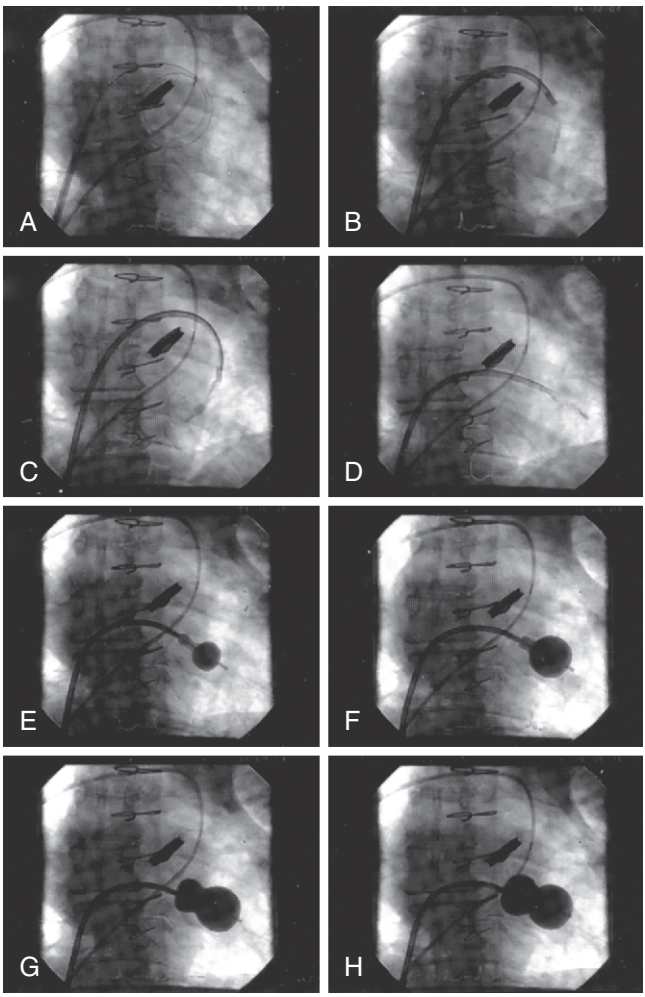

Figure 16-6 The major steps in percutaneous transvenous mitral commissurotomy. **A,** A 14F dilator is advanced over a spring-coiled guidewire. The guidewire has been introduced into the left atrium via a transseptal puncture. The 14F dilator dilates both the subcutaneous tissue at the groin catheter insertion site and the left atrial puncture. A prosthetic aortic valve marks the location of the aortic root. A pulmonary artery catheter traverses the right atrium, right ventricular outflow, and pulmonary artery. **B,** The uninflated balloon catheter has been introduced over the course of the spring wire. The wire has been removed. The tip of the catheter overlays the mitral orifice. **C,** The tip of the balloon catheter is partially inflated so that it may be manipulated across the mitral valve using a steering stylet. This is analogous to crossing the tricuspid valve from balloon-tipped catheter. **D,** The uninflated balloon is now in the left ventricular apex. **E,** The front portion of the balloon has been inflated and pulled back until it engages the mitral valve orifice. **F,** The balloon is inflated further. **G,** Additional inflation of the balloon causes the proximal portion to inflate, leaving a waist in the middle. **H,** Full inflation of the balloon results in expansion of the center of the balloon, splitting the fused mitral commissures.

After dilatations, as the balloon deflates, it usually falls back into the left atrium with no specific manipulation. If it does not, a gentle clockwise rotation of the balloon catheter will move the balloon back into the left atrium.The stylet is withdrawn and the balloon shaft is connected to a pressure transducer for reassessment of the transmitral pressure gradient.

A Doppler and echocardiographic examination can be performed to evaluate changes in mitral regurgitation and assess whether either fused commissure has been opened, as is best seen in a short-axis view.

In addition to evaluating the transmitral gradient, it is important to consider the magnitude of left atrial pressure and changes in left ventricular filling pressure. Often, after PTMC has been performed, there is only a modest decline in left atrial pressure. Left ventricular filling pressure may rise significantly. In addition, with atrial fibrillation, the heart rate is irregular. Together, these factors may make evaluation of the success of a PTMC procedure difficult.

Stepwise Balloon Inflation

If a transmitral gradient persists and no significant increase in mitral regurgitation has occurred, another balloon inflation is performed at an inflated diameter 1 mm greater than the preceding inflation, as shown in Figure 16-7. This sequence is repeated until either an increase in mitral regurgitation or a sufficient decrease in the transmitral gradient occurs. Balloons can be overinflated by 1 to 2 mm diameter by using an additional 1 to 2 mL inflation volume above the maximal calibrated balloon size. If sufficient reduction in gradient is not achieved after maximal or supermaximal inflation, a larger balloon size can be used.

It is very useful to monitor the effect of each balloon inflation in the mitral valve by echocardiography in the catheterization laboratory. Of course, the procedure may be performed without this adjunct, but monitoring of the results is facilitated by echo examination. An in-lab Doppler examination will demonstrate if mitral regurgitation is increased. More importantly, the short-axis two-dimensional examination will show the degree of commissural separation (Fig. 16-8). Note the degree of commissural fusion in the short-axis examination before the balloon dilatation. Separation of one commissure while the other remains fused will facilitate the decision to proceed with further balloon inflations. If mitral regurgitation is not worsened, attempts to complete commissurotomy may be pursued. Conversely, if one commissure is opened completely and a significant amount of mitral regurgitation has developed, this will signify at least an adequate result.

The transmitral pressure gradient is the simplest parameter to monitor between balloon inflations. The absolute level of left atrial pressure is extremely important as well. In general, if the left atrial pressure remains constant or decreases after successive balloon inflations, mitral regurgitation has not yet become limiting. When the mean left atrial pressure rises following balloon inflation, even if a large V wave has not occurred, mitral regurgitation may have worsened significantly. If in-lab

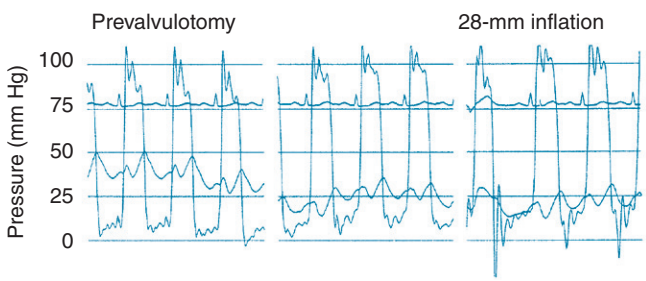

Figure 16-7 Stepwise dilatations result in a progressive decline in left atrial pressure and transmitral pressure gradient. In the prevalvulotomy tracing, the mean left atrial pressure is well over 25 mm Hg and the gradient is extreme. After a 28-mm diameter balloon inflation, the transmitral gradient and left atrial pressure have declined significantly. On the right, after only a 1-mm increment in inflated balloon diameter, there is dramatic improvement in the transmitral gradient. (From Feldman T, Herrmann HC, Inoue K. Technique of percutaneous transvenous mitral commissurotomy using the Inoue balloon catheter. *Cathet Cardiovasc Diagn Suppl* 1994;2:26–34.)

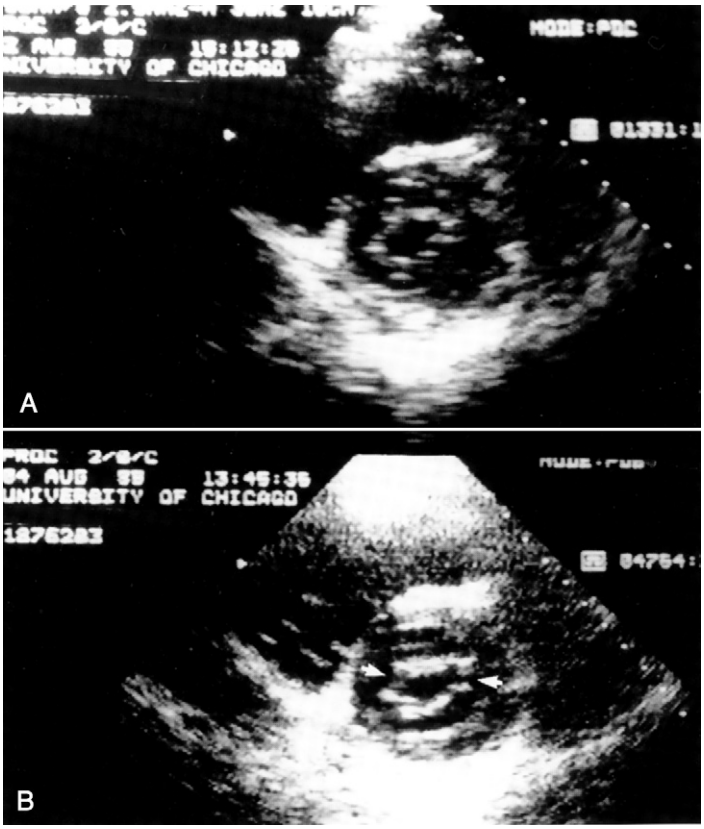

Figure 16-8 Short-axis echocardiogram illustrating commissural splitting following balloon dilatation. **A,** Fishmouth orifice of the mitral valve. **B,** Bilateral commissural splitting, indicated by solid white arrows. (From Feldman T, Carroll JD: Cardiac catheterization, balloon angioplasty, and percutaneous valvuloplasty. In Hall JB, Schmidt GA, Wood LDH, eds. *Principles of critical care.* New York: McGraw-Hill, 1992:343–360.)

echocardiography is not available and left atrial pressure is increasing, a repeat left ventriculogram should be performed. The decision to proceed with further balloon inflations is among the most difficult to make. Use of all available information, including two-dimensional and Doppler echocardiography, left atrial pressure and wave form (Fig. 16-7), auscultation, and ventriculography, is important. Hemodynamics before and after Inoue balloon valvuloplasty are shown in Figure 16-9.

Technical Considerations

If the interatrial septum is crossed in a relatively superior or anterior location, passing the balloon across the mitral valve may be difficult. In this circumstance, clockwise rather than counterclockwise rotation of the stylette will "bank" the balloon off the posterior atrial wall and allow it to cross into the left ventricle after making a loop, as seen in Figure 16-10. This alternative approach is sometimes limited by the short length of the balloon catheter shaft.

In the event the balloon is withdrawn toward the septal puncture during manipulations across the mitral valve, it is sometimes necessary to reinsert the coiled-spring-tipped guidewire into the left atrium to be able to advance the balloon catheter toward the mitral valve. This is particularly true when the septum is markedly thickened and the septal dilatation does not result in free movement of the balloon catheter shaft through the atrial septum.

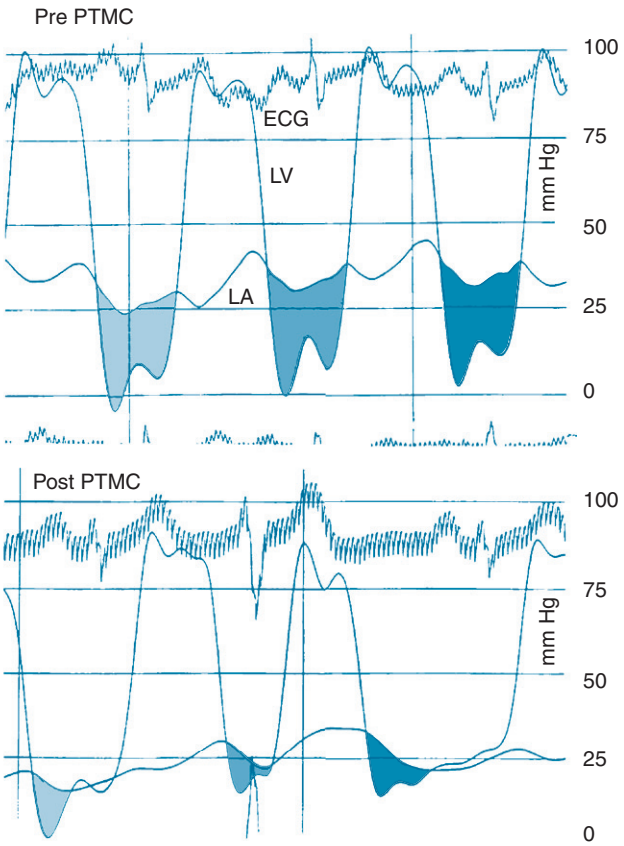

Figure 16-9 Transmitral valve pressure gradients before and after percutaneous transvenous mitral commissurotomy (PTMC).

Occasionally the catheter shaft may be seen to be pinched or bound by the atrial septum. Advancing the shaft of the catheter may cause it to buckle in the right atrium without causing the balloon to move forward in the left atrium toward the mitral valve. Redilatation of the interatrial septum with a 14F dilator or even a 6- to 8-mm diameter peripheral angioplasty balloon may sometimes be necessary.

Postprocedure Evaluation and Balloon Withdrawal

Following dilatation, a left ventriculogram is repeated to evaluate mitral regurgitation. Cardiac output measurement is repeated while the balloon catheter remains across the interatrial septum. It is important to leave the atrial septum occluded because withdrawal of the balloon might allow shunt flow across the atrial septal puncture site with a spurious increase in cardiac output. This has been demonstrated to yield valve area results that are falsely elevated.

The balloon catheter must then be withdrawn across the atrial septum. This is accomplished by reintroducing the balloon-stretching tube, which has been preloaded with the 0.025-inch spring-tipped guidewire. The guidewire is advanced and curled in the left atrium. The balloon-stretching tube is then locked to the gold metal hub of the balloon catheter. These two metal units are then advanced together into the plastic Luer lock to stretch the balloon. Special care must be taken not to stretch and stiffen the balloon through the roof of the left atrium. This is best accomplished by withdrawing the balloon backward onto the stretching metal tube and then withdrawing the plastic Luer lock onto the assembled metal hub apparatus. The balloon

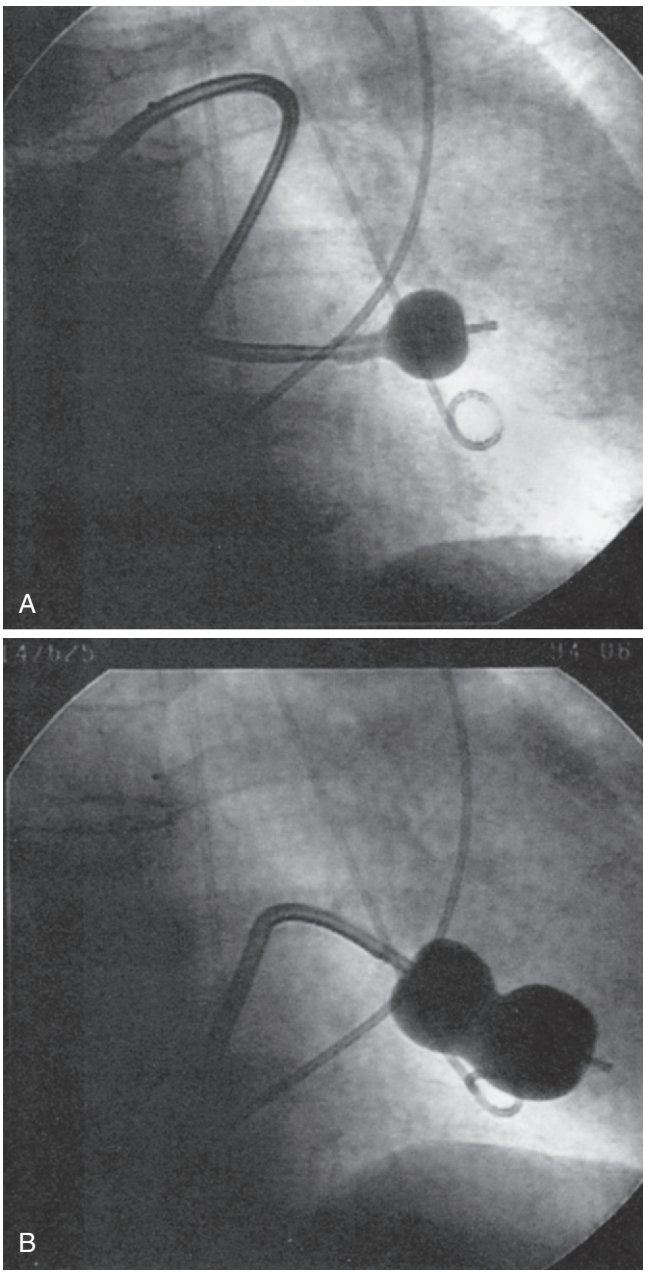

Figure 16-10 When the balloon catheter will not cross the mitral valve using the conventional method, the catheter may be rotated clockwise and manipulated across the mitral valve using an alternative approach. The balloon is introduced into the left atrium in the usual manner and guided past the mitral orifice. **A,** With clockwise rotation of the stylet and catheter shaft, a loop is made directing the balloon off the posterior left atrial wall. **B,** Withdrawal of the stylet and advancement of the catheter shaft direct the balloon catheter across the mitral valve into the left ventricle.

catheter is thus pulled back across the atrial septum as it is stretched and elongated rather than pushing the stretching metal tube forward through the septum. The balloon and wire can then be withdrawn from the left atrium. The wire is best removed while the stretched balloon is partly across the septum to avoid any "slicing" action of the wire on the septal puncture site, which can enlarge the septal defect.

Finally, oximetry may be repeated to evaluate left-to-right shunting across the atrial septal puncture site.

Atrial Shunting

Following double balloon mitral valvotomy, the occurrence of some left-to-right shunting results in a spurious increase in cardiac output and an artificially increased Gorlin mitral valve area calculation. Because the final cardiac output measurements after Inoue balloon PTMC are made while the shaft of the catheter remains across the atrial septal puncture, the magnitude of this spurious increase and calculated mitral valve area is insignificant. Use of a small balloon catheter to occlude the interatrial septum following balloon dilatation is not necessary for accurate post-PTMC valve area measurements with the Inoue catheter.

The best method for measurement of valve area following catheter commissurotomy is probably planimetric echo determination. This is ideally performed 24 hours after the procedure. Doppler estimates are highly variable because of the large swings in left atrial compliance and cardiac output associated with the acute changes of the valve dilatation procedure.

Recognition and Management of Complications

The two most serious complications of PTMC are cardiac tamponade and acute mitral regurgitation. Recognition of pericardial tamponade requires a high degree of suspicion on an ongoing basis. It is important to assess any chest, shoulder, or back pain of which the patient may complain during the procedure. Continuous attention to the pulsatile fluoroscopic cardiac borders is important. Make use of right heart pressures as well. An intraprocedure echo is essential when the patient is hemodynamically unstable. It is not reasonable to perform PTMC without the ability to perform pericardiocentesis as well.

Acute mitral regurgitation is easily recognized by the left atrial pressure magnitude and waveform. It occurs in some cases even with a single balloon inflation or sometimes a 0.5-mm diameter increment in balloon inflation size. Confirmation of the diagnosis with ventriculography is important. Nitroprusside therapy or intravenous nitroglycerin is the mainstay of immediate management of this hemodynamic complication. Between 1% and 2% of patients undergoing PTMC will develop severe acute mitral regurgitation requiring valve replacement as a result of the procedure.

Postprocedure Care and Sheath Removal

The left femoral 5F arterial sheath and the right femoral large venous sheath do not require any special management. Sheaths may be removed when the activated clotting time falls below 180 seconds. Younger patients with excellent hemodynamic results can be sent home on an outpatient basis at the end of the day of the procedure. For patients who require warfarin therapy, it is our usual practice to reinstitute warfarin therapy 1 day post-PTMC without a loading dose. In patients who are at special risk for thrombosis or a history of prior thrombotic episodes, heparin therapy or outpatient subcutaneous low-molecular-weight heparin therapy following sheath removal and a transition to warfarin therapy may be necessary.

The availability of femoral closure devices has facilitated the rapid discharge of patients who are candidates for this procedure on an outpatient basis. In some cases we have used percutaneous suture closure

for the arterial puncture and both venous punctures in these patients. Another option for the 14F venous sheath is temporary subcutaneous suture closure using a figure-of-8 silk suture.

Balloon Aortic Valvuloplasty

Balloon aortic valvuloplasty (BAV) showed great promise as an alternative to surgical aortic valve replacement when the procedure was initially described in the early 1980s. Balloon dilatation of the aortic valve results in an immediate increase in aortic valve area with the expected fall in the transvalvular pressure gradient and a rise in cardiac output. Most patients have immediate clinical improvement and this is accomplished with a percutaneous procedure resulting in substantially less morbidity than valve replacement surgery. Unfortunately it was quickly discovered that the durability of these results is short-lived. Disappointment with the clinical results of this procedure over a 1- to 2-year follow-up resulted in a pendulum-like movement away from the performance of BAV. With the introduction of transaortic valve implantation methods, the use of BAV is now an integral procedural step.

Indications

There are currently six clinical situations in which BAV is useful.

1. Predilation during transcatheter aortic valve implantation procedures. This method will be discussed in Chapter 17.
2. Cardiogenic shock. Patients who present with aortic stenosis and cardiogenic shock may be stabilized for the short term.
3. Congestive heart failure preceding aortic valve replacement. Among patients with severe left ventricular dysfunction or shock in whom aortic valve replacement is planned, balloon dilatation may be performed to allow improvement in left ventricular performance before surgery. Prerenal azotemia associated with their medical therapy may improve after aortic valve prolapse.
4. Preparation for major noncardiac surgery. Patients found to have aortic stenosis during the evaluation for major noncardiac surgery may undergo valvuloplasty. This is especially useful for patients with malignancies.
5. Preparation for hospice transfer. Hospital-bound patients with severe aortic stenosis who are not candidates for valve replacement surgery may undergo balloon dilatation with successful short-term improvement. This is useful for patients who are dependent on intravenous pressors and in an intensive care unit. Although valvuloplasty does not improve their long-term prognosis, it may allow them to be transferred to a regular floor or discharged from the hospital so that they may have a better quality of life, at least in the short term.
6. Diagnostic test in low gradient, low output aortic stenosis. There is a group of patients in whom balloon valvuloplasty may be performed as a diagnostic test. This is useful when the valve area is between 0.8 and 1.0 cm^2 with low cardiac output and a low transvalvular pressure gradient. In this group of patients, the severity of valvular stenosis is especially difficult to ascertain. Poor ventricular function has made therapy in this group difficult. In the past, valve replacement could be performed and, if the patient had improvement in left ventricular function, then survival was good. Unfortunately, for those patients who did not show improvement in left ventricular performance, perioperative mortality was very high. Balloon dilatation may be performed and serial echocardiography used to monitor changes in left ventricular function. If symptoms and left ventricular performance improve with opening of the aortic valve using valvuloplasty, later valve replacement surgery can be undertaken with a high expectation of long-term success.

BAV for Bioprosthetic Aortic Valves

In vitro evaluation of balloon dilatation for stenotic bioprosthetic valves has been disappointing. Prosthetic tissue is often friable and is frequently not severely calcified, but the potential for leaflet perforation or avulsion is significant in this group of patients. Thus, balloon dilation of bioprosthetic aortic valves alone is infrequently performed.

Results of Balloon Dilatation for Aortic Stenosis

The aortic valve area usually increases between 80% and 100% after valvuloplasty. The transvalvular pressure gradient declines by more than 50%. Postdilatation valve area ranges between 0.7 and 1.1 cm^2. An increase in valve area of 0.5 to 0.7 cm^2 or more will be associated with dramatic clinical improvement in most patients. Predilatation valve areas >0.5 cm^2 may ultimately yield postdilatation valve areas of 1 cm^2 or more. It is notable that prosthetic aortic valves have an area between 1.0 and 1.4 cm^2, smaller among women with small aortic annuli.

The greatest limitation of BAV is the almost inevitable occurrence of restenosis following dilatation. The majority of patients have anatomical and symptomatic restenosis between 6 and 18 months after the procedure. Survival is not clearly improved with aortic valvuloplasty. The mechanism of restenosis may be related to the mechanism of relief of aortic stenosis. The majority of these elderly patients have calcific tri-leaflet aortic stenosis with calcification and thickening of the valve cusps and no commissural fusion. The calcium deposits are acellular and nodular. Histologically the nodules are encased densely in fibrous tissue. This explains the striking lack of embolization during this procedure. After balloon dilatation, small fractures or cracks may be seen in the calcified nodules. This allows increased leaflet mobility due to the presence of many "hinge points" or fissures. The restenosis process probably involves regrowth of granulation tissue, fibrosis, and possibly true ossification of these fissures. This active process of restenosis follows a time course that is consistent with new scar formation.

Technique of BAV

In most cases diagnostic coronary arteriography and ventriculography are performed immediately before balloon dilatation. It is unusual to encounter a new patient with aortic stenosis who has not had adequate echocardiographic evaluation before catheterization. An assessment of aortic insufficiency is usually accomplished echocardiographically prior to cardiac catheterization, obviating the need for routine aortography. Single-session diagnostic and therapeutic catheterization procedures may decrease morbidity in this very elderly and ill population.

Arterial Access

It is important to place the femoral puncture comparatively high (cranial) so that the large sheath necessary for valvuloplasty will not be inserted into a branch vessel. Laying a hemostat or thin-walled needle on the femoral crease and using fluoroscopy to locate the mid-femoral head prior to puncture helps with accurate puncture placement. The puncture should be at the level of the mid-femoral head to have the greatest chance of a common femoral artery puncture.

A method to be sure of the level of the puncture is to use a micropuncture needle with a 3-mL syringe of contrast. When the femoral artery is entered, a contrast injection of 1 to 2 mL will verify the level of the puncture relative to the femoral bifurcation. If the entry site is too high or too low, the needle can be removed with no "penalty" and the

puncture repeated. Ultrasound guidance may also be helpful to guide needle insertion above the femoral bifurcation.

After the puncture has been accomplished and before placing a sheath, it is our practice to examine the course of the wire fluoroscopically. If the iliofemoral system is extremely tortuous, we may pass a wire on the contralateral side and choose the straighter course for sheath placement and eventual passage of the balloon. Lower abdominal angiography may be helpful. Sheath angiography is always performed prior to insertion of the large sheath. A 6F or 8F sheath can be inserted in the arterial system after the initial puncture and sheath angiography will verify that it is in the common femoral artery rather than a branch. Placing a 10F to 14F sheath in the superficial or profunda femoris can cause complications.

Heparin

Heparinization is recommended at a dose necessary to achieve an activated clotting time of between 220 and 275 seconds. Early sheath removal is important in this elderly population, so excessive anticoagulation is to be avoided.

Retrograde Technique

After the transvalvular gradient and cardiac output determinations have confirmed the presence of severe aortic stenosis, the arterial sheath is exchanged for a 10F or 12F sheath. This exchange is performed over an extra-stiff 0.035- or 0.038-inch guidewire to minimize the chance of the large arterial dilator perforating the iliac vessels. The sheath is exchanged over a 360-cm extra-stiff wire that is left curled in the left ventricular apex. To maximize the safety of the tip of this wire in the left ventricle, a "ram's horn" curve is put on the end of the guidewire (Fig. 16-11). This is done by grasping the wire between the thumb and the edge of a curved hemostat and pulling along the wire rapidly in the same manner one uses to put a curl on gift wrapping ribbon. After the sheath has been exchanged and flushed, it is connected to arterial pressure, and a valvuloplasty balloon catheter is passed over the wire and across the aortic valve. The balloon diameter is selected to approximate a balloon to aortic annulus ratio of between 0.9 and 1.2. The annulus is most easily measured echocardiographically. The optimal

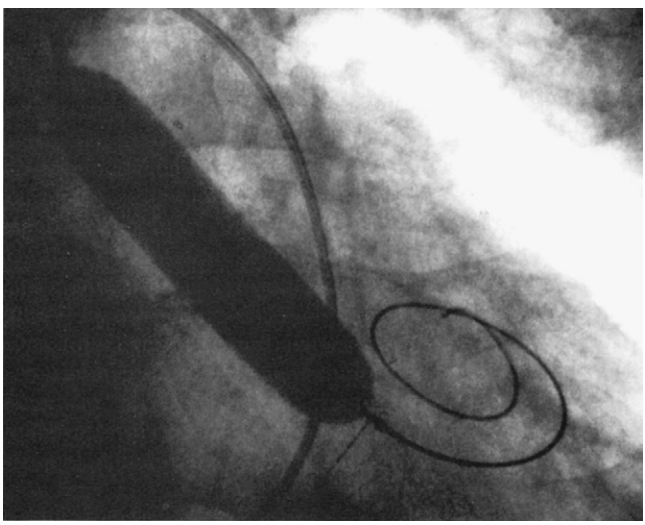

Figure 16-11 A 5.5-cm long, 20-mm diameter Mansfield aortic valvuloplasty catheter. The extra-support exchange guidewire has been looped into a ram's horn configuration by pulling it over the end of a hemostat as one would curl ribbon when wrapping a package.

balloon-to-annulus ratio has not been established. Most females can be treated with a 20-mm balloon and most males with a 22-mm balloon, but a smaller annulus size should be an indication for a smaller balloon. The necessary arterial sheath size varies among the currently available balloon manufacturers and balloon sizes.

Balloon Inflation

The technique of balloon inflation in the aortic valve is especially important. To stabilize the balloon position, temporary right ventricular pacing at a rate of 180 to 220 bpm is used to achieve a systemic pressure <50–60 mm Hg. This diminishes forward flow and allows for a stable balloon position during balloon inflation. The balloon is positioned midway across the valve. When ventricular function is poor, maintaining valve position may be very simple. A dynamic or vigorous left ventricle will typically eject the balloon during attempts to inflate it if rapid pacing is not used. Substantial forward pressure may be necessary to maintain the position of the balloon in the valve in that case.

Initially the balloon is inflated via a high-pressure stopcock using a 60-mL syringe partially filled with dilute saline and contrast mixture. The dilute mix (7 to 9 parts of saline to 1 part of contrast) minimizes the viscosity of the solution while at the same time maintaining fluoroscopic visibility. In addition, high-osmolarity conventional contrast is less viscous than low osmolarity. A 10-mL syringe filled with contrast mixture is placed on the sidearm of the high-pressure stopcock used for inflating the balloon. After the 60-mL syringe has been used to inflate the balloon as much as possible, the operator flips the stopcock so that the smaller syringe can be used to inject additional saline/contrast mixture under very high pressure. This "boost" in inflation is very important to achieve maximal balloon expansion. The balloon can be appreciated to completely expand or to "plump" out along its sides when this is done. Adequate valve dilatation is usually not achieved unless this can be accomplished. Hypotension and ventricular tachycardia are typical during balloon inflations (Fig. 16-12).

As soon as balloon deflation commences, pacing can be stopped and the balloon can be pulled back in the aortic root while maintaining the guidewire in the left ventricle. It is obviously important to minimize the time of rapid pacing. It requires some practice with a team to start pacing, inflate the balloon, deflate the balloon, and stop pacing smoothly. This allows pressure to recover as rapidly as possible. Once the balloon inflation has been performed without boosting to determine how well the patient will tolerate the inflations, a second inflation is performed to maximal balloon inflation (Fig. 16-13). If the balloon has not ruptured, a third inflation can be performed to ensure optimal dilatation. It is thus important to prepare the balloon very carefully to be

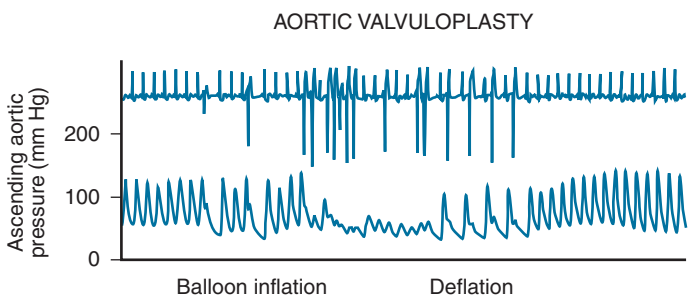

Figure 16-12 Hemodynamic tracing during balloon inflation in a patient undergoing aortic valvuloplasty. Ventricular tachycardia and hypotension are usual during balloon inflations. (From Feldman T, Carroll JD. Cardiac catheterization, balloon angioplasty, and percutaneous valvuloplasty. In Hall JB, Schmidt GA, Wood LDH, eds. *Principles of critical care.* New York: McGraw-Hill, 1992:343–360.)

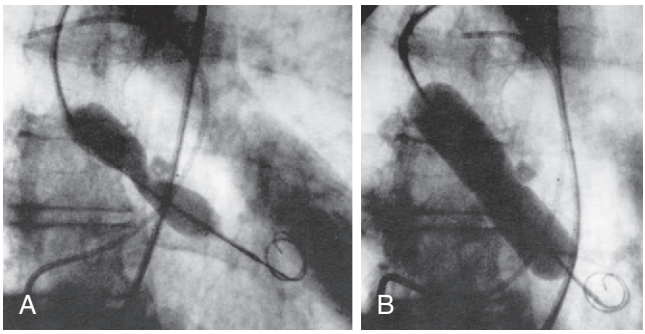

Figure 16-13 Aortic valvuloplasty. **A,** The valvuloplasty balloon can be seen to be indented by the calcified aortic valve leaflets. **B,** The indentation has expanded as the calcific nodules in the rigid valve leaflets have been fractured. (From Feldman T, Carroll JD. Cardiac catheterization, balloon angioplasty, and percutaneous valvuloplasty. In Hall JB, Schmidt GA, Wood LDH, eds. *Principles of critical care.* New York: McGraw-Hill, 1992:343–360.)

sure that no small air bubbles remain during test inflations outside the body. After maximal inflation, the balloon is withdrawn over the guidewire and removed from the sheath. Current generation balloons rupture infrequently, but when they do, the balloon and sheath are removed together as a unit. The ruptured balloon material is often hard to get all the way back into the sheath. Pulling too forcefully will tear off the end of the balloon shaft. Frequently, as the balloon is pulled into the sheath, it will cause the sheath to concertina; thus firm pressure to withdraw the balloon partway into the sheath is important, and then the combined catheter and sheath are removed as a unit. A new sheath can be introduced over the wire and a diagnostic pigtail catheter inserted in the left ventricle to evaluate the final valvuloplasty result.

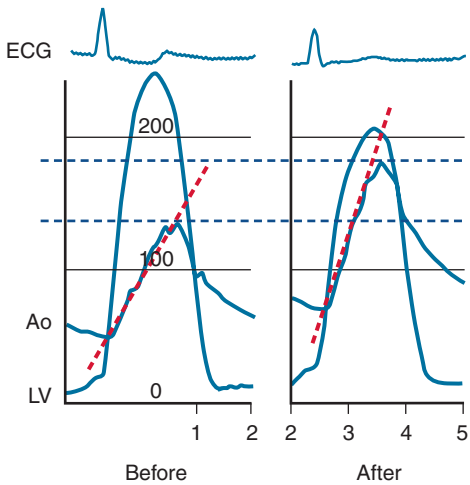

Figure 16-14 Pre- and post-aortic-valvuloplasty pressure tracings. Not only has there been a marked decline in the transaortic pressure gradient but aortic pressure has risen and left ventricular systolic pressure has fallen. The upstroke of the aortic pressure wave has become steeper. The left ventricular end-diastolic pressure has fallen. This 64-year-old man had an increase in valve area from 0.5 cm^2 to 1.0 cm^2.

$$\left[\frac{\text{Mean gradient}}{\left(\frac{\text{CO (L/min)}}{\text{SEP (sec/min)}}\right)\times 60}\right]\times 80$$

Figure 16-15 Calculation of valve resistance (dynes/sec/cm^{-5}) may be very helpful in evaluating patients before and after aortic valvuloplasty. *CO,* cardiac output; *SEP,* systolic ejection period. (From Kern MJ, Deligonul U, Donohue T, *et al.* Hemodynamic data. In *The cardiac catheterization handbook.* St Louis, MO: Mosby, 1994:124.)

Procedural End Point

If the transvalvular gradient has fallen by more than 50% and if cardiac output is at least unchanged or has risen, successful valve dilation has been accomplished (Fig. 16-14). In some cases evaluation of valve resistance is helpful (Fig. 16-15). Resistance over 250 dynes/sec/cm^{-5} is consistent with persistent stenosis while values below 200 dynes/sec/cm^{-5} signify relief of obstruction.

Sheath Removal and Postprocedure Management

Heparin has been given during the procedure, and in our usual practice none is given afterward. Antibiotic prophylaxis is not used for these procedures. The sheaths are removed as soon as the activated clotting time falls below 180 seconds if manual compression is to be used. It has become our practice in the past few years to "preclose" the puncture using percutaneous suture closure (Perclose, Abbott Vascular, Menlo Park CA). For this technique a 6F or 8F sheath is placed on the femoral artery and, if angiography demonstrates appropriate location in the common femoral artery, a wire is replaced in the sheath. A 10F Perclose device is passed over the wire. The Perclose sutures are delivered into the puncture and the needle is pulled back through the skin. The needle is clipped off the suture, and the four ends of the two sutures are left dangling outside the puncture. Alternatively the 6F ProGlide (Abbott Vascular, Menlo Park CA) device has been used, and in some instances, two 6F devices are placed. The Perclose delivery system is partially withdrawn and a guidewire is reinserted through the device. This leads the wire through the purse string in the femoral artery. The Perclose delivery system is removed and disposed of and the large French sheath is passed over the wire. At this point the sheath is in between the sutures. At the conclusion of the procedure, the sheath can be removed and the Perclose sutures tied in the usual fashion. This approach is successful in more than 90% of cases.

If manual compression is to be used, it is important to use a FemoStop (St. Jude Medical, St. Paul, MN) for at least 30 to 60 minutes after manual compression has been completed since this large puncture has a strong tendency to rebleed. Clamp devices are harder to place and require careful monitoring, whereas the FemoStop can be adjusted more easily. Ambulation must be very gradual.

Patients who are not in critical condition before the procedure are able to leave the hospital on the morning following aortic valvuloplasty. It is important to obtain a postprocedure echocardiogram prior to hospital discharge so that serial comparisons can be made.

Antegrade Technique for Aortic Valvuloplasty

It is possible to perform aortic valvuloplasty via a transseptal puncture with passage of the balloon through the left ventricle and antegrade across the aortic valve. Advantages of this approach include obviating

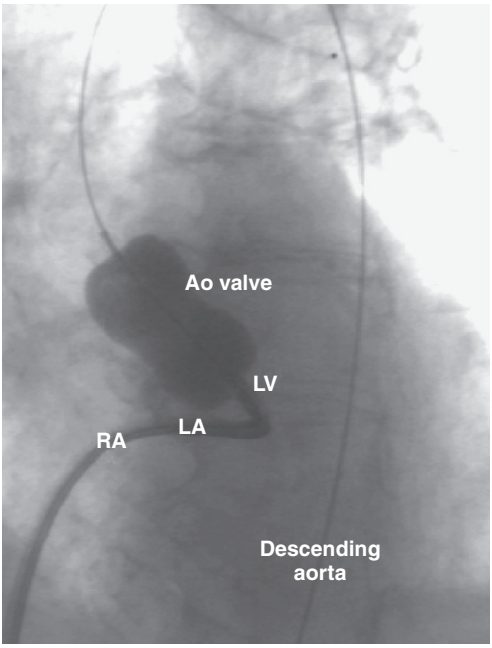

Figure 16-16 Antegrade aortic valvuloplasty using the Inoue balloon. Beginning at the lower left corner of the figure, a guidewire traverses the right atrium (RA) and then the left atrium (LA) via transseptal puncture and is then curled in the left ventricle (LV) and passed across the aortic (Ao) valve through the arch into the descending aorta. Passage of the wire requires a flexible, single-lumen balloon catheter to be floated through a transseptal sheath with a loop in the left ventricular apex. Then an extra-stiff guidewire is passed through the balloon catheter and is snared in the descending aorta and exteriorized through a femoral arterial sheath. This rigid, stable wire rail is necessary to provide support for antegrade passage of the balloon catheter through the left ventricle and across the aortic valve. This figure shows an Inoue balloon catheter fully inflated in the aortic valve.

the need for a large-caliber arterial sheath and the potential to use larger balloons that can be easily inserted on the arterial side. A 14F sheath is placed in the right femoral vein. An image of antegrade aortic valvuloplasty is shown in Figure 16-16.

After transseptal puncture, the Mullins sheath is directed into the left ventricle with the use of a 7F single-lumen balloon flotation catheter. This catheter can be looped in the left ventricle and floated across the aortic valve. It is our usual practice to advance a guidewire across the aortic valve via the balloon catheter positioned just below the valve and to deflate the balloon just prior to passing it through the aortic valve, since the valve calcifications may cause balloon rupture. Once the balloon is in the aortic root, a 0.032 inch × 260 cm extra-stiff guidewire can be passed through the balloon catheter into the descending aorta. Via a 6F arterial sheath, using a 10-mm gooseneck snare, the wire is snared and the snare left in place in the aorta to stabilize the wire loop through the circulation. The wire thus enters the right femoral vein and passes into the right and then left atria, across the mitral valve, through the aortic valve into the aortic root, and ultimately the snare exits out of the femoral artery sheath.

It is important to maintain a loop of wire in the left ventricle throughout this procedure to keep from putting too much tension on the mitral valve and causing mitral regurgitation. At this point an extremely stable rail has been created throughout the circulation. It is possible to pass either a conventional balloon or an Inoue balloon antegrade across the septal puncture and into the aortic valve using this approach. This is useful when the aortic valve cannot be crossed retrograde as well. Some

patients do not tolerate the wire, possibly because the mitral and/or aortic valves can be "propped" open.

If an Inoue balloon is to be used, the 26-mm maximum-sized balloon is passed into the left atrium using the same technique as in the mitral dilatation procedure. The wire is left in place throughout the procedure. The balloon is tracked into the aortic valve with the stretching metal tube withdrawn partway into the balloon shaft.

An advantage of the Inoue balloon catheter is that the inflate and deflate cycle is rapid, so that the hemodynamic tolerability of the procedure is enhanced. Conventional balloons can be passed antegrade without too much difficulty, but after they have become "winged" it may be difficult to withdraw them back across the atrial septal puncture. At the conclusion of the procedure, a 5F or 6F pigtail can be passed over the wire from the femoral vein and into the aorta to provide a sleeve for reduced friction when removing the wire.

There is some theoretical benefit to the Inoue balloon in that the waist of the Inoue balloon may fit in the aortic valve annulus while the larger distal bulbous portion may stretch the aortic leaflets more fully into the sinuses of Valsalva. This may result in larger valve areas after aortic valvuloplasty using the Inoue technique in this manner. Comparisons of antegrade and retrograde approaches show the major advantage of the antegrade technique to be diminished vascular complications.

Complications

The major complications of aortic balloon valvuloplasty are ventricular perforation from the balloon or guidewires used in the left ventricle, and femoral artery complications related to the large sheath size that is necessary for the retrograde technique.

Cardiac tamponade from catheter perforation has been reported in about 1% of cases. Vascular surgery for femoral arterial complications is required in as many as 5% of patients. This has been dramatically reduced in our recent experience using suture closure in association with retrograde aortic valvuloplasty or with the antegrade approach. We have also been able to "preclose" 14F venous punctures with suture closure with good success. Superficial suture closure with the figure-of-8 temporary suture technique has greatly simplified venous puncture management. Significant hematomas occur in up to 10% of the patients treated with manual compression, and transfusion rates in some series are as high as 20%. The need for transfusion has been almost completely eliminated in our practice using suture preclosure. Since the balloon catheter abrades the ventricular septum during balloon inflations, bundle branch block may occur and requires pacing in some cases. Rarely, permanent pacemaker implantation is necessary. It is critical to place a temporary pacemaker prior to balloon dilatation in patients who have bundle branch block or high grades of heart block preprocedurally.

Severe aortic regurgitation is infrequent. Leaflet avulsion may occur, usually with oversized balloons. Aortic valvuloplasty in the setting of regurgitation as the predominant valve lesion will not result in clinical improvement for the patient.

Rarely, a progressive low-output state has been encountered after valvuloplasty, sometimes ending in death. Each balloon inflation causes a transient but substantial stress on the left ventricle. Outflow obstruction is acutely worsened and chamber dilatation occurs. Ventricular pressure generation decreases and coronary perfusion pressure drops. Several technical factors can cause this disastrous syndrome. First, inadequate valve dilatation results from an inability to position the balloon properly. Second, repeated inflations may be excessively prolonged. Third, ventricular tachycardia may contribute to left ventricular depression. Lastly, a "rest" between inflations of several minutes is often needed. During this rest period, one should observe a rebound in the aortic

pressure, resolution of any ischemic electrocardiography changes, and resolution of any symptoms that have occurred during inflations.

In patients with a low initial cardiac output (<2.5 L/min), it is useful to initiate a dobutamine infusion prior to balloon dilatation. Some support for the blood pressure and cardiac output makes the procedure much more reasonable for both the patient and the operator to tolerate.

Compared with degenerated trileaflet valves, bicuspid valves may be more resistant to dilatation in adult patients.

Summary

Mitral stenosis can be treated successfully with catheter commissurotomy with good long-term results and an acceptably low complication rate.

Aortic balloon valvuloplasty is routinely performed during transcatheter aortic valve implantation but, as a stand-alone procedure, is reserved for selected patients at high risk of death from aortic valve surgery or those that require a bridge to surgery or percutaneous valve replacement, or temporary relief of aortic stenosis to facilitate other medical treatment or noncardiac surgery.

Suggested Readings

American College of Cardiology/American Heart Association. ACC/AHA guidelines for the management of patients with valvular heart disease. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee on Management of Patients with Valvular Heart Disease). *J Am Coll Cardiol* 1998;32:1486–1588.

Bahl VK, Chandra S, Goswami KC, *et al*. Balloon aortic valvuloplasty in young adults by antegrade, transseptal approach using Inoue balloon. *Cathet Cardiovasc Diagn* 1998;44:297–301.

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17

Transcatheter Valve Therapies

WILLIAM M. SUH · CHRISTINE CABILING · IGOR F. PALACIOS

Recent advances in percutaneous-based catheter technologies have allowed for development of novel therapies for valvular heart disease, including transcatheter valve implantation and transcatheter mitral valve repair (Table 17-1). Although these devices are still investigational in the United States, many have incorporated transcatheter valve procedures into their daily practice. This chapter briefly reviews two transcatheter valve procedures: transcatheter aortic valve replacement and percutaneous edge-to-edge mitral valve repair.

Transcatheter Aortic Valve Replacement (TAVR)

Age-related calcific aortic valve degeneration is the most common cause of aortic stenosis (AS) in adults and its prevalence steadily increases with age. Survival in patients with AS dramatically decreases with onset of symptoms (angina, syncope, congestive heart failure) with an average of 1 to 3 years and the poorest survival seen in patients with failing left ventricles. Aortic valve replacement is a proven treatment to prolong survival in patients with severe AS.

Indications

Aortic valve replacement (AVR) is indicated in all symptomatic patients with severe AS (2006 ACC/AHA Valvular Heart Disease Guidelines, Class I recommendation, Level of Evidence: B). Despite this recommendation, a significant number of elderly patients (up to one third) do not undergo AVR because of comorbidities, including advanced age and the associated increased morbidity and mortality with surgery.

Table 17-1

Transcatheter Valve Therapies

Transcatheter Valve Implantation
• Aortic position—Edwards SAPIEN, Medtronic CoreValve
• Pulmonic position—Edwards SAPIEN, Medtronic Melody
• Mitral position—Endovalve
Percutaneous Mitral Valve Repair
• Edge-to-edge—Abbott MitraClip, Edwards MOBIUS
• Coronary sinus annuloplasty—Cardiac Dimensions Carillon, Edwards MONARC
• Direct annuloplasty—Mitralign, QuantumCor, MiCardia
• Chamber and annular remodeling—Ample PS3, Myocor iCoapsys

Table 17-2

Indications for TAVR
• The patient has senile degenerative aortic valve stenosis with echocardiographically derived criteria: mean gradient >40 mm Hg, jet velocity >4.0 m/sec, or an initial aortic valve area of <0.8 cm^2
• Aortic annular diameter 18–24 mm
• NYHA functional class II or greater symptoms
• Patients must have comorbidities such that he or she has a minimum STS score of >10

STS, Society of Thoracic Surgeons; *TAVR*, transcatheter aortic valve replacement.

Additionally, many elderly patients that are suitable surgical candidates will refuse surgery because they perceive themselves as "too old" to survive open AVR. Transcatheter aortic valve replacement (TAVR) is a promising alternative to surgical AVR in those patients deemed high risk for surgery (Table 17-2).

Transcatheter Valves

There are two catheter-implantable valves commercially available overseas. They are the balloon-expandable Edwards SAPIEN valve and the self-expanding Medtronic CoreValve (Fig. 17-1). The Edwards SAPIEN valve was studied in the PARTNER trial, which completed randomized enrollment in fall 2009. The Medtronic CoreValve randomized trial started enrollment in December 2010. The initial international experience and the results of PARTNER cohort A and B suggest that outcomes compare favorably with conventional valve surgery in selected patients. In November 2011, the Edwards SAPIEN valve was FDA approved and became commercially available in the United States for PARTNER cohort B (inoperable) patients.

Patient Selection

A thorough clinical evaluation of the patient is performed with special attention to vascular access and potential sources of complications. The evaluation includes history and physical examination, laboratories, chest radiograph, electrocardiogram, transthoracic echocardiography,

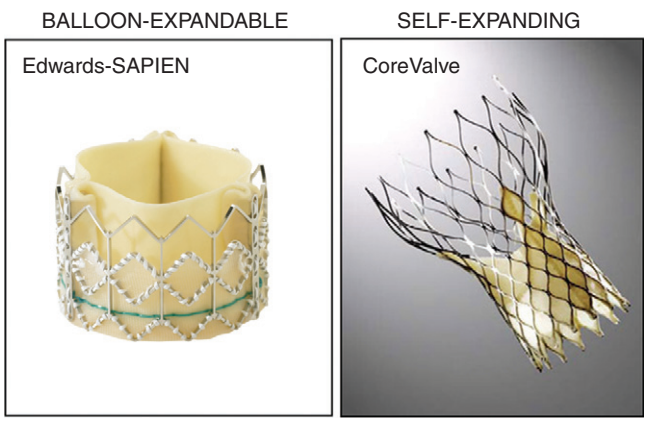

Figure 17-1 **Left,** Photograph of the Edwards SAPIEN transcatheter heart valve, which consists of a stainless steel stent with bovine pericardial tissue leaflets sewn onto the balloon-expandable stent. **Right,** Photograph of the Medtronic CoreValve transcatheter aortic valve system, which consists of a nitinol-based frame with porcine pericardial tissue leaflets affixed to the self-expanding stent.

pulmonary function testing, carotid ultrasound, right and left cardiac catheterization, coronary angiography, and computed tomography angiography (CTA) of the chest, abdomen, and pelvis. The CTA is performed to assess aortoiliac patency, dimensions, and tortuosity. Occlusive peripheral arterial disease, small vessels (<7 mm), and excessive tortuosity are characteristics that would preclude a transfemoral approach since the delivery systems for the SAPIEN valve are currently 22F and 24F sheaths for the 23-mm and the 26-mm valves, respectively. The second-generation Edwards valve, SAPIEN XT, is comprised of a cobalt chromium frame and allows for an 18F delivery system. Patients with unfavorable aortoiliac characteristics can have TAVR via a transapical approach with the Edwards valve. The advantage of the CoreValve system is the smaller 18F profile of its delivery system, but CoreValve can be delivered only in a retrograde fashion. If femoral access is not available, CoreValve may be delivered from subclavian and carotid approaches.

Risk of mortality is calculated using a validated scoring method such as the EuroScore or Society of Thoracic Surgeons (STS) score. Online calculators are available for both scores. These scores take patient characteristics (e.g., age, acuity, pulmonary function, renal function, neurologic function, type of surgery) to calculate risk of mortality and morbidity. An STS score of >10% mortality was an inclusion criterion in the PARTNER trial.

Transfemoral TAVR Procedure With Edwards SAPIEN valve

The procedure is typically performed in a cardiac catheterization laboratory or hybrid operating room suite. The implant procedure involves the cooperation of a multidisciplinary team, including cardiac surgery, interventional cardiology, echocardiography, and anesthesia. A surgical team and cardiopulmonary bypass machine are on stand-by in case bailout surgery is required.

Preprocedure planning includes identification of the implant side from the CTA scan and measurement of the aortic annulus to choose valve size, which will determine the size of the delivery system. Transesophageal echocardiogram (TEE) is used to size the annulus and to assist in valve positioning. Placement of the probe can be done once the patient is adequately sedated. A 23-mm valve is used for annular dimensions of 18 to 21 mm and a 26-mm valve is used for annular dimensions of 22 to 24 mm.

Femoral arterial and venous accesses are obtained on the non-implant side, and 6F sheaths are placed. These will be used for the temporary pacemaker (rapid pacing) and pigtail catheter (aortography), but they also provide rapid access in case the patient needs to be placed on emergency cardiopulmonary bypass. Pulmonary artery catheterization is done via jugular vein access. Due to the large delivery systems, surgical femoral artery cutdown and repair are best performed on the implant side. After cutdown, an 8F sheath is placed in the artery and a 6F sheath in the vein. Successful arterial closure with a Prostar XL closure device or two Perclose closure devices has been performed, making the procedure truly percutaneous. Weight-based heparin is administered intravenously once access has been obtained. Target activated clotting time (ACT) is 250 to 300 seconds.

A temporary pacemaker wire (used for rapid ventricular pacing during balloon inflations) is positioned in the right ventricle through the venous sheath on the non-implant side. A pigtail catheter is advanced to the ascending aorta and supravalvular aortography is performed in the left anterior oblique cranial and right anterior oblique caudal projections. The projection that best lays out all three aortic valve leaflets in a single plane is chosen for valve positioning.

The implant-side arterial access must be serially dilated with hydrophilic-coated dilators over a stiff 0.038-inch guidewire. From 8F, the artery is serially dilated with 10F to 24F dilators. The delivery sheaths for the 23-mm and 26-mm valves are 22F and 24F, respectively. The delivery sheath is advanced over the wire and positioned in the abdominal aorta.

The stenotic aortic valve is crossed using standard technique. After crossing the valve with the straight wire, the catheter is advanced into the left ventricle (LV) and the straight wire is exchanged for an Amplatz super stiff (1-cm tip) guidewire with a pigtail curve. A double-lumen pigtail catheter is advanced over this wire and positioned in the LV. Baseline LV-aortic gradient is measured. The stiff wire is then advanced into the left ventricle, and the pigtail catheter is exchanged for the valvuloplasty balloon. The balloon (typically 20 × 40 mm) is positioned across the aortic valve, rapid ventricular pacing at 180 bpm is initiated, and the balloon is inflated once the systolic blood pressure has fallen below 50 mm Hg (5-sec inflation). The balloon catheter is removed with the stiff wire remaining in the LV.

Next, the RetroFlex 3 delivery prosthetic valve system with the crimped SAPIEN valve is advanced through the delivery sheath over the stiff wire. The delivery system has a flexing mechanism that assists in steering through the aortic arch and minimizes trauma on the outer curvature of the arch (Fig. 17-2). When crossing the native aortic valve, the delivery system is fully retroflexed, which gives a central and coaxial orientation of the prosthesis to the native valve. The delivery catheter also has a nose cone, which facilitates crossing of the native valve (Fig. 17-3). After the valve has been crossed, the retroflex catheter is retracted to fully expose the delivery balloon. The valve is positioned using fluoroscopy, aortography, and TEE (Fig. 17-4). Approximately 60% of the valve assembly should be on the ventricular side of the aligned sinuses. Once positioning is confirmed, rapid pacing is performed and the delivery balloon is inflated when the blood pressure falls below 50 mm Hg (Fig. 17-5). The balloon is inflated for 5 seconds, then deflated. After stent valve deployment, aortography is repeated to assess for

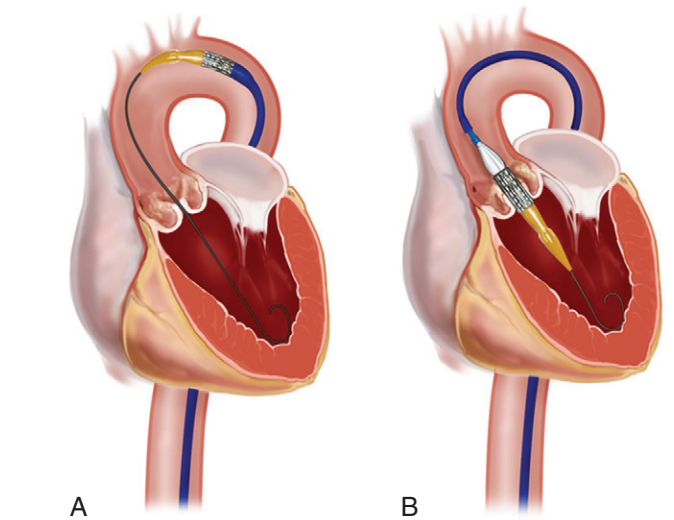

Figure 17-2 Diagrams of the Edwards RetroFlex 3 delivery system. **A,** As the delivery system approaches the transverse aortic arch, the operator retroflexes the delivery system by turning a knob on the delivery system handle. This maneuver assists in the transit across the aortic arch. **B,** The stent is positioned across the aortic valve. The retroflex position of the delivery system allows for a central and coaxial orientation of the prosthetic valve to the native aortic valve.

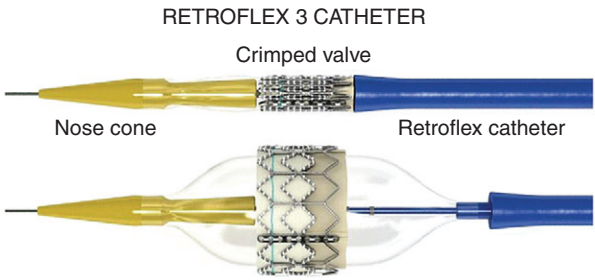

Figure 17-3 Diagram of the Edwards RetroFlex 3 delivery system. The tapered yellow nose cone facilitates crossing of the native aortic valve. The blue retroflex catheter acts as a pusher while the valve is advanced. It is important that the catheter is retracted to fully expose the delivery balloon before deployment.

paravalvular leak, and if significant, repeat balloon inflations may be necessary. The double-lumen pigtail catheter is again placed and final LV-aortic gradients are measured.

Potential complications of TAVR are listed in Table 17-3.

Vascular Hemostasis

At the end of the procedure, protamine is given to reverse anticoagulation. The delivery sheath is removed, and the femoral arteriotomy is either surgically repaired or the artery is closed with the Prostar or Perclose sutures if preclosure was done. To assist in hemostasis, an 8- to 10-mm peripheral balloon can be inflated proximally to reduce blood loss.

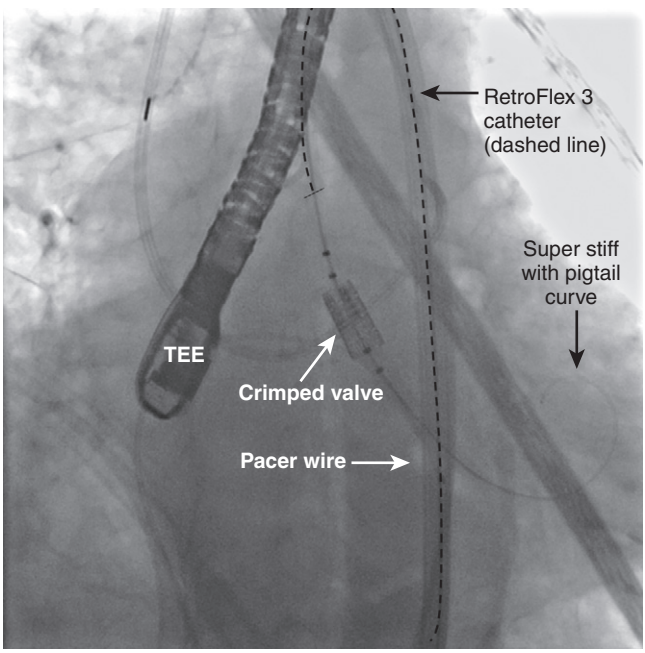

Figure 17-4 Fluoroscopic view before valve deployment. Transesophageal echocardiogram (TEE) is used adjunctively for proper positioning. A pacer wire is present in the right ventricle for rapid pacing. A super stiff guidewire with a pigtail curve resides in the left ventricle. The RetroFlex catheter is retracted back to fully expose the delivery balloon. A pigtail catheter (behind the TEE probe) is also present, which was used to perform supravalvular aortography.

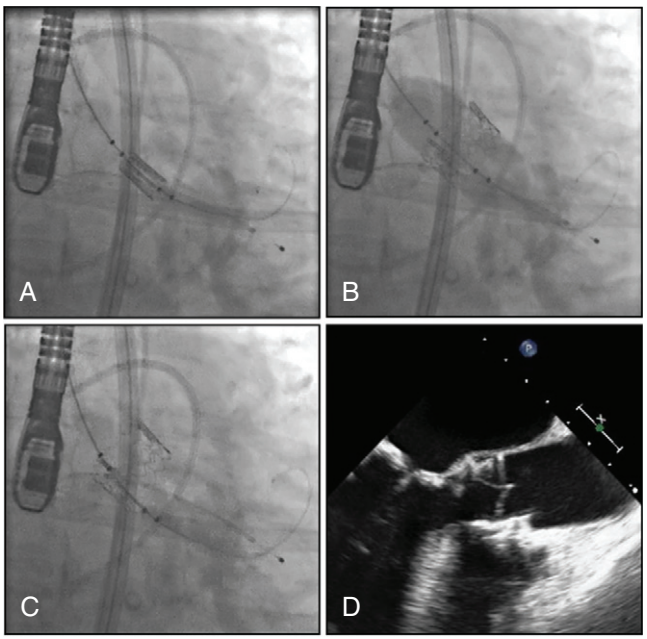

Figure 17-5 SAPIEN valve implantation. **A,** The SAPIEN valve is positioned across the native aortic valve. **B,** With rapid ventricular pacing, the delivery balloon is inflated to deploy the valve. **C,** The delivery balloon is deflated, revealing a fully expanded stent valve. **D,** Transesophageal echocardiogram after deployment shows two of the pericardial leaflets coapting during diastole.

Clinical Results

The PARTNER trial is the only completed randomized trial evaluating TAVR with the SAPIEN valve versus medical therapy or surgery. In cohort B, 358 inoperable patients were randomized 1:1 to transfemoral TAVR versus standard therapy (including balloon aortic valvuloplasty in 84%). At 12 months, there was an absolute mortality reduction of 20% in the TAVR arm (number needed to treat to prevent 1 death at 1 year = 5). With regard to the safety end points, there were significant increases in stroke, vascular complications, and major bleeding with TAVR, which were largely attributed to the bulky delivery systems of the first-generation device. In cohort A, 700 patients were randomized 1:1 to TAVR (transfemoral or transapical) versus surgical AVR. The results of cohort A presented in April 2011 showed noninferiority for mortality between the two techniques. There was a higher rate of stroke observed with TAVR and increased bleeding with AVR. Based on the results of PARTNER cohort B, the FDA approved the SAPIEN valve only for those patients deemed inoperable. Approval for high risk patients (cohort A) is still pending.

Table 17-3

Complications From TAVR
• Arterial dissection/perforation
• Myocardial ischemia
• Coronary obstruction by the valved stent
• Cardiogenic shock
• Stroke
• Bradyarrhythmias
• Paravalvular leak

TAVR, transcatheter aortic valve replacement

Percutaneous Mitral Valve Repair

The mitral valve is composed of two leaflets (anterior and posterior), the mitral annulus, the chordae, and the papillary muscles (Fig. 17-6). Dysfunction of any of these structures can cause incompetence of the valve and result in regurgitation. Mitral regurgitation (MR) is the most common form of valvular heart disease, and about half of the cases are due to myxomatous degeneration of the valve, which leads to stretching of the valve leaflets and chordae tendineae. Elongation of these structures causes prolapse of the leaflets into the left atrium and failure of the leaflets to coapt properly. If left untreated, severe MR leads to LV failure due to chronic volume overload.

Surgical mortality is significantly better when the mitral valve is repaired rather than replaced. With mitral valve replacement, the mitral valve apparatus is disrupted, which causes adverse effects on LV geometry, volume, and function. Therefore, whenever possible, all efforts should be made to repair the valve and preserve the subvalvular apparatus. In the Euro Heart Survey, almost half of the patients with severe MR were denied surgery. Impaired LV function, older age, and comorbidity were associated with surgery denial.

Percutaneous transcatheter mitral valve therapies have evolved less rapidly when compared to the aortic and pulmonary valves. Endovascular access is more difficult with transcatheter mitral valve therapies since a transseptal puncture is required to have access to the mitral valve. More importantly, the inherent complexity of the mitral valve apparatus poses a challenge to catheter-based techniques. Any derangement of one or more of its components may result in significant valvular dysfunction. A clear understanding of these anatomical and functional properties becomes essential when distinguishing the pathophysiologic mechanisms that differentiate primary from secondary valvular disease as well as in the development of surgical and new alternative percutaneous transcatheter therapies.

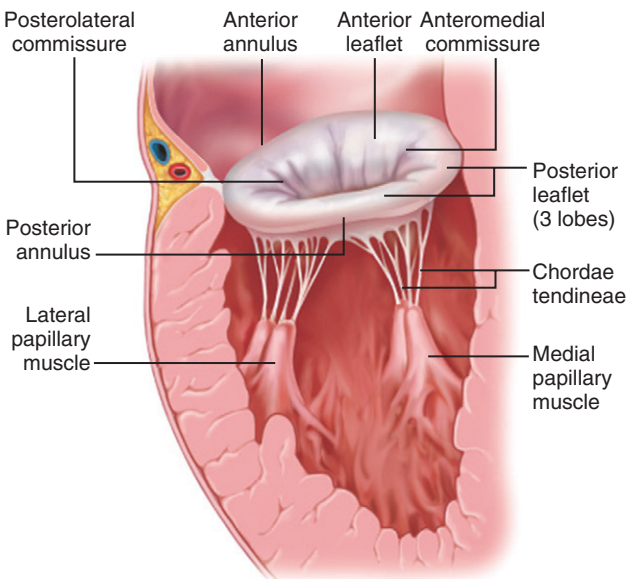

Figure 17-6 Mitral valve apparatus is a composite anatomical structure that requires integral preservation for its proper function and is dependent on the intricate interplay between the annulus, the commissures, the mitral leaflets, the chordae tendineae, and the subvalvular apparatus, including the papillary muscles and the left ventricular wall.

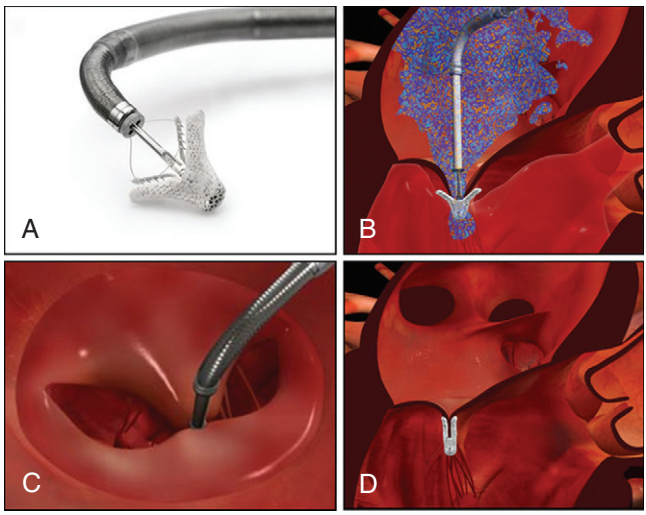

Figure 17-7 MitraClip mitral valve repair system. **A,** The device is covered with polyester fabric to facilitate tissue in-growth. The distal gripping elements help with leaflet fixation. **B,** The clip is delivered via a transseptal guiding catheter. The MitraClip is steered until axially aligned and centered over the origin of the regurgitant jet. **C,** The clip mechanically coapts the anterior and posterior leaflets in a similar fashion to the Alfieri stitch technique, creating a double orifice valve. **D,** The clip is deployed and mitral regurgitation is reduced.

There are numerous transcatheter mitral valve repair strategies that have been developed over the recent years. These include leaflet repair, direct and indirect annuloplasty, and ventricular and annular remodeling devices (see Table 17-1).

The MitraClip (Fig. 17-7) currently represents the most widely used percutaneous repair technique. In 1991, Dr. Alfieri performed a mitral valve repair without annuloplasty using a stitch "edge-to-edge" technique to create a double-orifice valve. The durability of this procedure (>1500 patients) led to the development of a percutaneous technique using a clip to approximate the valve leaflets instead of a suture. The MitraClip system has been evaluated in the EVEREST I and EVEREST II studies.

Indications

Patients with a class I indication for mitral valve surgery according to the AHA/ACC 2006 guidelines for valvular heart disease were eligible for the EVEREST studies (Table 17-4). Mitral valve surgery is indicated in all symptomatic patients with severe MR in the absence of severe

Table 17-4

Inclusion Criteria for MitraClip
• Candidates for mitral valve repair or replacement surgery • Moderate to severe (3+) or severe (4+) chronic mitral valve regurgitation • NYHA functional class II or greater symptoms with EF >25% and LV end-systolic dimension <55 mm • If asymptomatic, evidence of left ventricular dysfunction (EF < 60% but >25% and/or LV end-systolic dimension >40–50 mm) • Appropriate valve anatomy • Exclusion criteria included recent MI, any interventional or surgical procedure within 30 days, mitral valve orifice area <4 cm^2, renal failure, and endocarditis

EF, ejection fraction; *LV,* left ventricular; *MI,* myocardial infarction; *NYHA,* New York Heart Association.

LV dysfunction and/or LV end-systolic dimension >55 mm (Class I recommendation, Level of Evidence: B). In asymptomatic patients with severe MR, mitral valve surgery is indicated if LV dysfunction is present (Class I recommendation, Level of Evidence: B). Additionally, patients with severe MR and new onset of atrial fibrillation or pulmonary hypertension were also candidates.

Mitral Valve Anatomy

The mitral valve anatomy must have sufficient leaflet tissue amenable for mechanical coaptation with the MitraClip. A key anatomical inclusion criterion includes a regurgitant jet origin associated with the A2 to P2 segments of the mitral valve (Fig. 17-8). For patients with functional MR, a coaptation length of at least 2 mm and a coaptation depth of no more than 11 mm are required. For patients with leaflet flail, a flail gap less than 10 mm and a flail width less than 15 mm are required (Fig. 17-9).

MitraClip Procedure

The procedure is performed with the patient under general anesthesia with the use of fluoroscopy and TEE for device guidance. The right femoral vein is accessed and an 8F sheath is inserted. Right heart catheterization is then performed.

Transseptal puncture is then performed using standard technique via the right femoral vein. Heparin is administered after transseptal puncture with a goal ACT of >300 seconds. The steerable guide catheter is 24F proximally and 22F at the atrial septum. The transseptal sheath is exchanged for the guide catheter and tapered dilator. The clip delivery system is advanced through the guide catheter and into the left atrium. Controls on the guiding catheter allow deflection of the distal

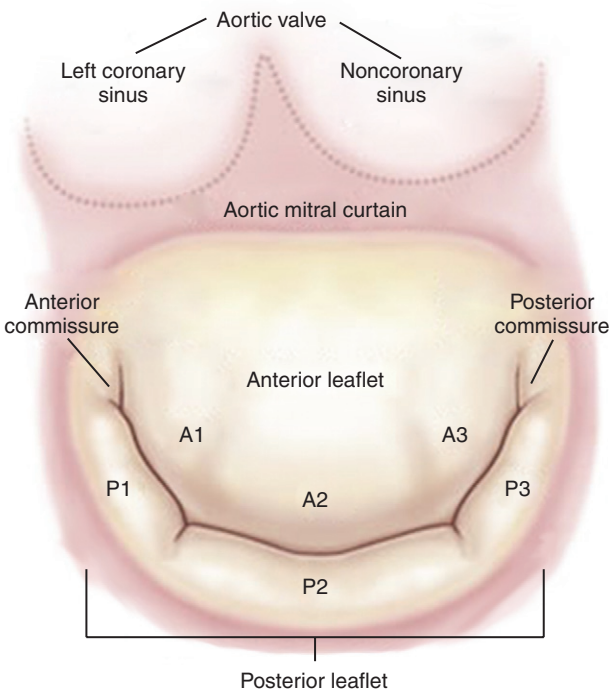

Figure 17-8 Nomenclature of the anterior and posterior leaflets of the mitral valve. A key anatomical inclusion criterion in the EVEREST trials was a regurgitant jet origin associated with the A2 to P2 segments.

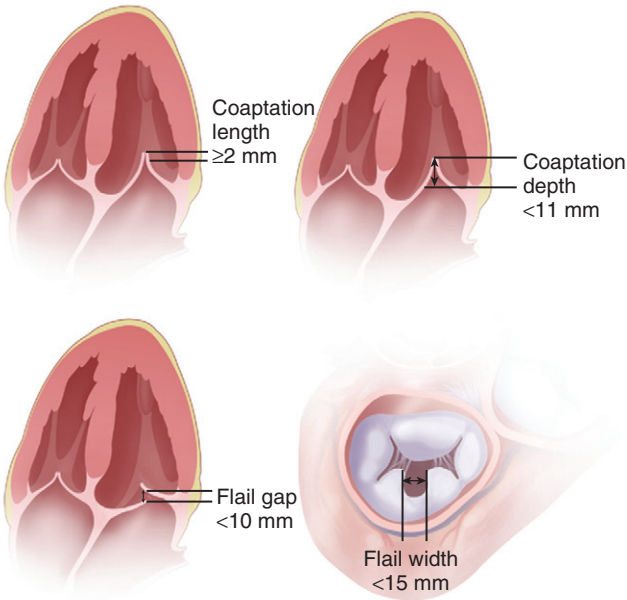

Figure 17-9 Key anatomical eligibility criteria. The coaptation length must be ≥ 2 mm. Coaptation depth must be <11 mm. If a flail leaflet exists, the flail gap must be <10 mm, and the flail width must be <15 mm. These anatomical characteristics are necessary for sufficient leaflet tissue for mechanical coaptation when the MitraClip device is used.

tip. The clip delivery system has two dials that permit medial-lateral and anteroposterior steering. Using fluoroscopic and echocardiographic guidance, the MitraClip is steered until axially aligned and centered over the origin of the regurgitant jet. The clip is opened to extend the two arms and advanced into the LV below the mitral leaflets. The clip is retracted so that each leaflet is grasped by an extended arm and then closed to coapt the mitral leaflets. The inner portion of the clip has two "grippers" adjacent to each arm to secure the leaflets as the clip is closed. Leaflet insertion into the clip and MR reduction are assessed by two-dimensional and Doppler echocardiography. If reduction in MR is not adequate, the clip can be re-opened releasing the leaflets, and the clip can be repositioned. After adequate reduction of MR has been achieved, the clip is deployed and the delivery system and guide catheter are removed.

Complications from the MitraClip procedure are listed in Table 17-5.

Clinical Results

The clinical experience with the MitraClip (n = 1115) include (1) EVEREST I, feasibility nonrandomized trial (n = 55); (2) EVEREST II, prerandomization (n = 60); (3) EVEREST II, high registry (n = 78); (4) EVEREST II, pivotal, 2:1 randomization to MitraClip vs. surgery (n = 279);

Table 17-5

Complications From MitraClip
• Complication from transseptal puncture, including pericardial effusion/tamponade and aortic puncture
• Stroke
• Bleeding
• Prolonged mechanical ventilation
• Partial clip detachment

(5) REALISM, continued Access High Risk & Non High Risk (n = 266); and (6) European Experience (n = 472).

In EVEREST I, 27 patients with a mean age of 69 years were enrolled. Of the 24 patients in whom the MitraClip was successfully deployed, 67% had less than 2+ MR upon discharge. At 30 days, MR severity grade decreased from 3.7 to 1.6. One patient experienced a stroke, and three others developed clip detachment without embolization. There were no cases of emergent cardiac surgery, myocardial infarction, cardiac tamponade, or septicemia. Furthermore, ability to undergo surgical repair was preserved in those who, at the 30-day follow-up, had inadequate MR control.

The randomized arm of EVEREST II enrolled 279 patients at 37 sites. These patients were randomized in a 2:1 fashion to the MitraClip procedure versus mitral valve surgery. In terms of safety, the major adverse event rate in the MitraClip arm was 9.6% versus 57.0% in the surgery arm ($P < 0.0001$). The safety benefit with device closure was largely driven by higher blood transfusion requirements >2 units in the surgery arm (53.2% vs. 8.8%).

In terms of effectiveness, the noninferiority hypothesis was met with the clinical success rate in the MitraClip arm being 72.4% versus 87.8% in the surgery arm ($p_{NI} = 0.0012$). At 12 months, MR reduction was greater in the surgery arm with 97% of patients with less than 2+ MR versus 81.5% in the device arm. Despite this, more patients in the device arm had NYHA functional class I or II versus the surgical arm (97.6% vs. 87.9%; $P < 0.0001$). Two-year data from the EVEREST II trial were presented in April 2011 showing that treatment with MitraClip remained effective (composite end point of freedom from death, no new mitral valve surgery, and MR lower than pretreatment minimum of 3+) compared to surgery at the 2-year follow-up. The data from EVEREST II suggest that percutaneous mitral valve repair with the MitraClip system is a viable alternative to surgery in those patients with mitral valve anatomy amenable to mechanical coaptation.

In a substudy of the EVEREST I and II trials looking at patients with functional MR, MitraClip not only reduces the severity of MR but also stimulates reverse left ventricular remodeling. LV chamber size decreased significantly at the 1-year follow-up, suggesting the presence of reverse remodeling. Acute procedural success, defined as freedom from MR > 2+ was 89%; in the 12 of 19 patients for whom the 1-year follow-up was complete, freedom from death, surgery for valve dysfunction, and MR > 2+ was 79% after 12 months. NYHA class and measures of reverse remodeling showed significant improvement in the follow-up period.

Conclusion

As with the initial phases of coronary intervention, rapid technological advances in parallel with good clinical results will ultimately permit routine use of these novel methods in a broader population. Too many patients with significant valvular dysfunction are not being offered potentially life-preserving therapy. Transcatheter valve procedures thus far appear to be durable alternative treatments for valvular heart disease in select patients.

Suggested Readings

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18

Pericardiocentesis

PAUL SORAJJA

Cardiac tamponade is a life-threatening disorder that can result from any condition that causes a pericardial effusion. Although the most frequent cause is malignancy, tamponade may also occur from pericarditis (e.g., viral, uremic, inflammatory, or idiopathic), aortic dissection (with disruption of the aortic annulus), or ventricular rupture from myocardial infarction. In the cardiac catheterization laboratory, tamponade can result as a complication of a variety of invasive procedures and lead to rapid demise of the patient due to the swift accumulation of fluid in a poorly compliant pericardial space. Prompt recognition of the salient hemodynamic features and immediate pericardiocentesis are essential to the successful treatment of cardiac tamponade. The rate of pericardial fluid accumulation relative to the stiffness of the pericardium determines how quickly the clinical syndrome of tamponade will occur. Figure 18-1 shows a normal pericardial membrane and the mechanisms of pericardial tamponade.

Diagnosis of Tamponade

The hemodynamic effects of a pericardial effusion may be acute or gradual, depending on the amount and rate of fluid accumulation. Normally, the pericardial space contains 15 to 50mL of fluid with an intrapericardial pressure that approximates intrapleural pressure (–5 to +5cm H_2O). Fluid accumulation and pericardial restraint lead to rises in intrapericardial pressure. Tamponade occurs when intrapericardial pressure exceeds intracardiac pressure, leading to impaired ventricular filling, increases in pulmonary venous and jugular venous pressures, and reduction in forward stroke volume. During interventional procedures, tamponade may be signaled by hypotension. Tachycardia, which usually occurs, may not be present in patients receiving beta blockers. A high index of suspicion of tamponade should accompany any procedure in which a distal guidewire position appears unusual or in which oversized stents are used. All procedures with rotational atherectomy have a higher incidence of perforation and subsequent tamponade.

Echocardiography

Two-dimensional and Doppler echocardiography are commonly used for diagnosing cardiac tamponade. Specific signs of tamponade include collapse of the right atrium and right ventricle, ventricular septal shifting with respiration, and plethora (enlargement) of the inferior vena cava (Fig. 18-2). Respiratory variation in the Doppler mitral inflow is a highly sensitive measure that occurs early in tamponade, and may precede changes in cardiac output, blood pressure, and other echocardiographic findings.

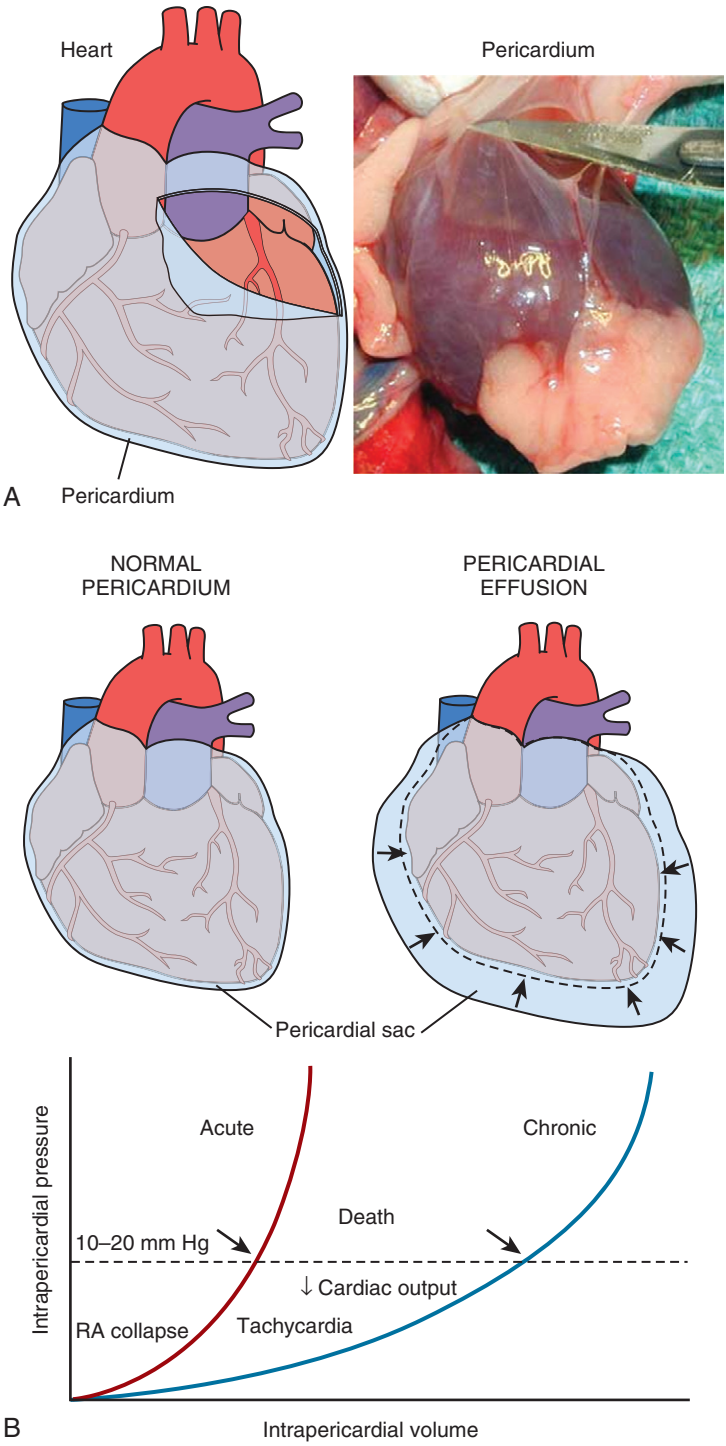

Figure 18-1 **A,** Pericardium is normally a thin membrane but can thicken with disease and can produce tamponade with a small amount of fluid when not compliant. **B,** Illustration of compliance curves and cardiac tamponade. Normal pericardium (**A**) has steep low compliance pressure-volume relationship as compared to chronic pericardial effusion with a distensible pericardium (**B**) producing tamponade only later in its course. (From Holmes DR, *et al. JACC Cardiovasc Interv* 2009;2:705–717 with permission.)

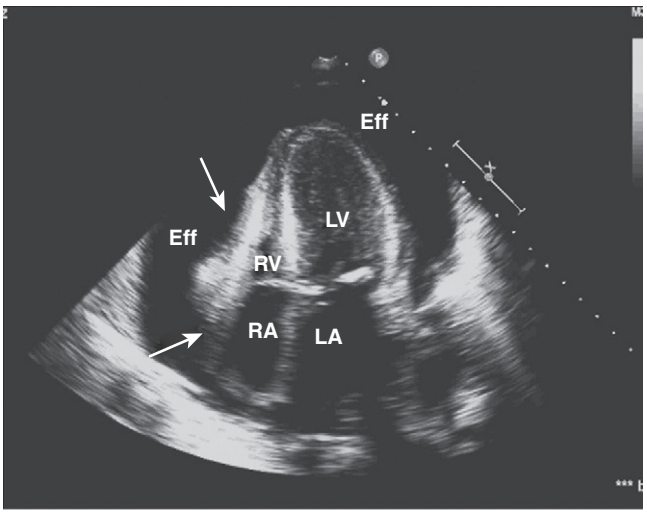

Figure 18-2 Echocardiographic image of pericardial tamponade with right-sided chamber collapse. *LA,* left atrium; *LV,* left ventricle; *RA,* right atrium; *RV,* right ventricle; *Eff*, (pericardial) effusion. (From Holmes DR, *et al. JACC Cardiovasc Interv* 2009;2:705–717 with permission.)

Hemodynamics

The invasive hemodynamic hallmarks of cardiac tamponade include pulsus paradoxus on the arterial tracing (Fig. 18-3) and prominent *x* descents and blunted *y* descents in the atrial pressure tracings (Fig. 18-4). Preservation of the *x* descent occurs because of the decrease in intracardiac volume during systolic ejection, which leads to a temporary reduction in intrapericardial and right atrial pressures (See Kern (2011) *The Cardiac Catheterization Handbook* 5th ed., Chapter 3 Hemodynamics). Elevated intrapericardial pressure impairs ventricular filling during the remainder of the cardiac cycle, resulting in blunting of the *y* descent. In patients with cardiac tamponade, the driving pressure to fill the left ventricle falls during inspiration. Consequently, there is a reduction in left ventricular filling and stroke volume, which manifests as a decrease in aortic pulse pressure during inspiration in a manner analogous to the bedside finding of pulsus paradoxus (see Fig. 18-3).

On relief of pericardial pressure and removal of the effusion, right atrial pressure and pericardial pressure fall usually to normal values if

Figure 18-3 Arterial pressure in a patient with dyspnea at rest demonstrating pulsus paradoxus due to cardiac tamponade.

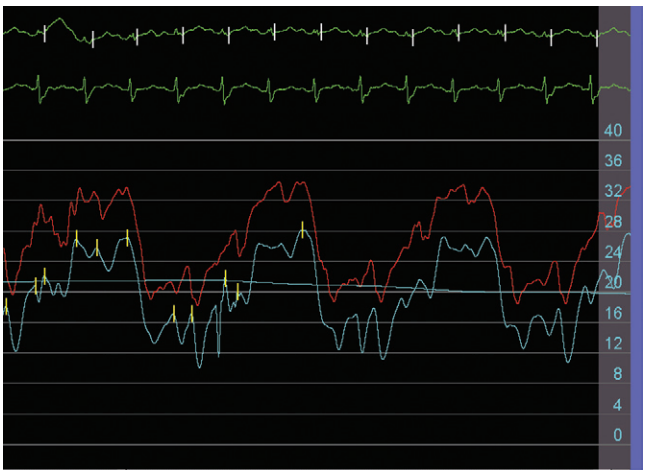

Figure 18-4 Hemodynamics of right atrial (RA) pressure (*red*) and pericardial pressure (*blue*); scale is 0–40 mm Hg. There is matching of phasic waveforms but RA is higher due to zero offset.

no residual pericardial disease is present (Fig. 18-5). However, in some cases, although pericardiocentesis empties the pericardial space and pericardial pressure falls to near zero, right atrial pressure may be unaffected, signifying the syndrome of effusive-constrictive pericardial disease (Fig. 18-6).

Cardiac tamponade should be suspected in any patient in the cardiac catheterization laboratory with unexplained hypotension, elevated venous pressure, and a compatible history. Unusual manifestations also can occur. Tamponade may occur without elevated jugular venous pressure because of low intracardiac filling pressures (i.e., low-pressure tamponade), such as in dehydrated patients with malignant effusions. Localized tamponade can result from loculated pericardial effusions, such as those that may be present adjacent to the atria in the postoperative setting. Of note, pericardiocentesis should not be performed in patients with tamponade and aortic dissection. In such patients, relief of the tamponade will lead to an abrupt increase in systolic blood pressure that may exacerbate the aortic dissection. Careful imaging with transthoracic or transesophageal echocardiography is required to determine the presence of these manifestations of tamponade.

Technique for Pericardiocentesis

The basic technique of pericardiocentesis is discussed in Table 18-1 lists the equipment used for the procedure. For most patients, pericardiocentesis is performed with echocardiographic guidance.

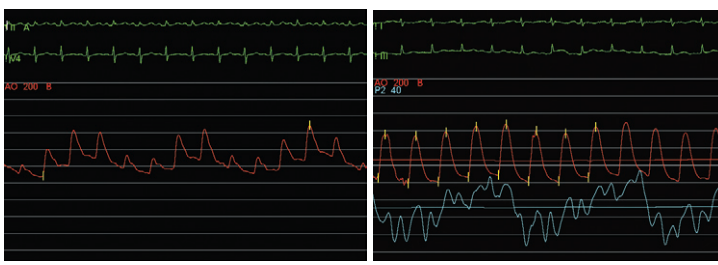

Figure 18-5 Hemodynamics of arterial pressure before pericardiocentesis (*left*) and after pericardiocentesis (*right*). Pericardial pressure is reduced from 24 to 10 mm Hg (*blue*); scale is 0–40 mm Hg.

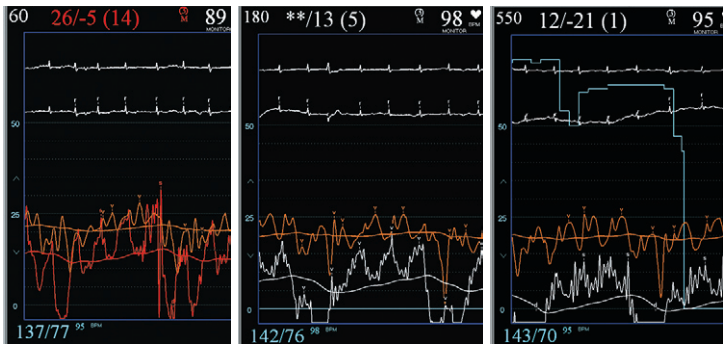

Figure 18-6 Hemodynamics of pericardiocentesis with near normalization of pericardial pressure without change in right atrial (RA) pressure consistent with effusive constrictive pericardial disease.

In some cases, additional use of hemodynamic monitoring through the pericardial needle adds important information during both puncture and after withdrawal of fluid to verify procedural findings. Certainly, in emergent situations where echocardiography is not immediately available, pericardiocentesis can be performed in a blinded or electrocardiogram (ECG)-guided fashion, usually from the subxiphoid approach. However, adjunctive echocardiography plays a significant role in the evaluation of patients with cardiac tamponade and will reduce the incidence of complications related to pericardiocentesis. Figure 18-7 shows several points of pericardial access.

For all patients, *volume resuscitation* can help provide hemodynamic stability and should be performed in patients with cardiac tamponade. Reversal of anticoagulation and antiplatelet therapy should be performed as clinically permitted. During pericardiocentesis, right heart catheterization with simultaneous measurement of right atrial and pulmonary capillary wedge pressures assist in the diagnosis and for determining efficacy of the procedure.

Patient positioning. The patient usually is positioned with head raised approximately 30 degrees to facilitate inferior and apical pooling of the pericardial effusion.

Site of entry. Echocardiography helps to determine the most appropriate site of entry and needle direction. Most frequently, the echocardiographic window that is closest to the effusion is selected. Common portals of entry are subxiphoid and apical, but other locations have included axillary, and left or right parasternal (see Fig. 18-7). Advantages

Table 18-1

Equipment for Pericardiocentesis
Sterile gloves, mask, and gown
Povidone-iodine solution or other skin antiseptic
Sterile transparent plastic drape
20- or 25-gauge needle for local anesthesia administration
Local anesthesia (e.g., 1% lidocaine)
18-gauge polytef-sheathed venous needles of varying lengths (5–8 cm)
Syringes (10 mL, 20 mL, and 50 mL)
0.035-inch J-tipped guidewire
Scalpel (no. 11 blade)
5F or 6F introducer sheath
5F or 6F 65-cm pigtail catheter with multiple side holes
4 × 4 inch gauze for dressing and ointment
1-L vacuum bottle or comparable fluid receptacle
Labels for specimen collection
Sterile isotonic saline (for catheter flush)

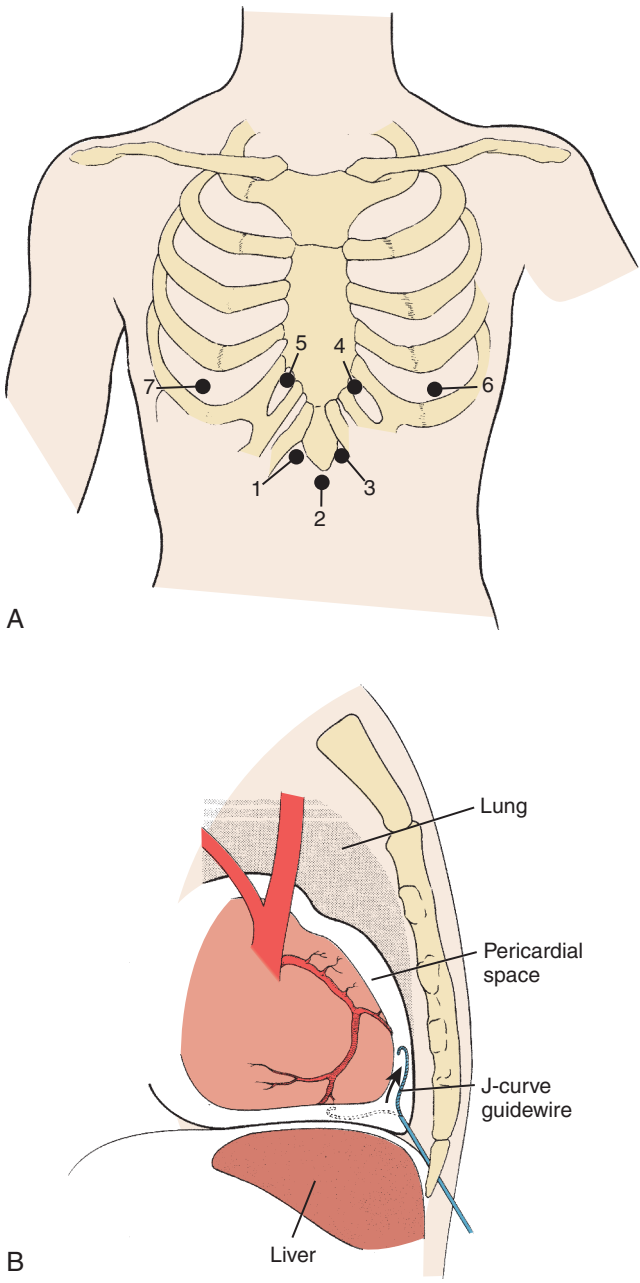

Figure 18-7 **A,** Locations for pericardiocentesis. (*1, 2, 3*) Xiphoid approaches, (*4*) Fifth left intercostal space at sternal border, (*5*) Fifth right intercostal space at the sternal border, (*6*) Apical approach, (*7*) Approach for major fluid accumulation on the right side. (Modified from Spodick DH. *Acute pericarditis.* New York: Grune & Stratton, 1959.) **B,** Passing a flexible J-curve guidewire through pericardial needle into the pericardial space. (From Tilkian AG, Daily EK. *Cardiovascular procedures: diagnostic techniques and therapeutic procedures.* St Louis, MO: Mosby, 1986.)

of the subxiphoid approach are a lower risk of pneumothorax and laceration of internal mammary or intercostal arteries. For the subxiphoid approach, the needle must be angled clear below the bottom rib as it attaches to the inferolateral surface above the xiphoid process (typically one fingerbreadth inferior and lateral to the edge of the xiphoid).

Punctures that are too high and near the recess at the xiphoid angle can pose challenges to delivering the needle under the rib. When using a parasternal approach, the needle should pass 1 cm lateral to the sternum to avoid injury to the internal mammary artery; the risk of pneumothorax increases with further lateral positioning. For intercostal approaches, the needle should pass superior to the rib margins to reduce the risk of injury to the neurovascular bundle. The angle of entry and direction should be transfixed in the operator's mind. The site of entry can be marked with an indelible pen. The precordial or subxiphoid area is sterilized with antiseptic solution and covered with a sterile drape.

Needle insertion. Following local anesthesia, an 18-gauge, thin-walled polytef-sheathed needle is inserted at the entry site using the predetermined angulation. The needle is advanced with gentle aspiration into the pericardial space. Aggressive aspiration may cause tissue occlusion of the needle and inhibit detection of pericardial fluid. Once fluid has been obtained, the needle is advanced slightly further (~2 mm) to ensure placement of the sheath into the pericardial space. Figure 18-8 shows a pericardial needle and stopcock arrangement designed to check pericardial pressure and then aspirate pericardial fluid and discharge the fluid into a pericardial drainage bag. Alternately, a needle and sheath system can be used. Once the needle is in the pericardial space, the polytef sheath then is advanced over the needle, followed by withdrawal of the needle. The needle should not be re-advanced once it has been removed from the sheath.

Confirmation of location. Agitated saline is injected into the sheath via a three-way stopcock with echocardiographic imaging (Fig. 18-9). If the agitated saline does not enhance the pericardial space, then repositioning of the needle by either withdrawal or another needle passage is performed. Radiographic contrast can also be administered under fluoroscopy. Small test injections should be given initially to exclude myocardial positioning, which is seen as myocardial staining. Contrast swirling will indicate a ventricular location, while pooling suggests intrapericardial positioning. Alternatively, the needle (before it is withdrawn) or the sheath can be connected to tubing connectors for pressure transduction. Intrapericardial pressure will be similar to the atrial pressure, while ventricular systolic pressure waveforms can immediately alert the operator to inadvertent ventricular perforation. For operators using an ECG-guided approach, the needle is connected to an alligator-tipped electrode. With myocardial contact, ST-segment elevation (i.e., injury

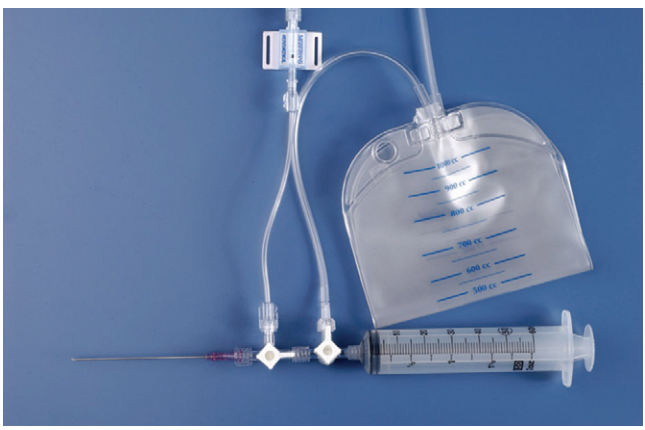

Figure 18-8 Pericardial needle attached to stopcocks which connect to pressure line and drainage bag. (Courtesy of Merit Medical, Inc.)

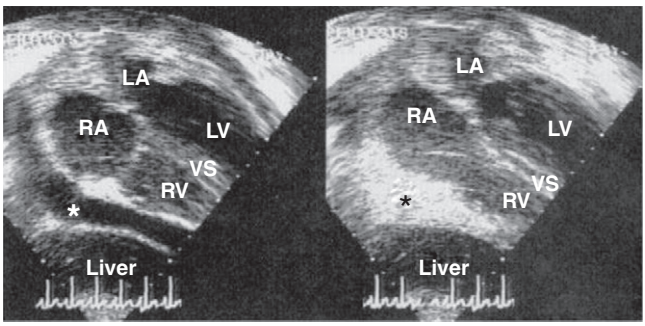

Figure 18-9 Use of agitated saline contrast medium for confirmation of sheath position in pericardial space. Pericardial effusion was visualized by imaging from subcostal position remote from entry site on chest wall, before injection of agitated saline contrast medium (*left*). Injection of agitated saline contrast medium provides dense opacification of pericardial space, confirming sheath position (*right*). *LA,* left atrium; *LV,* left ventricle; *RA,* right atrium; *RV,* right ventricle; *VS,* ventricular septum; *, pericardial space. (Reprinted with permission from Tsang TS, Freeman WK, Sinak LJ, *et al.* Echocardiographically guided pericardiocentesis: evolution and state-of-the-art technique. *Mayo Clin Proc* 1998;73:647–652.)

current) will be detected that may not appear on other electrocardiographic leads (Fig. 18-10).

Catheter placement. Following confirmation of position, a J-tipped guidewire is inserted through the polytef sheath into the pericardial space. A small skin incision with a scalpel is made, followed by exchange for a 5F or 6F introducer sheath and removal of the dilator. A multihole pigtail catheter is then inserted, followed by removal of the introducer sheath, leaving only the smooth-walled pigtail catheter in place. Positioning of the pigtail catheter can be reconfirmed using either echocardiography or pressure measurement.

Aspiration. Manual techniques or vacuum bottle can be used to remove the pericardial effusion. For patients with tamponade due to cardiac perforation, care should be taken to remove as much pericardial fluid as possible as this will facilitate sealing of the perforated site. For patients with other causes of pericardial effusion, complete apposition of the parietal and visceral layers also will reduce risk of recurrence. Inability to aspirate despite a persistent pericardial effusion on echocardiography should lead to repositioning of the pigtail catheter. Occasionally, puncture of a tense pericardium will lead to discharge of pericardial contents into a pleural space, resulting in less than expected removal via aspiration. Normalization of atrial pressures documented with simultaneous right heart catheterization helps to ensure successful removal of the pericardial effusion and relief of cardiac tamponade. For patients with large volume removal due to acute hemorrhage, cell savers often are used to minimize blood loss.

Post-pericardiocentesis management. The pigtail catheter is sutured to the chest wall, connected to a stopcock, and flushed every 4 to 6 hours with heparinized saline to maintain patency. Standard indwelling catheter care with complete dressing changes every 72 hours is recommended. When drainage becomes minimal (<25 mL/day) and echocardiography shows no recurrent effusion, the pigtail catheter can be removed. For completely drained pericardial effusions, the risk of recurrence is low (<10%) with the exception of certain etiologies (e.g., bacterial infection, malignancy).

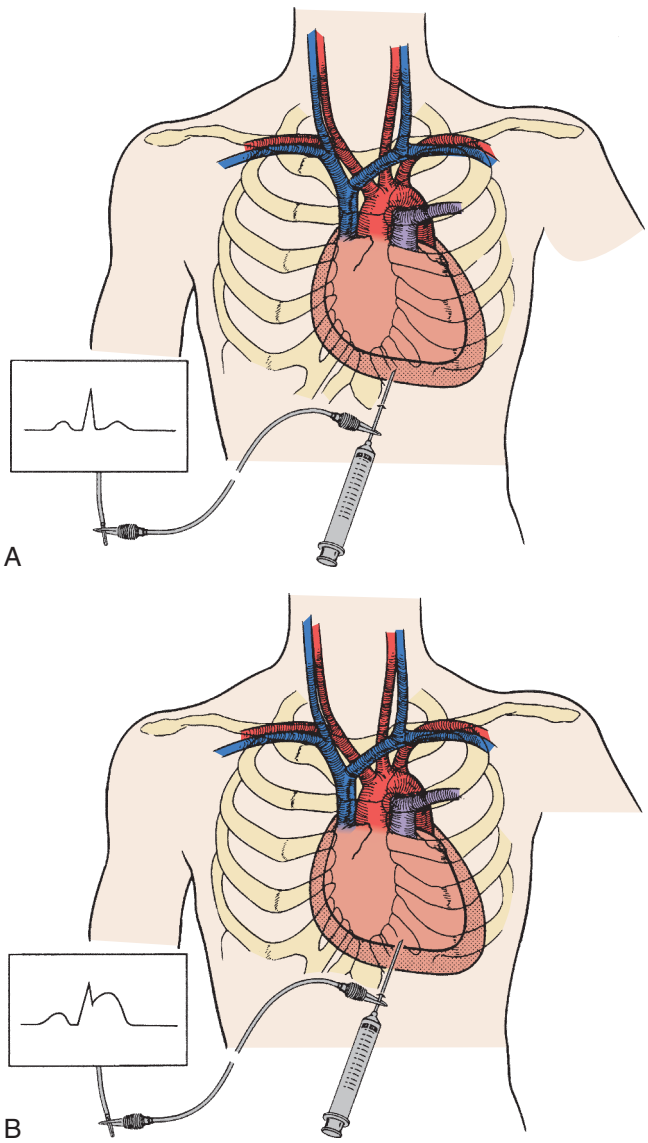

Figure 18-10 **A,** Electrocardiographic monitoring of pericardial needle tip. Note normal ST segment while tip is not touching the epicardium. **B,** When needle tip touches epicardium, current of injury ("contact" current) with elevated ST segment is seen. (From Tilkian AG, Daily EK. *Cardiovascular procedures: diagnostic techniques and therapeutic procedures.* St. Louis, MO: Mosby, 1986.)

Complications

When pericardiocentesis is performed by experienced operators, complications are infrequent (<1.5% of patients). The most serious complication is laceration of a coronary artery. Perforation of either the right or left ventricle also may occur, but this is rarely of clinical significance. Bleeding and tamponade from coronary or ventricular perforation can be detected by continuous monitoring of atrial pressure, which will increase in the event of these complications. Acute left ventricular failure with pulmonary edema has been reported as a complication of pericardiocentesis, but the cause of this phenomenon is not known.

While most pericardial effusions can be treated percutaneously, a surgical approach may still be required. Loculated effusions, posterior effusions, or pericardial clot formation from recent hemorrhage may be difficult to remove percutaneously. Large surgical drainage often is required for effusions due to bacterial infection. For patients with refractory pericardial effusions (e.g., due to malignancy), balloon pericardiotomy to allow drainage into the pleural or peritoneal space may be a therapeutic option.

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19

Septal Ablation for Obstructive Hypertrophic Cardiomyopathy

PAUL SORAJJA

Hypertrophic cardiomyopathy (HCM) is a common, inheritable cardiac disorder with a prevalence of 1 in 500 persons. Dynamic left ventricular outflow tract (LVOT) obstruction frequently is present, affecting up to two thirds of these patients. Although the clinical significance of LVOT obstruction in HCM has been debated, recent studies have linked the presence of obstruction to heightened risk for heart failure and, in some reports, an increased risk of death. Negative inotropic agents, such as beta-receptor antagonists, disopyramide, or calcium-channel blockers (i.e., verapamil, diltiazem), are the cornerstone of drug therapy for symptomatic LVOT obstruction. When severe symptoms persist despite drug therapy, definitive septal reduction therapy should be considered.

The time-honored standard for septal reduction therapy has been surgical myectomy, in which a surgeon uses a transaortic approach to resect ventricular septal hypertrophy. In 1995, percutaneous alcohol septal ablation was introduced as an alternative to surgical myectomy for the relief of LVOT obstruction in patients with HCM. The aim of alcohol septal ablation is to induce a localized myocardial infarction and thinning of the basal ventricular septum, thereby leading to a reduction in septal thickening and systolic excursion into the LVOT.

Patient Selection

Proper patient selection is critical to the success of septal ablation. A comprehensive clinical evaluation and echocardiogram should be performed in all candidates, ideally in a center with expertise in the care of HCM patients. Criteria for septal ablation include:

1. Severe, drug-refractory cardiac symptoms (New York Heart Association functional class III/IV dyspnea or Canadian Cardiac Society angina class III/IV) due to obstructive HCM;
2. Dynamic LVOT obstruction (gradient ≥30 mmHg at rest or ≥ 50 mmHg with provocation) that is due to septal hypertrophy and systolic anterior motion of the mitral valve;
3. Ventricular septal thickness ≥15 mm;
4. Absence of significant intrinsic mitral valve disease;
5. Absence of the need for concomitant cardiac surgical procedure (e.g., bypass grafting, valve replacement); and
6. Informed patient consent. Informed consent requires a full understanding of the limited data on long-term survival after the procedure, the risk of pacemaker dependency, the relatively lower success rate due to its dependence on coronary anatomy,

and potential complications related to cardiac catheterization and instrumentation of the coronary arteries. Although younger age has not been an absolute contraindication to the procedure, septal ablation generally has been reserved for older adult patients due to the limited data on long-term survival of the procedure. A comprehensive two-dimensional and Doppler echocardiogram is elementary to proper patient selection. This evaluation should document the dynamic nature of the LVOT obstruction and exclude anatomical findings that would impede the clinical efficacy of the procedure (Fig. 19-1).

Technique

Hemodynamic Evaluation

Proper performance of septal ablation requires a complete and accurate evaluation of the severity of LVOT obstruction due to HCM. Characteristically, LVOT obstruction in HCM is dynamic and exquisitely sensitive to ventricular loading conditions and contractility. The operator should be cognizant of this sensitivity when examining hemodynamic data from both the echocardiogram and invasive catheterization. Careful attention must be given not only to the initial LVOT gradient observed at rest, but all dynamic and provocable gradients (e.g., variation with respiration, post-premature ventricular contraction accentuation) observed during the procedure.

Transseptal Hemodynamic Assessment

The most accurate method for the invasive evaluation of LVOT obstruction in HCM entails a transseptal approach with positioning of a balloon-tipped catheter (e.g., a 7F Berman catheter, Arrow International Inc., Reading, PA) at the left ventricular inflow region and a pigtail catheter placed retrograde in the ascending aorta for simultaneous measurement of the LVOT gradient. The transseptal approach helps to avoid

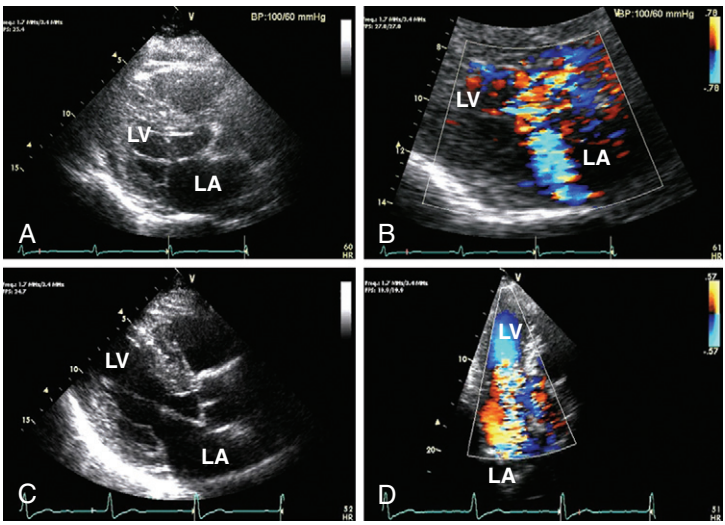

Figure 19-1 Patient selection for septal ablation. **A** and **B,** Appropriate patient for septal ablation. There is septal hypertrophy, systolic anterior motion of the mitral valve, and posteriorly directed mitral regurgitation that is secondary to the outflow obstruction. **C** and **D,** This patient has obstructive hypertrophic cardiomyopathy, but the mitral regurgitation is secondary to a flail mitral leaflet. Note the anterior course of the mitral regurgitant jet, which is not typical for that due to outflow obstruction. *LA,* left atrium; *LV,* left ventricle.

catheter entrapment, which can be difficult to distinguish from changes in left ventricular pressure that occur due to the dynamic nature of LVOT obstruction. Use of an 8F Mullins sheath for transseptal access also enables recording of left atrial pressure via the side arm for assessment for concomitant diastolic dysfunction.

Retrograde Hemodynamic Assessment

Alternatively, left ventricular pressure can be assessed with a 5F or 6F catheter placed retrograde across the aortic valve. In this technique, a catheter with shaft side holes should not be used because some or all of the holes will be positioned above the level of subaortic obstruction, leading to erroneous measurements of left ventricular pressure and the LVOT gradient. Catheters that may be used for this purpose are a multipurpose or a Halo pigtail catheter. Absence of catheter entrapment should be confirmed with hand contrast injections or demonstration of pulsatile flow from the catheter with disconnection from the extenders used for pressure transduction.

Temporary Pacemaker Placement

The risk of pacemaker dependency from septal ablation varies according to the baseline electrocardiographic abnormalities. Septal ablation frequently results in right bundle branch block (approximately 50% of cases). Thus, for those patients with left bundle branch block, severe left axis deviation, or a very wide QRS interval, the rate of pacemaker dependency approaches 50%. However, permanent pacemaker dependency from complete atrioventricular block still occurs in 10% to 15% of patients with a normal electrocardiogram. Thus, for patients without a permanent pacemaker, a temporary device is placed at the right ventricular septum via the right internal jugular vein prior to septal ablation. Conventional 5F or 6F temporary pacemakers or balloon-tipped catheters can be utilized. Of note, however, some pacemaker catheters have been associated with cardiac perforation, at least partly due to their long dwelling time while patients are observed in the intensive care unit after the procedure. In our practice, we have observed no cardiac perforations with the use of a low-profile, less traumatic temporary pacemaker. The temporary pacemaker should be placed distal or away from the target site of ablation to ensure continuous capture during induction of the septal infarction.

Coronary Angiography

The primary goal of coronary angiography is to determine the most appropriate septal artery for the procedure. Both arteries should be evaluated, as basal septal branches occasionally arise from the proximal right coronary artery. With a right anterior oblique angulation of the left coronary artery, straight and caudal views facilitate examination of the angulation of the origin of the septal artery, while cranial projections can assist with the length of the vessel. Left anterior oblique projections should be used to demonstrate the course of the artery in the ventricular septum.

Alcohol Ablation

Conventional 6F or 7F guide catheters are used to engage the left coronary artery with standard procedural anticoagulation (e.g., heparin 70–100 U/kg). Both a primary and a large secondary bend should be placed on the tip of a 0.014-inch guidewire to facilitate entry into the candidate septal artery. A slightly oversized, short-length, over-the-wire balloon (2.0–2.5 mm × 8–10 mm length) is placed entirely into the septal artery using standard catheter techniques. Oversizing of the balloon allows occlusion of the artery at low pressures (3–4 atm), which permits

relatively easier injection of material through the wire lumen of the catheter. Following inflation of the balloon catheter, the guidewire is withdrawn.

Angiography of the left coronary then is performed to demonstrate no communication between the septal artery and left anterior descending, and also to confirm the course of the target vessel through the ventricular septum on fluoroscopy. Next, using full-strength contrast, angiography of the septal artery through the balloon catheter confirms patency of the vessel for ablation and localization (i.e., no untoward collateralization). Both angiographic and echocardiographic contrast media are injected to identify the perfusion bed of the septal perforator artery with simultaneous two-dimensional echocardiography (Fig. 19-2). Multiple echocardiographic views are used to confirm enhancement of the septal hypertrophy intimately related to LVOT obstruction but no targeting of undesirable locations, such as the right ventricle, free walls, or papillary muscles.

After delineation of the targeted myocardium, 1 to 3 mL of desiccated ethanol is infused slowly over a period of 3 to 5 minutes followed by slow normal saline flush. The use of alcohol is preferred because this agent immediately results in a discrete myocardial infarction. In other percutaneous methods (e.g., vascular coiling, covered stent placement), septal infarction may not result due to septal collateralization that is either preexisting or develops during follow-up. Hemodynamics are monitored during alcohol instillation.

The balloon should be left inflated following saline flush for 5 to 10 minutes to reduce likelihood of alcohol extravasation. For patient comfort, intravenous analgesia (e.g., fentanyl 25 mg) frequently is given prophylactically or intermittently as needed. For patients without significant reduction of either the resting or provoked LVOT gradient, other septal perforator arteries can be targeted and treated in similar fashion.

Clinical Outcomes

Acute Procedural Success

In published series, the magnitude of LVOT gradient reduction with septal ablation has ranged from 55% to 75%. Acute procedural success, when defined as a ≥50% reduction in the peak resting or provoked LVOT gradient with a final residual resting gradient of <20 mmHg, occurs in 80% to 85% of patients. In addition to proper patient selection, factors associated with higher likelihood of acute hemodynamic success include relatively less septal hypertrophy, lower LVOT gradients, and operator experience. Further reduction in the LVOT gradient over 3 to 6 months after the procedure also occurs due to ventricular remodeling and basal septal thinning. Regression of myocardium both at the site of LVOT obstruction and remote from the ventricular septum has been demonstrated using cardiac magnetic resonance imaging.

The major limitation to higher success rates is the lack of an appropriate septal artery, which may be absent in up to 20% of patients. The most common complication of septal ablation is temporary or complete atrioventricular block. Other potential complications are cardiac tamponade, dissection of the left anterior descending artery, ventricular tachycardia or fibrillation, and free wall myocardial infarction. For these reasons, patients are observed in an intensive care setting for at least 3 days after the procedure. Overall, the published peri-procedural mortality rates are 1% to 2%.

Symptom Improvement

Septal ablation leads to significant clinical improvement, as measured by both subjective functional class and objective testing, such as treadmill exercise time and peak myocardial oxygen consumption.

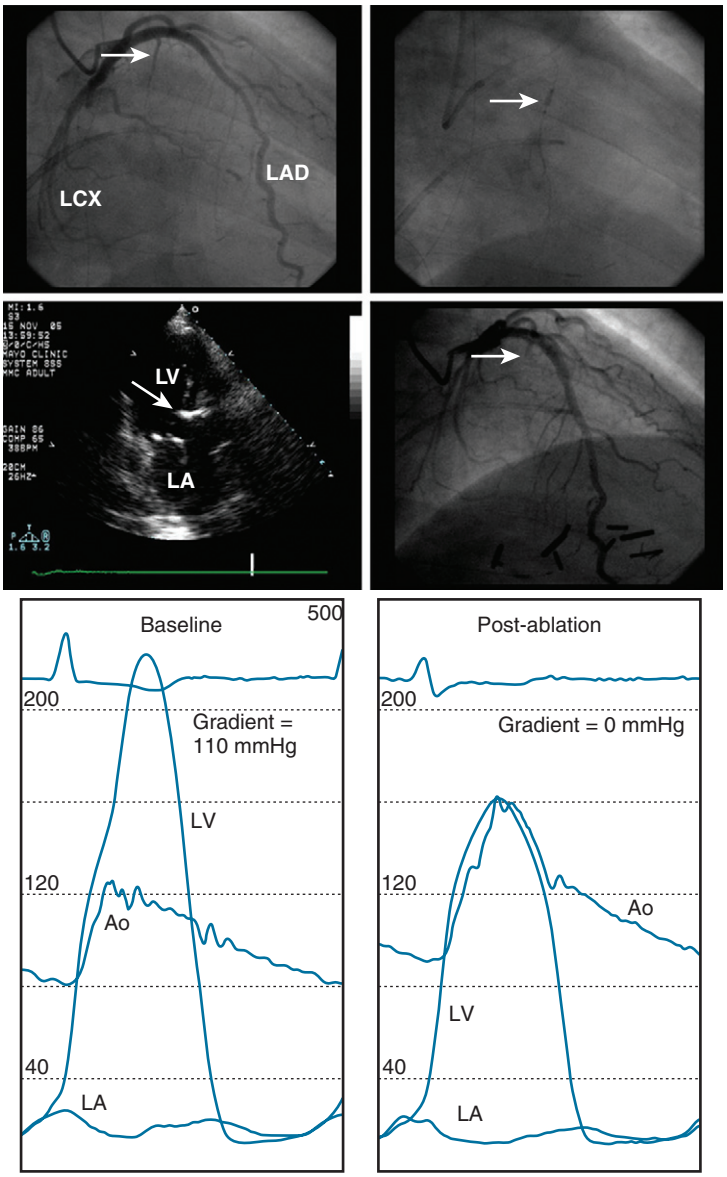

Figure 19-2 Percutaneous septal alcohol ablation. *Top left*, Baseline angiogram of the left coronary artery showing the septal perforator artery (*arrow*) to be used for ablation. *Top right*, An over-the-wire balloon (*arrow*) is inflated in the perforator artery followed by contrast injection through the balloon. *Middle left*, Echocardiographic contrast is injected through the balloon and visualized with simultaneous echocardiography. *Middle right*, Following injection of alcohol, the septal artery (*arrow*) is obliterated. *Bottom left*, Before septal ablation, the left ventricular outflow tract gradient is 110 mmHg. *Bottom right*, Following septal ablation, there is no left ventricular outflow tract gradient. *Ao,* ascending aorta; *LA,* left atrium; *LAD,* left anterior descending; *LCX,* left circumflex; *LV,* left ventricle. (Reprinted from Sorajja P, Nishimura RA. Myocardial and pericardial disease. In *CathSap version 3*, by permission from American College of Cardiology Foundation.)

The clinical efficacy of septal ablation is related to the degree of reduction in severity of the LVOT gradient. Overall, septal ablation typically results in a 20% to 30% increase in objective measures of functional capacity.

Several studies have shown these clinical improvements to be sustained in follow-up ≥1 yr, with several reports showing effects

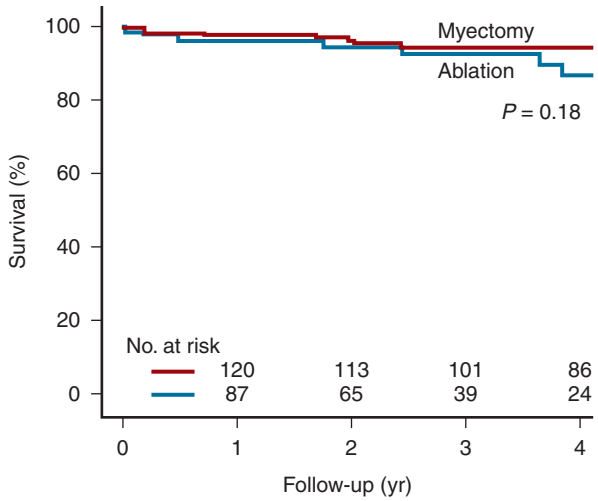

Figure 19-3 Comparison of survival after septal ablation to a matched cohort of surgical myectomy patients. The 4-year survival free of all mortality (including defibrillator discharge for lethal arrhythmia) among septal ablation patients was similar to that observed among age- and sex-matched patients who underwent isolated surgical myectomy. (Reprinted from Sorajja P, *et al.* Outcome of alcohol septal ablation for obstructive hypertrophic cardiomyopathy. *Circulation* 2008;118:131–139, by permission from Lippincott Wilkins.)

comparable to that of surgical myectomy (Fig. 19-3). Nonetheless, in younger patients (age <65 yr), symptom relief may be greater with surgical myectomy (Fig. 19-4). The reasons for this observation are not clear but may be related to the residual gradients present after ablation (typically 10–20 mmHg) that are higher than those after surgical myectomy (typically <10 mmHg). These relatively higher residual gradients may be less tolerated by younger, more active individuals.

Survival

Presently, five published studies have compared the results of septal ablation to surgical myectomy with follow-up ranging from 3 months to 4 years. Overall survival has been comparable to that of myectomy, although the total number of ablation patients examined remains relatively small (n = 286 for all series combined) (see Fig. 19-4). In the Mayo Clinic study (n = 140), 4-year survival free of all-cause mortality (including appropriate defibrillator discharge) after septal ablation was 88.0%; sudden death occurred in 2.2% of patients. Although the current studies suggest that there is no impairment of early to midterm survival after septal ablation, the long-term effects and risk of sudden death remain largely unknown due to limited data on follow-up beyond 3 to 5 years.

Perspective

Although septal ablation has established itself as an alternative therapy in selected HCM patients, its introduction has been met with skepticism and controversy about its appropriate role in the management of these patients. These concerns have arisen primarily because of the established safety and durable efficacy of surgical myectomy, procedural morbidity of septal ablation (e.g., pacemaker dependency), and the paucity of long-term data with septal ablation.

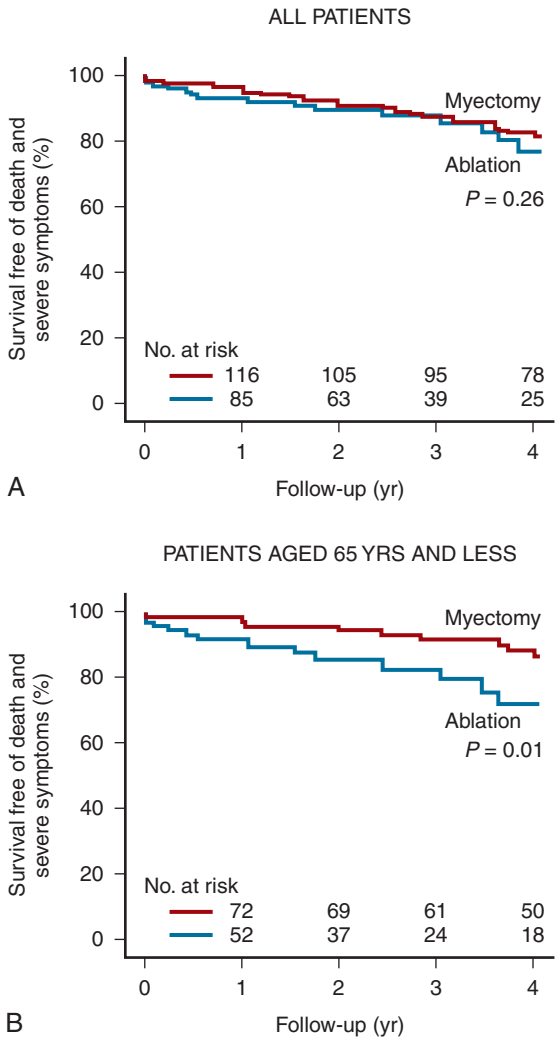

Figure 19-4 Symptom-free survival for septal ablation patients in comparison to surgical myectomy. Survival free of severe symptoms and death was comparable in the overall population (*top*), but was inferior among patients < 65 years (*bottom*). (Reprinted from Sorajja P, *et al.* Outcome of alcohol septal ablation for obstructive hypertrophic cardiomyopathy. *Circulation* 2008;118:131–9, by permission from Lippincott Wilkins.)

Although there have been calls for a randomized trial of alcohol ablation versus surgical myectomy, there are a number of significant practical challenges. For an adequately powered trial to determine differences in mortality, screening of >34,000 HCM patients would be required. This number far surpasses the number of HCM patients currently under care at medical centers that have expertise in both percutaneous and surgical modalities. Management of these patients thus will continue to rely on carefully performed observational data and expert consensus.

Presently, septal ablation cannot be advocated as a therapy to replace surgical myectomy. For some patients, septal ablation may be the only option for definitive relief of LVOT obstruction due to poor candidacy for surgery. In others, septal ablation can be offered as an alternative treatment only after the risks of the procedure and lack of long-term data are discussed fully with the patient. Importantly, even though septal ablation uses conventional coronary angioplasty equipment, the

procedure is complex with a steep learning curve and unique complications. In addition, the clinical evaluation of patients with HCM can be significantly challenging, with many factors that should be taken into account when considering septal reduction therapy. Current guidelines recommend that these considerations be made in a tertiary center, where expertise in both percutaneous and surgical options can be offered.

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20

Transcatheter Closure of Atrial Septal Defects and Patent Foramen Ovale

WAIL AL KASHKARI · QI LING CAO · ZIYAD M. HIJAZI

An atrial septal defect (ASD) is a communication between the right atrium and left atrium due to an abnormal septation. There are four types of ASD:

- Primum
- Secundum
- Sinus venosus (superior vena cava [SVC] type and inferior vena cava [IVC] type)
- Coronary sinus septal defect

ASDs are among the most common congenital heart defects. At present, only the secundum type is amenable to transcatheter closure.

Secundum ASD

This is a defect or deficiency in the septum primum in which the overlap with the septum secundum is incomplete, leading to the defect. The defect is therefore bordered by the limbus of the fossa ovalis or the C-shaped septum secundum. It comprises 10% of all congenital heart defects and is twice as common in females as in males. Associated anatomical lesions include mitral valve prolapse, partial anomalous pulmonary venous return, and complex congenital heart defects.

The hemodynamic pathophysiology typically involves a left-to-right shunt at the atrial level. The flow across an ASD or other atrial level shunt occurs mainly in diastole, and its direction depends on the differences in the atrial pressures and compliance rather than on pulmonary vascular resistance (PVR) or systemic vascular resistance (SVR), although these resistances are indirect factors. The compliance of the atria is determined by their respective ventricular compliance, which is dependent on ventricular wall thickness, a function of ventricular pressure and the resistance (e.g., PVR for the right ventricle and SVR for the left ventricle). As right ventricular pressure and PVR increase, the wall thickness of the right ventricle increases, leading to a fall in right ventricular and right atrial compliance (i.e., atrial wall becomes stiffer). Normally the mean left atrial (LA) pressure is 6 to 9 mmHg and the mean right atrial (RA) pressure is 1 to 4 mmHg. This favors a left-to-right shunt.

The pressure in the respective atria is dependent on the compliance of the respective ventricles. If the ventricles are poorly compliant or stiff, a higher atrial pressure is required for filling to occur. Unless the communicating defect is small, the amount of flow is dependent on the difference in compliance of the ventricles rather than the pressure, since a large defect will equalize the pressures in the atria. Normally, the right ventricular compliance is much higher than that in the left ventricle, resulting in a left-to-right shunt across the ASD, and its magnitude is dependent on the relative difference between the right ventricular and left ventricular compliance.

Left ventricular compliance is relatively stable for the first 20 to 30 years of life. As aging occurs, the arteriolar elasticity decreases and SVR increases, leading to higher blood pressure. This leads to higher energy expenditure by the left ventricle, to overcome increased afterload, and subsequent left ventricular hypertrophy. The compliance of the left ventricle decreases, with a subsequent elevation in LA pressure and increased left-to-right atrial level shunt. The shunt results in right-sided volume overload. Thus, the right atrium, right ventricle, pulmonary arteries, and pulmonary vascular bed are enlarged because of the increased volume of the shunt. There is increased flow across an otherwise normal tricuspid and pulmonary valve, leading to increased turbulence or a flow-related gradient across these valves.

Clinical Presentation

Most children with an ASD present with a murmur and are asymptomatic. Occasionally, infants may present with breathlessness, recurrent chest infections, and even heart failure. Failure to thrive is an uncommon presentation.

Adults with an ASD typically have a prolonged asymptomatic course. Symptom onset is insidious, most often occurring after the age of 40 or 50. Women may become symptomatic during the physiologic demands of pregnancy or labor. In adults with an ASD who are less than 40 years of age, there is no correlation between symptoms (New York Heart Association [NYHA] class) and the size of a shunt. Even patients with small (<10 mm) defects can present with significant symptoms. However, the development of symptoms does correlate with age. Major and limiting problems are often experienced after age 65 years.

The clinical course of an unrepaired ASD in adulthood may be significantly affected by hypertension, coronary artery disease, and mitral regurgitation. Patients with unrepaired ASD over 60 years of age often develop atrial fibrillation, an age-related reflection of atrial stretch, which seldom occurs in those younger than 40 years of age.

Symptoms may include the following:

- Reduced exercise tolerance or fatigue
- Exertional dyspnea
- Palpitations (due to supraventricular arrhythmias, frequent atrial fibrillation/atrial flutter in older age), or syncope for sick sinus syndrome
- Atypical chest pain (right ventricular ischemia)
- Frequent respiratory tract infections
- Signs of right-heart failure
- Paradoxical embolism from peripheral venous or pelvic vein thrombosis, atrial arrhythmias, unfiltered intravenous infusion, or indwelling venous catheters

The physical examination findings depend on the stage of presentation and pathophysiology. For example, cyanosis suggests severe pulmonary hypertension with reversed shunting in the presence of a secundum ASD or superior sinus venosus defect. A diastolic murmur at the lower right sternal border suggests increased blood flow through the tricuspid orifice, especially if the Qp:Qs ratio is more than 2.5:1 (relative tricuspid stenosis). The clinical findings and auscultation may also be completely unremarkable.

Echocardiography

In the current era of percutaneous device closure of interatrial communications, evaluation with transesophageal echocardiography (TEE) or intracardiac echocardiography (ICE) is mandatory prior to consideration of device closure.

Table 20-1

Transesophageal Echocardiogram Features to Consider for Atrial Septal Defect Closure

1. Demonstration of all four pulmonary veins draining to the left atrium is essential prior to device closure of fossa ovalis defects. Ten percent of secundum atrial septal defect (ASD) have anomalous pulmonary venous drainage, most commonly of the right upper pulmonary vein.
2. Exclude a superior sinus venosus defect, in the long axis 90-degree view and at zero degrees rotation.
3. Measure the margins of the atrial septum for suitability for device closure.
4. A detailed mitral valve assessment is mandatory prior to closure as mitral incompetence is a potential complication of device closure. The severity of mitral stenosis and regurgitation are often underestimated in the presence of an ASD.
5. Closure of a defect in the context of significant mitral valve disease will likely worsen symptoms rather than improve them.
6. Exclude intracardiac thrombus.

Initial screening imaging with transthoracic echocardiography (TTE) may demonstrate a clearly visible defect in the atrial septum, best seen in the apical four chamber and subcostal long-axis views. However, it is common to see "echo dropout" in the region of the interatrial septum, and this may lead to misdiagnosis. Bubble contrast echocardiography with provocation (e.g., including a sharp nasal sniff, a cough, or the relaxation phase of the Valsalva maneuver) improves diagnostic accuracy. A positive test reveals the rapid transit of bubbles from the right to the left heart within three to five cardiac cycles. The amount of bubbles seen is related to the size of the defect. Late transit (more than five cardiac cycles) of bubbles is associated with intrapulmonary shunting. Intravenous contrast injection in the left arm may diagnose a persistent left SVC with anomalous drainage to the left atrium.

Table 20-1 summarizes the key points regarding TEE evaluation of intracardiac anatomy.

Cardiac catheterization is not usually required for diagnosis. However, in older patients a diagnostic cardiac catheterization with full hemodynamic and coronary assessment may be justified.

Indications for Percutaneous Closure of Secundum ASD

Large ASDs should be closed to reduce the risk of complications; these may include premature death, atrial arrhythmias, reduced exercise tolerance, hemodynamically significant regurgitation, right-to-left shunting and embolism during pregnancy, congestive heart failure, or pulmonary vascular disease. Large defects with *evidence of right ventricular volume overload* on echocardiography may only cause symptoms in the third decade of life or beyond; however, regardless of symptoms, closure is usually indicated to *prevent long-term complications*.

Symptoms or complications of an ASD are indications for closure regardless of age. ASD closure will prevent further deterioration and probably will reverse or normalize right ventricular dilation right ventricular failure, and tricuspid regurgitation (TR). Atrial flutter or fibrillation after defect closure may be treated with radiofrequency ablation, ablation of the cavotricuspid isthmus, or atrial surgery (Maze procedure).

If the patient presents with pulmonary arterial hypertension (PAH), complete assessment of the reversibility of pulmonary vascular disease should be done prior to closure. Closure may be considered in the presence of net left-to-right shunting, pulmonary artery pressure less than two-thirds systemic levels, PVR less than two-thirds SVR, or when PAH is responsive to either vasodilator therapy or test occlusion of the defect. Patients should be treated in conjunction with providers who have expertise in the management of pulmonary hypertensive syndromes.

Closure of an ASD also is reasonable in the presence of paradoxical embolism and documented orthodeoxia-platypnea.

Closure of ASD should be considered in some cases as prophylaxis even if the defect is small. For example, patients who are professional divers or patients undergoing pacemaker implantation will benefit due to a reduced risk of paradoxical embolism.

Pregnancy and delivery are generally well tolerated, even by patients with an unclosed ASD with a significant left-to-right shunt. However, clinical symptoms may emerge during pregnancy or after childbirth. During pregnancy and delivery there is an increased risk of paradoxical embolism, regardless of the defect size. In our practice we close the defect before planned pregnancy, even if it is hemodynamically insignificant.

Contraindications for Percutaneous Closure of Secundum ASD

Small ASDs with a diameter of <5 mm and no evidence of right ventricular volume overload do not impact the natural history of the individual and do not require closure unless associated with paradoxical embolism.

An absolute contraindication for percutaneous ASD closure is the presence of severe and irreversible PAH, with no evidence of a left-to-right shunt. See Table 20-2 for a summary of the indications and contraindications to ASD closure.

Table 20-2

Indications and Contraindications to Atrial Septal Defect Closure

Indications

1. Symptoms or complications of an atrial septal defect (ASD)
2. Paradoxical embolism and documented orthodeoxia-platypnea
3. Prophylaxis for professional divers or those undergoing pacemaker implantation
4. Pregnancy and delivery

Contraindications

1. Small ASD (diameter <5 mm) and no evidence of right ventricular volume overload
2. Irreversible pulmonary hypertension
3. Other contraindications include the following:
   - Poor state of the patient with other serious conditions or comorbidities
   - Patients with associated cardiac anomalies requiring cardiac surgery
   - Patients with current systemic or local infection or sepsis within 1 month of device placement
   - Patients with bleeding disorder or with other contraindications to aspirin therapy, unless another antiplatelet drug can be administered for 6 months
   - Presence of intracardiac thrombus
   - Unsuitable defect anatomy including deficient rims, superior/inferior or posterior. Deficient anterior rim is not a contraindication for the use of percutaneous closure devices.
   - Patients allergic to nickel may suffer an allergic reaction. This is a relative contraindication. Most nickel allergies are contact reactions. It is unclear if intracardiac devices will mount a similar reaction. A consultation with an allergist may be needed.

Outcomes of ASD Closure

In patients undergoing successful ASD closure before they are 24 years of age, the long-term survival matches that seen in the general population. Significantly shorter survival in patients with pulmonary hypertension (PAP = 40 mmHg) after age 24 has been reported. Closure in patients over 40 years of age, while reducing mortality, improving symptoms, limiting functional deterioration, and limiting the incidence of heart failure compared with a conservatively managed control group, did not reduce arrhythmias or stroke on long-term follow-up. Independent predictors of mortality include functional NYHA Class III-IV, PAP > 40 mmHg and Qp/Qs > 3.5:1.

ASD Closure Devices

Currently the only two devices approved for the percutaneous closure of secundum ASD are the Amplatzer septal occluder and HELEX septal occluder device.

Amplatzer Septal Occluder (ASO)

The Amplatzer septal occluder (ASO) is a self-expandable double disc device made of nitinol (55% nickel, 45% titanium) wire mesh. The ASO is tightly woven into two flat discs (Fig. 20-1). There is a 3- to 4-mm connecting waist between the two discs, corresponding to the thickness of the atrial septum. Nitinol has super elastic properties, with shape memory. This allows the device to be stretched into an almost linear configuration and placed inside a small sheath for delivery and then return to its original configuration within the heart when not constrained by the sheath. The device size is determined by the diameter of its waist and is constructed in various sizes ranging from 4 to 40 mm (1-mm increments up to 20 mm; 2-mm increments up to the largest device currently available, 40 mm; the 40-mm size is not available in the United States). The two flat discs extend radially beyond the central waist to provide secure anchorage.

The LA disc is larger than the RA disc. For devices 4 to 10 mm in size, the LA disc is 12 mm and the RA disc is 8 mm larger than the waist. However, for devices larger than 11 mm and up to 32 mm in size, the LA disc is 14 mm and the RA disc is 10 mm larger than the connecting waist. For devices >32 mm, the LA disc is 16 mm larger than the waist and the RA disc is 10 mm larger than the waist. Both discs are angled slightly toward each other to ensure firm contact of the discs to the atrial septum.

A total of three Dacron polyester patches are sewn securely with polyester thread into each disc and the connecting waist to increase the thrombogenicity and endothelialization of the device. A stainless steel sleeve with a female thread is laser-welded to the RA disc. This sleeve is used to screw the delivery cable to the device. Each device costs US $5500.

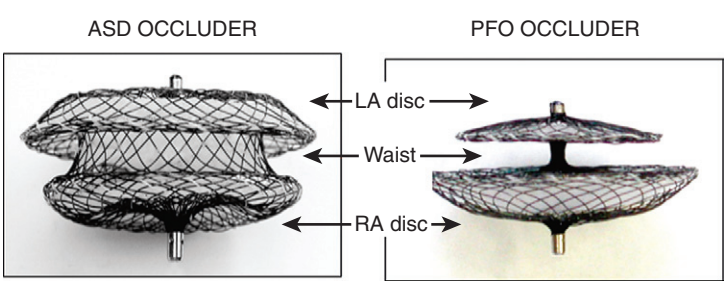

Figure 20-1 Amplatzer. Atrial septal defect occluder and patent foramen ovale occluder. *LA,* left atrial; *RA,* right atrial.

Table 20-3

Sheath Delivery System Sizing for Atrial Septal Defect Devices
6F delivery system for devices <10 mm in diameter
7F delivery system for devices 10–15 mm
8F sheath for devices 16–19 mm
9F sheath for devices 20–26 mm
10F sheath for devices 28–34 mm
12 F sheath for the 36-mm and 38-mm device
14 F sheath for the 40-mm device

Amplatzer Delivery System

For device deployment, we recommend using appropriately sized sheaths for the device as summarized in Table 20-3. The delivery system is supplied sterilized and separate from the device. It contains all the equipment needed to facilitate device deployment. It consists of the following:

1. Delivery sheath of specified French size and length, and appropriate dilator
2. Loading device, used to collapse the device and introduce it into the delivery sheath
3. Delivery cable (internal diameter [ID] 0.081 inch): the device is screwed onto its distal end allowing for loading for loading, placement, and retrieval of the device
4. Plastic Pin-vice: this facilitates unscrewing of the delivery cable from the device during device deployment
5. Tuohy Borst valve adapter with a side arm for the sheath, to act as a one-way stop-bleed valve

All delivery sheaths have a 45-degree angled tip. The 6F sheath has a length of 60 cm, the 7F sheath is available in lengths of 60 and 80 cm and the 8F, 9F, 10F, and 12F sheaths are all 80 cm long. The delivery system costs US $580.

Amplatzer Exchange (Rescue) System

This is made up of the same components as the Amplatzer delivery system except that the inner lumen and tip of the dilator can accommodate the delivery cable. It is available in two sizes: 9F (dilator ID 0.087 inch) and 12F (dilator ID 0.113 inch), with a 45-degree curve and 80 cm in length. The distal tip of the delivery cable can screw into the back of another delivery cable. This allows it to become an exchange length cable. The damaged sheath then can be removed and the rescue sheath with its dilator can be inserted over the cable to recapture the device. The exchange system costs $580.

Optional but Recommended Equipment

Amplatzer Sizing Balloon

The Amplatzer sizing balloon is a double-lumen balloon catheter with a 7F shaft size. The balloon is made from nylon and is very compliant, making it ideal for sizing the secundum ASD by flow occlusion ("stop-flow") without overstretching of the defect. The balloon catheter is angled at 45 degrees and there are radiopaque markers for calibration at 2, 5, and 10 mm. The balloon catheters are available in three sizes: 18 mm (maximum volume is 20 mm and is used for defects up to 20 mm); 24 mm (maximum volume 30 mL and used to size defects up to 22 mm); and 34 mm (maximum volume 90 mL and used to size defects up to 40 mm).

Table 20-4

Materials/Equipment Required for Transcatheter ASD Closure Procedures

Item	Size	Cost each (US$)
Amplatzer Septal Occluder	4–40 mm	5500
Amplatzer PFO Occluder	18, 25, 35 mm	5000
Amplatzer Delivery System	7–12F	580
Amplatzer Super Stiff exchange	0.035-inch, 100 cm length guidewire	45
Multipurpose catheter	6–7F	10
Amplatzer Sizing Balloon	24, 34 mm	265
Amplatzer Rescue System	9F, 12F	580

PFO, patent foremen ovale.

Amplatzer Super Stiff Guidewire

The 0.035-inch Amplatzer super stiff exchange guidewire is used to advance the delivery sheath and dilator into the left upper pulmonary vein. Table 20-4 summarizes all the necessary materials for ASD closure.

Step-by-Step Technique: Transcatheter Device Closure of Secundum ASD

Materials and Equipment

1. Single- or bi-plane cardiac catheterization laboratory
2. TEE or ICE
3. Full range of device sizes, delivery and exchange (rescue) systems, sizing balloons
4. A multipurpose catheter to engage the defect and the left upper pulmonary vein
5. Extra-stiff exchange length wire, for example, a 0.035-inch Amplatzer super stiff exchange length guidewire with a 1-cm floppy tip, but any extra-stiff J-tipped wire may be used.

Personnel

1. Interventional cardiologist appropriately proctored to perform device closure
2. Cardiologist (noninvasive) to facilitate TEE or ICE
3. Anesthesiologist if procedure is performed under TEE guidance
4. Nurse certified to administer conscious sedation if procedure is performed under ICE guidance
5. Catheterization laboratory technologists

Method

1. Preprocedure. Review all pertinent data relating to the patient and to the defect to be closed and ensure that appropriate devices and delivery systems are available. The procedure and complications should be explained and opportunity given to ask questions. All preprocedure orders should be given to the patient. Aspirin 81 to 325 mg should be started 48 hours prior to the procedure. If allergic to aspirin, clopidogrel 75 mg should be used.

2. Vascular Access. The right femoral vein is accessed using a 7F or 8F short sheath. An arterial monitoring line (e.g., 4F) can be inserted in the right femoral artery, especially if the patient's condition is marginal or if the procedure is performed under TEE and general endotracheal anesthesia. If a subclavian or internal jugular venous approach is used, it is very difficult to maneuver the device deployment, especially with large defects.

Heparin IV (e.g., 40U/kg) is given to achieve an activated clotting time (ACT) of more than 200 seconds at the time of device deployment. Antibiotic coverage for the procedure is recommended (e.g., cefazolin 1 g IV), the first dose at the time of procedure and two subsequent doses 6 to 8 hours apart.

3. Routine right heart catheterization should be performed in all cases to ensure presence of normal PVR. The left-to-right shunt can also be calculated.

4. Echocardiographic assessment of the secundum ASD is performed simultaneously using either TEE or ICE. Figure 20-2 demonstrates full assessment of the defect by ICE.

The important ASD rims to look for are:

- Superior/SVC rim—best achieved using the bicaval view
- Superior posterior/right upper pulmonary vein rim
- Anterior superior/aortic rim—the least important rim; often, patients lack it
- Inferior/IVC and coronary sinus rim—an important rim to have
- Posterior rim—seen best in the short-axis view at the aortic valve level

The rims must be sufficient (>5 mm) except for the anterior rim. A deficient anterior rim is not a contraindication to the procedure.

5. How to Cross the ASD. Use a multipurpose catheter. The MP A2 catheter has the ideal angle. Place the catheter at the junction of the IVC and the right atrium. The IVC angle should guide the catheter to the ASD. Keep a clockwise torque on the catheter while advancing it toward the septum (posterior). If unsuccessful, place the catheter in the SVC and slowly pull it into the right atrium; keep a clockwise posterior torque to orient the catheter along the atrial septum until it crosses the defect. TEE/ICE can be very useful to guide the catheter across difficult defects.

6. Perform a right upper pulmonary vein angiogram (Fig. 20-3*A*) in the hepatoclavicular projection (35-degree left anterior oblique/35-degree cranial). This delineates the anatomy, shape, and length of the septum. This may come in handy when the device is deployed but not

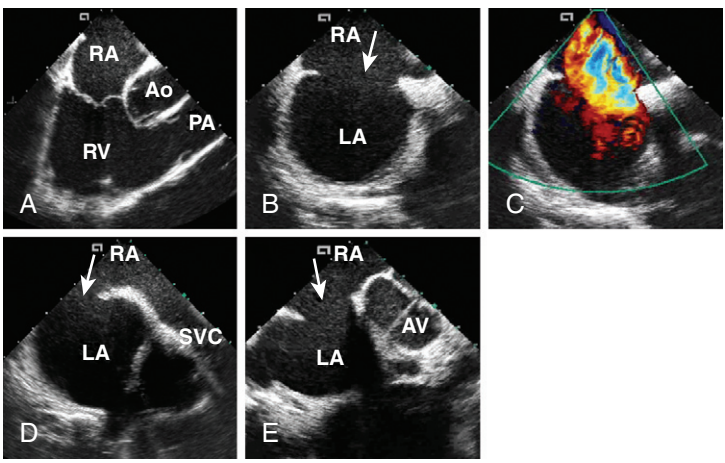

Figure 20-2 Intracardiac echocardiographic images in a patient with a large secundum atrial septal defect (ASD). **A,** Home view demonstrating the right atrium (RA), tricuspid valve, right ventricle (RV), aortic root (Ao) and pulmonary artery (PA). **B,** Septal view, demonstrating the large ASD (*arrow*), the RA and the left atrium (LA), and the superior and inferior rims. **C,** Same view with color Doppler. **D,** Caval view demonstrating the entire superior rim and the defect (*arrow*). **E,** Short-axis view demonstrating the defect (*arrow*), the aortic root, the absent anterior rim and good posterior rim, and both atria. *AV,* aortic valve *SVC,* superior vena cava.

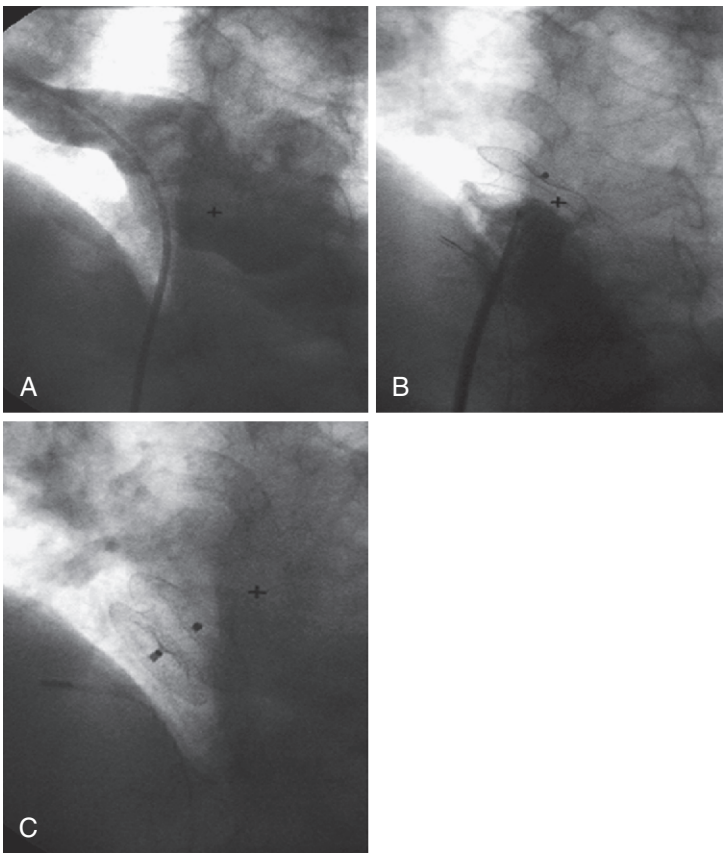

Figure 20-3 Cineangiographic images in a patient with secundum atrial septal defect (ASD). **A,** Angiogram in the right upper pulmonary vein in the hepatoclavicular projection (35 degrees left anterior oblique/35 degrees cranial) demonstrating left-to-right shunt. **B,** Angiogram in the right atrium in the hepatoclavicular projection prior to release of the device. Correct deployment manifest by opacification of the right atrial disc only and on levophase the left atrial disc only opacified. **C,** Cineangiographic image after the device has been released, demonstrating good device alignment with the septum.

released—the operator can position the imaging tube in the same view of the angiogram and compare the position of the device with that obtained during the deployment (Fig. 20-3*B, C*).

7. Defect Sizing. Position the multipurpose catheter in the left upper pulmonary vein. Prepare the appropriate size of balloon according to the manufacturer's guidelines. We prefer to use the 34-mm balloon because it is longer and during inflation it sits nicely across the defect. Pass an extra-stiff, floppy/J-tipped 0.035-inch exchange length guidewire (Fig. 20-4*A*). This gives the best support within the atrium for the balloon, especially in large defects. Remove the multipurpose catheter and the femoral sheath. We advance the sizing balloon catheter directly over the wire without a venous sheath. Most sizing balloons require an 8F or 9F sheath. The balloon catheter is advanced over the wire and placed across the defect under both fluoroscopic and echocardiographic guidance. The "stop-flow" balloon sizing is performed by inflating the balloon (previously prepared with 1:4 diluted contrast) until the left-to-right shunt ceases, as observed by color flow Doppler TEE/ICE. Once the shunt ceases, deflate the balloon slightly until shunt reappears. This "stop-flow" balloon sizing technique is used to select an ASO device size. The best echo view for measurement is to observe the balloon in its long axis (Fig. 20-4*B*). In this view the indentation made by the margins of the ASD can be visualized and precise measurement can be made.

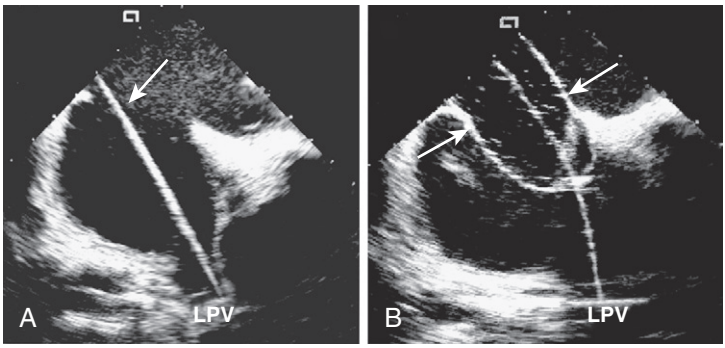

Figure 20-4 Intracardiac echocardiographic images of the patient in Figure 20-2, showing defect sizing. **A,** The exchange wire (*arrow*) across the defect into the left upper pulmonary vein (LPV). **B,** Sizing balloon occluding the defect. This is the stretched diameter (*arrows*) of the defect.

8. Fluoroscopic Measurement. Angulate the x-ray tube so the beam is perpendicular to the balloon. Various calibration markers can be helpful. Ensure that the markers are separated and discrete. Measure the balloon diameter at the site of the indentation (or at the middle of the balloon) as per the diagnostic function of the laboratory (Fig. 20-5). We have found that when a discrepancy exists between the echocardiographic and the fluoroscopic measurements, the echocardiographic measurement is usually more accurate.

Once the size has been determined, deflate the balloon and pull it back into the junction of the right atrium and IVC, leaving the wire in the left upper pulmonary vein.

Recheck the ACT and give the first dose of antibiotics.

9. Device Selection. If the defect has adequate rims (>5 mm), select a device ≤2 mm larger than the "stop-flow" diameter of the balloon. However, if the superior/anterior rim is deficient (5–7 mm), we tend to select a device 4 mm larger than the balloon "stop-flow" diameter.

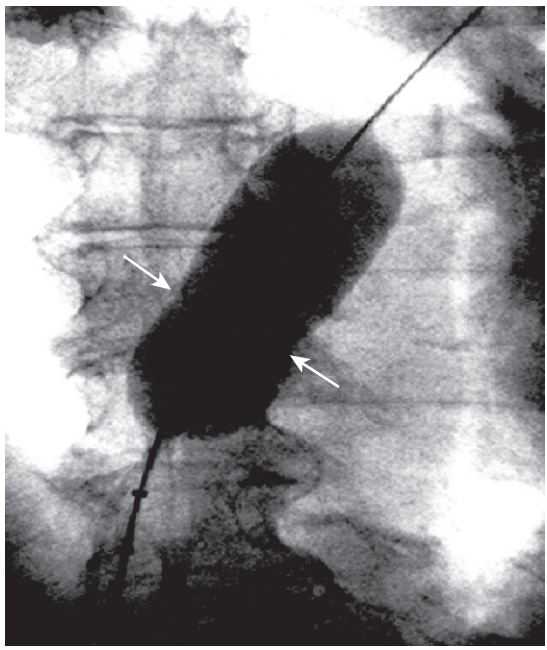

Figure 20-5 Cineangiographic image of the patient in Figure 20.3 during balloon sizing of the defect, demonstrating the stretched diameter (*arrows*) of the defect.

10. Device Delivery. Open the appropriate-sized delivery system. Flush the sheath and dilator. The delivery sheath is advanced over the guidewire to the left upper pulmonary vein (Fig. 20-6*A*). Both dilator and wire are removed, keeping the tip of the sheath inside the left upper pulmonary vein. Use extra care and do not allow air inside the delivery sheath. An alternative technique to minimize air embolism is passage of the sheath with the dilator over the wire until the IVC, at which point the dilator is removed and the sheath is advanced over the wire into the left atrium while continuously flushing the side arm of the sheath.

On the back table, the ASO device is then screwed to the tip of the delivery cable, immersed in normal saline to clear air bubbles, and drawn into the loader while under water injecting saline through the side arm of the loading sheath to expel air bubbles out of the system. A Y connector is applied to the proximal end of the loader to allow flushing with saline. The loader containing the device is attached to the proximal hub of the delivery sheath with a fluid-to-fluid connection. The cable with the ASO device is advanced to the distal tip of the sheath, taking care not to rotate the cable while advancing it in the long sheath to prevent premature unscrewing of the device. Both cable and delivery sheath are pulled back as one unit to the middle of the left atrium. Position of the sheath can be verified using fluoroscopy or TEE/ICE.

11. Device Deployment. The LA disc is deployed first under fluoroscopic and/or echocardiographic guidance by pulling back the sheath, while leaving the disc fixed in the LA away from the LA appendage (Fig. 20-6*B*). Part of the connecting waist should be deployed in the left atrium, very close (a few millimeters) to the atrial septum (the mechanism of ASD closure using the ASO is stenting of the defect). While applying constant tension on the entire assembly and withdrawing the delivery sheath off the cable, the connecting waist and the RA disc are deployed in the ASD itself and in the right atrium respectively (Fig. 20-6*C*).

12. Device Positioning. Proper device position can be verified using different techniques:

Fluoroscopy in the same projection as that of the angiogram. Good device position is evident by the presence of two discs that are parallel to each other and separated from each other by the atrial septum. In the same view the operator can perform the "Minnesota wiggle" (the cable

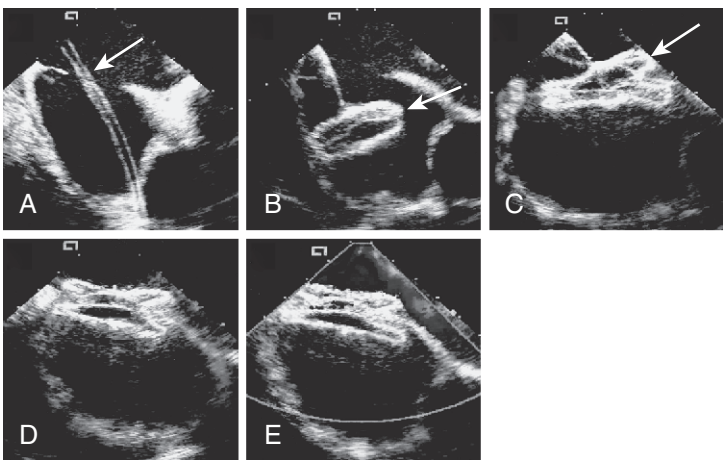

Figure 20-6 Intracardiac echocardiographic images of the patient in Figure 20-2, showing device delivery and deployment. **A,** Delivery sheath (*arrow*) across the defect into the left upper pulmonary vein. **B,** The left atrial disc (*arrow*) deployed in the left atrium. **C,** The right atrial disc (*arrow*) deployed in the right atrium. **D,** The device released, demonstrating good position. **E,** Color Doppler demonstrating no residual shunt and patent superior vena cava.

is pushed gently forward and pulled backward). Stable device position manifests by the lack of movement of the device in either direction.

TEE/ICE. The echocardiographer should make sure that one disc is in each chamber. The long-axis view should be sufficient to evaluate the superior and inferior part of the septum and the short-axis view for the anterior and posterior part of the disc (Fig. 20-6*D,E*).

Angiography. This is done with the camera in the same projection as for the first angiogram to profile the septum and device using either the side arm of the delivery sheath or a separate angiographic catheter, inserted in the sheath used for ICE or via a separate puncture site. Good device position manifests by opacification of the RA disc alone when the contrast is in the right atrium and opacification of the LA disc alone on pulmonary levophase.

If the position of the device is questionable, the device can be recaptured, entirely or partly, and repositioned following similar steps.

13. Device Release. Once the device position is verified, the device is released by counterclockwise rotation of the delivery cable using a pin vise. There is often a notable change in the angle of the device as it is released from the slight tension of the delivery cable and it self-centers within the ASD and aligns with the interatrial septum. To assess the results of closure, repeat TEE/ICE, color Doppler, and angiography (optional) in the four-chamber projection in the right atrium with pulmonary levophase are performed. Once the procedure is complete, recheck the ACT and, if appropriate, remove the sheath and achieve hemostasis. If ACT is above 250 seconds, reverse the effect of heparin by using protamine sulfate.

14. Postprocedure Care. Patients receive a dose of an appropriate antibiotic (commonly cefazolin 1 g) during the catheterization procedure and two further doses at 8-hour intervals. Patients are also asked to take endocarditis prophylaxis when necessary for 6 months after the procedure, as well as aspirin 81 to 325 mg orally once daily for 6 months. In addition, we have been adding 75 mg clopidogrel for 2 to 3 months. We have observed that the incidence of postclosure headaches is much less in those patients taking the clopidogrel. The patient is asked not to engage in contact sports for 1 month after the procedure. Full activity, including competitive sports, is usually allowed after 4 weeks of implantation. Magnetic resonance imaging (if required) can be performed any time after implantation.

15. Postprocedure Monitoring. Patients recover overnight in a telemetry ward. Some patients may experience an increase in atrial ectopic beats. Rarely, some patients may have sustained atrial tachycardias. The following day an ECG, a chest x-ray [optional] (posteroanterior and lateral), and a TTE with color Doppler should be performed to assess the position of the device and presence of residual shunt.

Recheck ECG, chest x-ray, and TTE/TEE at 6 months after the procedure to assess everything. If the device position is good with no residual shunt, antibiotic prophylaxis and aspirin can be discontinued. Clinical follow-up can be annually for the first 2 years, then every 3 to 5 years thereafter. Long-term follow-up of device performance should be assessed and any new information communicated to the patient.

Troubleshooting

Air Embolism. Meticulous technique should be used to prevent air entry. The sheath should be positioned at the mouth of the left upper pulmonary vein. Doing so allows free flow of blood into the sheath. Forceful negative pressure should not be applied to aspirate the sheath. If a large amount of air is introduced on the left side, it will usually pool in the right coronary sinus and right coronary artery. This may manifest with bradycardia, asystole, or profound hypotension. If this occurs, immediately place a right coronary catheter in the right coronary sinus and forcefully inject saline or contrast to displace the air and hence reperfuse the right coronary system.

Cobra-Head Formation. This describes the situation when the left disc maintains a high profile when deployed, mimicking a cobra head. This can occur if the left disc is opened in the pulmonary vein or the LA appendage, or if the left atrium is too small to accommodate the device. It can also occur if the device is defective or has been loaded with unusual strain on it. If this occurs, check the site of deployment; if appropriate, recapture the device and remove and inspect it. If the "cobra head" forms outside the body, use a different device. If the disc forms normally, try deploying the device again. Do not release a device if the left disc has a "cobra-head" appearance.

Device Embolization. If a device embolizes, it must be retrieved, preferably by transcatheter snare and a long sheath, otherwise by surgery. The transcatheter technique is difficult and should not be performed if the operator is inexperienced in snaring techniques. Furthermore, the catheter laboratory should be equipped with large Mullins-type sheaths (12F–16F) and also should have various-sized snares. We use the Gooseneck Snare (ev3, Plymouth, MN) or the EN Snare (Merit Medical, Salt Lake City, UT). The device should not be pulled across valves, since it may damage the chordae and leaflets. Always use a long sheath to pull the device outside the body. To snare a device, we usually use a sheath that is two French sizes larger than the sheath that was used to deliver the device. On rare occasions, if the LA disc cannot be collapsed inside the sheath, another snare is introduced from the right internal jugular vein to snare the stud of the microscrew of the LA disc and stretch it toward the internal jugular vein while the assistant pulls the device with the snare toward the femoral vein. This allows the device to collapse further and come out of the sheath in the femoral vein.

Prolapse of the Left Disc Across the Defect During Deployment. On occasion, especially in patients with large defects with deficient anterior/superior rims, when the left disc is deployed it opens perpendicular to the plane of the atrial septum and prolapses through the anterior superior part of the defect. To overcome this problem, use a device that is at 4 mm larger than the measured "stop-flow" balloon diameter. If this is not possible or it does not work, change the angle of the deployment by placing the sheath either in the left or right upper pulmonary vein rather than mid left atrium. This may change the orientation of the disc. Another potential solution is to use the Hausdorf sheath (Cook Medical, Bloomington, IN), which has two posterior curves at the end. This sine curve can be quite useful in changing the deployment angle.

The use of the dilator technique or balloon-assisted technique is also helpful in preventing prolapse of the LA disc to the right. The dilator technique implies the use of a long dilator from the contralateral femoral vein to hold the LA disc in the left atrium while the assistant/operator deploys the remainder of the device. The balloon-assisted technique is similar to the dilator technique. A guidewire is positioned in the left upper pulmonary vein from the contralateral femoral vein. A balloon is inflated in the right atrium very close to the septum. The device is deployed in the usual fashion. The presence of the balloon will prevent prolapse of the left disc. Once the device has been deployed, the balloon is deflated slowly. After complete deflation, the guidewire is pulled out carefully from the left atrium.

Recapture of the Device. To achieve the smallest sheath size for device delivery, the sheath wall thickness is small, with a resultant decrease in strength. To recapture a device prior to its release, the operator should hold the sheath at the groin with the left hand and, with the right hand, pull the delivery cable forcefully inside the sheath. If the sheath is damaged or kinked (accordion effect), use the exchange (rescue) system to change the damaged sheath. First, extend the length of the cable by screwing the tip of the rescue cable to the proximal end of the cable attached to the device. Then remove the sheath or, if the

sheath is 9F or 12F, introduce the dilator of the rescue system over the cable inside the sheath until it reaches a few centimeters from the tip of the sheath. This dilator will significantly strengthen the sheath, allowing the operator to pull back the cable with the dilator as one unit inside it. Then the operator can decide what to do next (change the entire sheath system or the device).

Release of the Device With a Prominent Eustachian Valve. To avoid the possibility of cable entrapment during release, advance the sheath to the hub of the right disc. Then release the cable and immediately draw back inside the sheath before the position of the sheath is changed.

Closure of Multiple Secundum ASD. If two defects are present and separated by more than 7 mm from each other, cross each defect separately. Size each one and then leave a delivery system in each defect. Initially deploy the smaller device, then the larger device, and release sequentially, starting with the smaller one.

If there are multiple fenestrations, use the Amplatzer multi-fenestrated septal occluder–"Cribriform" (these devices are similar in design to the Amplatzer PFO occluder except that the two discs are equal in size). The device should be deployed in the middle of the septum so that it can cover all fenestrations.

Complications

In the U.S. phase II trial comparing device closure to open surgical closure, the incidence of complications was 7.2% for device closure, far less than what was encountered when using an open surgical technique (24%). Most complications were related to rhythm disturbances, with very few patients requiring long-term medical therapy. Complications included the following:

1. Device embolization, the majority of which were encountered during the early learning curve of the investigators.
2. Heart block: rarely reported. Most likely related to the use of an oversized device.
3. Atrial arrhythmia: significant increase in atrial arrhythmias following device placement, generally resolving by 6 months.
4. Headaches: reported in about 5% of patients following device placement, resolving within 6 months. The use of clopidogrel for 2 to 3 months after device closure has minimized this complication significantly.

Results

Closure rates have been similar to those achieved by open surgical results. However, patients who underwent device closure were somewhat older than those who underwent open surgical closure. Furthermore, the cost of device closure was much less than open surgical closure and the length of hospital stay was shorter (1 day) for the device group than the surgical group (3.4 days). In a study by Kim and Hijazi, the mean cost for transcatheter closure was $11,541 whereas for surgical closure it was $21,780.

HELEX Septal Occluder Device

The Gore HELEX septal occluder device (WL Gore & Associates, Flagstaff, AZ) is a non-self-centering double-disc device made of nitinol and expanded polytetrafluoroethylene (ePTFE) (Fig. 20-7). The device is designed such that, following introduction across the septum, one disc is constituted on the LA side and the other on the RA side of the septum. The construction of the device consists of a curtain of ePTFE (gore-tex, WL Gore & Associates Flagstaff, Arizona)

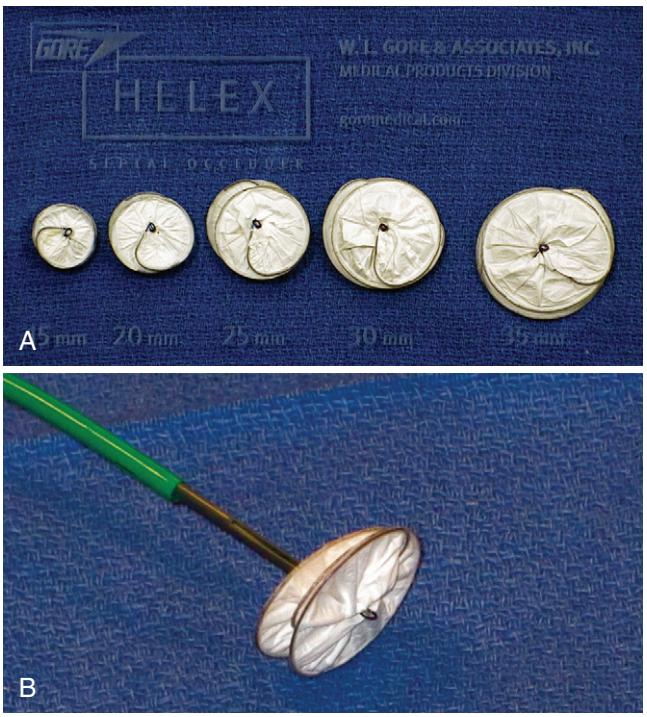

Figure 20-7 **A,** HELEX atrial septal defect (ASD) closure devices of various sizes. **B,** Closeup view of attached HELEX device to delivery cable.

bonded to a single-piece wire frame of nitinol (0.012 inch). The nitinol is manufactured into a helical pattern of opposing rotations which, on full configuration, assumes two parallel discs. The device is delivered through its own composite triaxial 10 F delivery catheter with a workable length of 75 cm. This obviates the need for a long transseptal sheath. For patent foramen ovale (PFO) closure, the delivery system can be "monorailed" through a hole close to its distal end using a wire placed through a diagnostic catheter positioned in one of the left pulmonary veins. The device is available in 15-, 20-, 25-, 30- and 35-mm diameters. The devices are delivered through a short 10 F femoral vein sheath; however, if using the monorail technique, a short 11F or 12F femoral sheath is required.

The HELEX device is designed to be flexible and atraumatic, molding itself to the atrial septum and contiguous structures, rendering it particularly appealing for use in a growing heart. Similarly the proven low thrombogenicity of ePTFE imparts confidence in delivering devices on the systemic side of the circulation (left atrium). This is of particular relevance in closure of the PFO where there are implications of thrombotic events to the systemic circulation, producing transient ischemic attacks and strokes. ePTFE has been used in various formats as patches and vascular tubes in the growing heart for almost 30 years and thus has proven longevity and biocompatibility with rapid endothelialization characteristics. Studies particular to the HELEX device have confirmed this excellent biocompatibility.

Patient Selection

The HELEX occluder is designed to occlude only the central (secundum) type ASD. The morphology of secundum ASDs is variable, and multiple defects, fenestrated, and aneurysmal ASDs can be closed using this device. A deficient anterior superior rim, where there is a lack of effacement of the atrial septum at the aorta, can also be accommodated by relative oversizing of the device.

With a non–self-centering device, a device-to-defect diameter ratio of 1.8-2:1 is recommended for ASD closure. With the largest available HELEX device being 35 mm, the largest diameter defect that would be closable would be in the range of 18 to 19 mm. In addition, children with large ASDs tend to have a relatively small left atrium; our experience has shown that the 30- and 35-mm devices do not sit effectively on the LA side of the septum in children weighing less than 25 kg. Operators should also be aware that defects measuring more than 15 mm on a standard TTE will balloon to size 18 mm or more and be unsuitable for the HELEX device.

Technique of Closure

Anesthesia. In children, general anesthesia is required, usually with endotracheal intubation. In adults, conscious sedation can be used if ICE is used; if TEE is planned, general anesthesia is required. In our practice we use ICE exclusively because it has excellent image quality and because endotracheal intubation can be avoided.

Vascular Access. Venous access is established in a manner similar to that described for the ASO device. Heparin 100 U/kg is administered intravenously. A hemodynamic study is performed to assess the shunt and pulmonary artery pressure and resistance. Echocardiography demonstrates the morphology of the ASD with respect to size, margins, proximity to the aorta, and atrioventricular valves. At this stage, multiple defects, not apparent on transthoracic echo, may be imaged, as well as fenestrations and aneurysms of the septum.

The same steps for the ASO are used when placing the HELEX occluder device. However, for device size, we use a device size that is 1.8-2:1 the size of the "balloon diameter."

Loading the Device. The HELEX device is supplied with its own delivery catheter (Fig. 20-8*A*) such that a long Mullins-type sheath is not necessary. The delivery system consists of three distal coaxial components transitioning to a parallel component arrangement at the proximal Y-arm hub: a 10 F green delivery catheter, a gray control catheter, and a tan mandrel (Fig. 20-8*B*). The proximal end of the control catheter

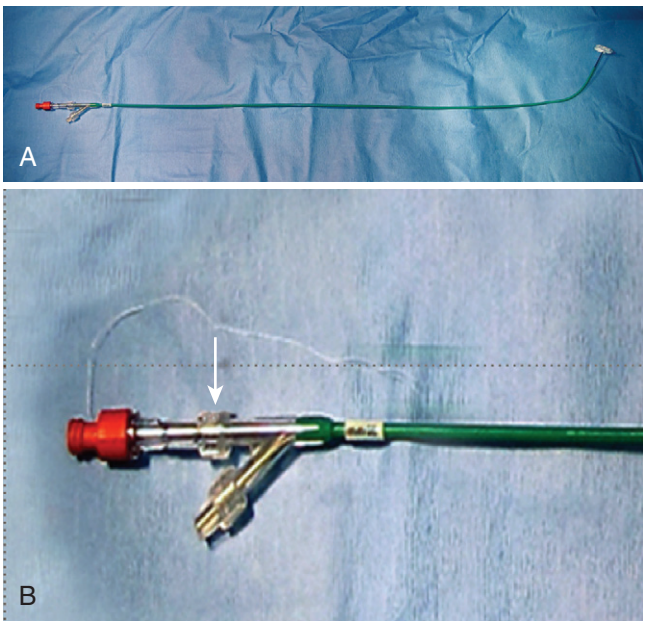

Figure 20-8 **A,** HELEX delivery device. **B,** Tuohy Borst Y connector for HELEX device.

exits the Y-arm hub and is terminated by a red retrieval cord cap. The proximal end of the mandrel exits the side port of the Y-arm hub and is terminated by a clear Luer-Lok. The control catheter is equipped with a retrieval cord if occluder repositioning or retrieval is deemed necessary (Fig. 20-8*B*). A 0.035-inch guidewire channel is incorporated into the distal end of the delivery catheter.

Loading the Occluder Into the Green Delivery Catheter. Remove the device from the sterile tray. Discard the sterile tray and follow the following steps:

1. To reduce the chance of air entrapment in the delivery system, loading of the occluder should be conducted with the occluder and catheter tip submerged in a heparinized saline bath.
2. Fill a large volume (20–30 mL) syringe with heparinized saline.
3. Attach the syringe to the red retrieval cord cap.
4. Tighten the mandrel Luer-Lok.
5. Loosen the control catheter Luer-Lok.
6. Flush the control catheter into the bowl or sterile tray.
7. When the initial flushing is completed, draw back on the gray control catheter with the attached syringe until only about 3 cm of the occluder remains outside the delivery catheter and the tan mandrel appears slightly curved (Fig. 20-9*A*).
8. Loosen the mandrel Luer-Lok.
9. Complete loading by continuing to draw back on the gray control catheter hub until the entire occluder has been withdrawn into the green delivery catheter (Fig. 20-9*B*).
10. Flush the control catheter into the bowl or sterile tray.
11. Keep the flushing syringe attached to the red cap to prevent the entrance of air into the delivery system until the catheter tip is placed inside the introducer sheath.

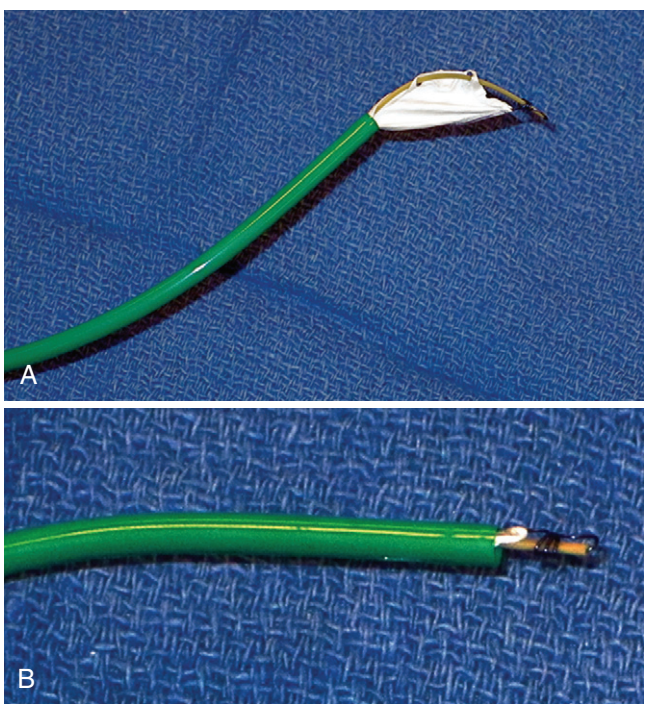

Figure 20-9 A, Pulling the HELEX device into the delivery sheath. **B,** Captured HELEX device.

Device Delivery. Load the delivery catheter onto a guidewire through the guidewire port from the luminal surface out; ensure that the occluder is sufficiently withdrawn into the green delivery catheter to avoid interference with the guidewire (monorail system) (Fig. 20-10*A*). Load the delivery system into the appropriately sized introducer sheath. At this stage, remove the flushing syringe. Verify that the red retrieval cord cap affixing the retrieval cord is securely attached to the gray control catheter.

Deployment

LA Disc Deployment

1. Under direct fluoroscopic visualization, advance the catheter tip across the ASD until the radiopaque marker at the tip of the green delivery catheter is positioned within the middle left atrium. Verify that the tip of the green delivery catheter is across the defect and away from the LA appendage using TEE or ICE.
2. At this stage, the guidewire should be removed before attempting to deploy the occluder.
3. Use the following "push-pinch-pull" method to deploy the LA occluder disc:
   (a) Push the gray control catheter, moving the occluder into the LA chamber off of the septum but do not push against the atrial wall, or if the chamber space is adequate, push until the tan mandrel Luer-Lok stops against the Y-arm hub (approximately 2 cm).
   (b) While holding the green delivery catheter to maintain position, pinch the gray control catheter.
   (c) Then pull the tan mandrel back approximately 2 cm or less to form exposed segment of occluder. Repeat the "push-pinch-pull" sequence until the center eyelet exits the green delivery catheter tip demarcated by the radiopaque marker (Fig. 20-10*B*, 20-11*A*).
4. Once the LA disc is deployed, hold the entire system as one unit and pull it back until the LA disc is in contact with the atrial septum under echocardiographic and fluoroscopic guidance.

RA Disc Deployment

1. To prepare for RA disc deployment, hold the gray control catheter in a fixed position and gently expose a portion of the RA side by withdrawing the green delivery catheter until the mandrel Luer-Lok stops on the Y-arm hub. Tighten the mandrel Luer-Lok.
2. Deploy the RA disc by holding the green delivery catheter in a fixed position with left hand and pushing the gray control catheter with the right hand until the control catheter Luer-Lok contacts the Y-arm hub. Then tighten the control catheter Luer-Lok.
3. Confirm that both left and right discs appear planar and apposed to the septum with septal tissue trapped between the discs (Figs. 20-10*C*, 20-11*B*).

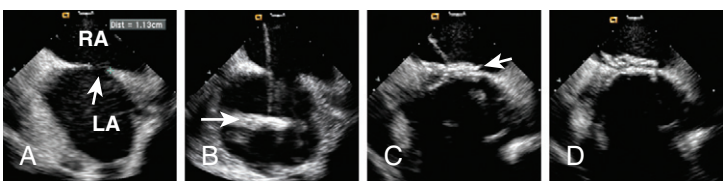

Figure 20-10 Intracardiac echocardiography in patient with atrial septal defect (ASD). **A,** Septal view, demonstrating the ASD (*arrow*), the right and left atria, and the superior and inferior rims. **B,** The left atrial disc (*arrow*) deployed in the left atrium. **C,** The right atrial disc (*arrow*) deployed in the right atrium. **D,** The device released, demonstrating good position.

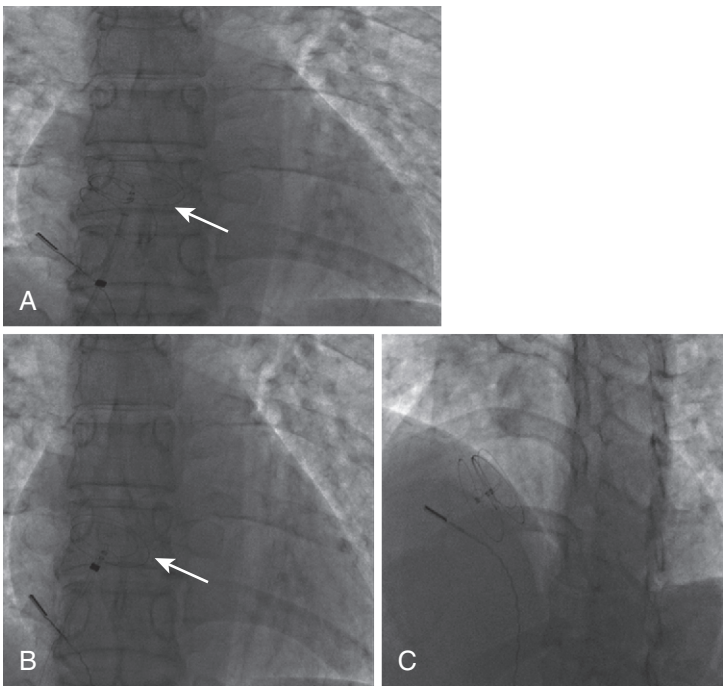

Figure 20-11 Cineangiographic image in the patient whose ICE is shown in Fig. 20-10. **A,** The left atrial disc (*arrow*) deployed in the left atrium. **B,** The right atrial disc (*arrow*) deployed in the right atrium. **C,** The device released, demonstrating good position.

4. Confirm proper position using TEE/ICE and angiography in the LAO-cranial (35-35) position (Figs. 20-10*D*, 20-11*C*). If the position is not correct, refer to the repositioning steps later in this chapter.
5. Completely remove the red retrieval cord cap and set it aside.

Occluder Lock and Release

1. It is important to note that the occluder can only be repositioned prior to lock release.
2. If position and occlusion are acceptable, loosen the mandrel Luer-Lok. Hold the green delivery catheter in a fixed position and release the lock by sharply pulling the tan mandrel at least 2 cm.
3. At the completion of the lock and release step, the occluder is still loosely attached to the gray control catheter by the retrieval cord. If the occluder position is not acceptable, refer to the section titled "Removing the Occluder With the Retrieval Cord," later in this chapter. Once the delivery system is withdrawn (next step), the occluder cannot be removed using the delivery system.
4. If position is acceptable, remove the entire delivery system as a single unit, making sure the retrieval cord moves smoothly through the control catheter hub.

Repositioning the Occluder

1. Replace and tighten the red retrieval cord cap and tighten the mandrel Luer-Lok.
2. Repeat steps mentioned in the earlier section "Loading the Occluder Into the Green Delivery Catheter" in order to bring the occluder back into the catheter.
3. Reposition across the defect.
4. Repeat steps listed in the "Deployment" section (earlier in this chapter).

5. During repositioning, if increased force is required to move the catheter components due to abnormal conditions (such as a kinked mandrel, curved mandrel-lock loop or premature lock release), remove the occluder and delivery system entirely and utilize a new device.

Removing the Occluder With the Retrieval Cord

1. If the lock is released and if the retrieval cord is still attached to the gray control catheter, the occluder can be removed by taking up any slack in the retrieval cord and securely reattaching the red retrieval cord cap.
2. Position the green delivery catheter in the right atrium. Withdraw the gray control catheter while pulling the occluder into a linear form and drawing the occluder back into the green delivery catheter.
3. Do not use excessive force in an attempt to withdraw all of the occluder into the green delivery catheter. Doing so could cause the retrieval cord to break or result in occluder fracture.

- *Note:* Without the mandrel to support the wire frame of the occluder, the operator must ensure that the lock loop and eyelets do not catch on the delivery catheter tip or introducer sheath. If the lock loop or eyelet catch and the delivery system are forcibly retracted, the retrieval cord or wire frame is at risk of fracture.

4. Normal removal practices withdraw 50% to 100% of the occluder into the green delivery catheter. If a portion of the locked or unlocked occluder remains outside of the delivery catheter, the control catheter and delivery catheter should be withdrawn together. If necessary, remove the introducer sheath and occluder together.

If the occluder is removed, it should be disposed of and a new occluder should be used to complete the procedure.

Recapture

1. In the event that the occluder is malpositioned or embolized, it can be recaptured with the aid of a loop snare. A long sheath (≥10 F) positioned close to the device is recommended for recapture.
2. Place the loop snare around any portion of the occluder frame.
3. Pull the occluder into the sheath using the snare. If a portion of the occluder frame cannot be retracted into the long sheath, it may be necessary to remove the occluder, loop snare, and long sheath as one unit.
4. Bring the recaptured occluder into the sheath to avoid pulling the unlocked device across valve tissue.

Postprocedure Management

See recommendations for ASO procedure (earlier in this chapter).

Complications

Serious complications following HELEX closure of an ASD are rare. Embolization occurs, but almost always the device can be retrieved using a snare device and a long 10F sheath. Wire fractures have been seen in a small percentage of patients (about 5%–6%) and are usually of no clinical consequence as the wire is held secure by the fabric of the device and its comprehensive endothelialization.

Results

Early experience has demonstrated the ease of use of this device, its complete retrievability, and excellent closure of small to moderate ASDs in children.

Results of the U.S. Multicenter Pivotal Study of the HELEX Septal Occluder for Percutaneous Closure of Secundum ASDs showed that closure of ASD with the HELEX septal occluder is safe and effective when compared with surgical repair, with reduced anesthesia time and hospital stay. Clinical success was achieved in 91.7% (100 of 109) of

device patients and in 83.7% (72 of 86) of surgical control patients. The most common major adverse event for the HELEX septal occluder group was device embolization requiring catheter retrieval (1.7%); in the surgery group, it was post-pericardiotomy syndrome (6.3%), including one death due to tamponade.

Patent Foramen Ovale

A PFO is part of normal fetal development. Following birth, an increase in pulmonary blood flow, and higher LA relative to RA pressure, the foramen ovale physiologically closes. The foramen is created by the overlap of the septum primum and septum secundum (Fig. 20-12) and fuses closed in latter life. This anatomy can behave like a flap valve, opening if the RA pressure exceeds the LA pressure. Pathologic studies have suggested that the foramen ovale may be probe-patent in 25% of the population.

There are three anatomical types:

1. "Flap" type
2. Tunnel type
3. Aneurysmal septum primum with a PFO

Clinical Significance

A PFO is a potential source for right-to-left intracardiac shunt and can result in paradoxical emboli. Presentation is usually in the third or fourth decade of life and rarely in adolescence.

Cerebrovascular Accident

Paradoxical emboli crossing the PFO with associated neurologic deficits (or stroke), or other systemic events are the most easily recognized manifestations of PFO. Cryptogenic stroke (stroke with no identifiable cause) accounts for 40% of stroke in young adults. Contrast echocardiography has demonstrated a higher than normal prevalence of PFO in cryptogenic stroke patients younger than 55 years old. In addition, the presence of an aneurysmal septum primum with a PFO enhances the

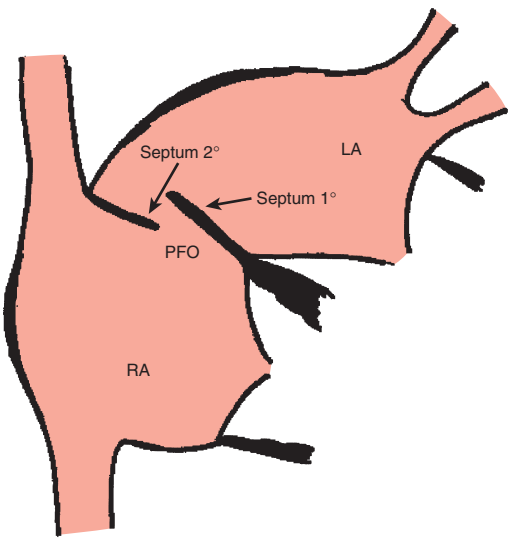

Figure 20-12 Schematic sketch demonstrating the patent foramen ovale (PFO) as a flaplike structure created between septum primum (1°) and septum secundum (2°).

risk of stroke. The presence of a prominent eustachian valve of the IVC has also been postulated to enhance the risk for paradoxical emboli, although no clear evidence exists for this hypothesis.

The recently reported PFO in Cryptogenic Stroke Study provides data from a large cohort of patients in a prospective manner. A PFO was present in 39% of the patients with cryptogenic stroke compared to 29% in patients with an identifiable cause for the stroke. Large PFOs (≥2 mm separation between septum primum and secundum or ≥10 microbubbles appearing in the left atrium with a contrast TEE) were present in 20% of the cryptogenic group versus 9.7% of the patients with an identifiable cause for their stroke.

Risk of Recurrence After a Presumed Cryptogenic Transient Ischemic Attack or Stroke

A recurrence risk of 3% to 5% has been reported in most series with medical management of embolic stroke. However, the Warfarin-Aspirin Recurrent Stroke Study (WARSS) yielded a recurrent event or death over a 2-year period of 15% with warfarin and 17% with aspirin when the subset of patients with cryptogenic stroke only was analyzed. The Mayo Clinic reported a 4.1% recurrence rate of any neurologic event following surgical closure of PFO. It is likely that a percentage of these represent patients in whom the hypothesis that their problem resulted from a paradoxical embolus was incorrect.

Divers

An interesting group of PFO patients are those who are deep-sea or scuba divers. This population may report decompression sickness with unusual symptoms despite following an appropriate and rigid protocol during a dive ascent. An incidence of neurologic symptoms as high as 61% has been reported. Decompression problems have also led to more brain defects in individuals with PFO than without.

Migraine

Migraine has a higher prevalence in patients with PFO—57% in one study. PFOs are a potential cause of postoperative complications in surgical procedures prone to venous fat or air embolism. Migraine headaches are not yet an approved indication for PFO closure.

Conditions Increasing Right-to-Left Shunt

Conditions associated with elevated RA pressure will enhance the potential for a right-to-left shunt. For example, chronic restrictive pulmonary or recurrent pulmonary embolus, hypercoagulable states, prothrombin gene G20210A, factor V Leiden mutations, anticardiolipin antibodies, protein S and C deficiencies, and thrombocytosis may promote venous thrombosis and increase the chance of a paradoxical embolus occurring.

Transcatheter Closure of PFO

Two devices are currently designed to specifically close PFO: the Amplatzer PFO occluder and the PFO Star devices. The CardioSEAL (NMT Medical) and the HELEX (WL Gore & Associates) were designed for ASD closure; however, they have also been used for PFO closure.

The Amplatzer PFO occluder is a self-expanding, double-disc device made from a nitinol wire mesh (see Fig. 20-1). The nitinol mesh wire is 0.005 to 0.006 inches in diameter.

The two discs are linked together by a connecting waist 2 mm in diameter and 4 mm in length. This thin waist allows free motion of each disc so that the device can conform to the PFO shape and position the two discs in the plane of the atrial septum. The discs are filled with a polyester fabric sewn securely to each disc by a polyester thread. The polyester

increases the closing ability of the device by trapping blood, thus forming the initial plug and promoting the endothelialization of the device.

The devices are available in three sizes, 18, 25, and 35 mm, corresponding to the diameter of the right disc. The diameter of the left disc is 18 mm for the 18- and 25-mm devices and 25 mm for the 35-mm device. The connecting waist is the same for both—2 mm in diameter and 4 mm in length. The devices are packaged individually and supplied sterilized ready for use. The device costs $5000.

Amplatzer Delivery System

This is the same as the secundum ASD delivery systems and the PFO occluder devices will deploy through a 7 F to 9 F sheath. The delivery system costs $580. The device is available in the United States and is under a clinical trial protocol.

Contraindications

See contraindications for secundum ASD device closure.

Step-by-Step Technique: Transcatheter Closure of PFO:

Materials, Equipment, and Personnel

These are the same as for secundum ASD. The preprocedure evaluation is also the same.

Vascular Access

Place a 7F sheath in the right femoral vein. An arterial monitoring line can be useful if the procedure is performed under TEE with general anesthesia. Administer a full heparin dose and administer antibiotics as for secundum ASD. Perform a right heart hemodynamic study. Perform a TEE/ICE to assess the anatomy of the PFO and to perform a contrast bubble study with and without Valsalva maneuver.

Some operators determine the septal length and the distance of the surrounding structures, especially the free wall of the atrium. The type of PFO—simple flap type, tunnel type, or PFO with an aneurysmal septum primum—may influence device selection.

Suggested Measurements With TEE/ICE Images

1. Total septal length and edge of the defect to the mitral valve in the four-chamber view
2. SVC to the edge of the defect (long-axis TEE view/caval view by ICE)
3. Edge of defect to the aorta in short-axis view. Do not implant a device if the distance either from the defect to the SVC or from defect to the aortic root is < 9 mm.

Device Selection

For defects without an aneurysmal septum primum use the 18- or 25-mm device, depending on the length of the septum. If there is a significant aneurysm or if the septum primum appears very thin and floppy, use the 35-mm device as long as the distance from the SVC to the edge of the defect and from the edge of the defect to the aortic root is >17.5 mm. If there is an aneurysm and the distance from the edge of the defect to either SVC or aortic root is between 12.5 and 17.5 mm, the 25-mm device should be used.

Procedure Steps

The procedure is identical to that described for secundum ASD except that balloon sizing is not performed. Prior to device release, careful reassessment of the edge of the device along the free atrial wall by TEE/ICE

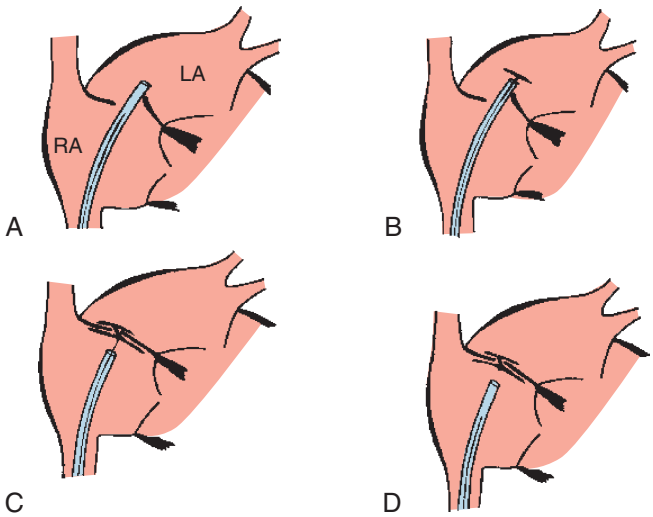

Figure 20-13 Schematic demonstration of patent foramen ovale (PFO) closure using the Amplatzer PFO occluder. **A,** Sheath in mid left atrium. **B,** Deployment of left atrial disc. **C,** Deployment of connecting waist and right atrial disc. **D,** Device released.

is needed. Do not release the device if it does not conform to its original configuration or if it appears unstable. In this case the operator should recapture and redeploy the device. Figures 20-13 and 20-14 demonstrate the steps of PFO closure.

Postprocedure follow-up is similar to that for secundum ASD closure except that most investigators maintain 81 to 325 mg aspirin per day for 6 months in combination with an antiplatelet agent, usually clopidogrel 75 mg/day, for 1 to 6 months. Follow-up echocardiogram at 3 to 6 months should include assessment for right-to-left atrial level shunt with a venous contrast injection, with Valsalva maneuver. (Figs. 20-15, 20-16)

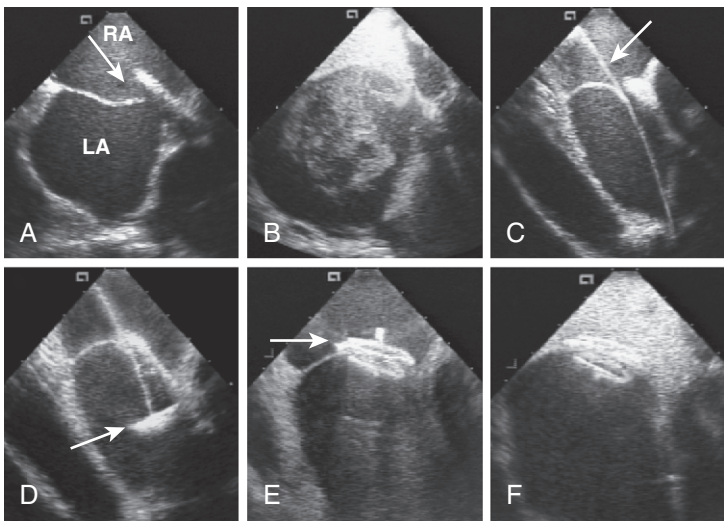

Figure 20-14 Intracardiac echocardiographic images in a young patient who has a patent foramen ovale (PFO), demonstrating the steps of closure. **A,** Septal view demonstrating the PFO (*arrow*) and the thin septum primum. **B,** Contrast bubble study demonstrating significant right-to-left shunt. **C,** Guidewire (*arrow*) positioned through the defect into the left pulmonary vein. **D,** Deployment of atrial the left disc (*arrow*). **E,** Deployment of the right atrial disc (*arrow*); release of the device. **F,** Contrast bubble study repeated after the device has been released, demonstrating successful closure.

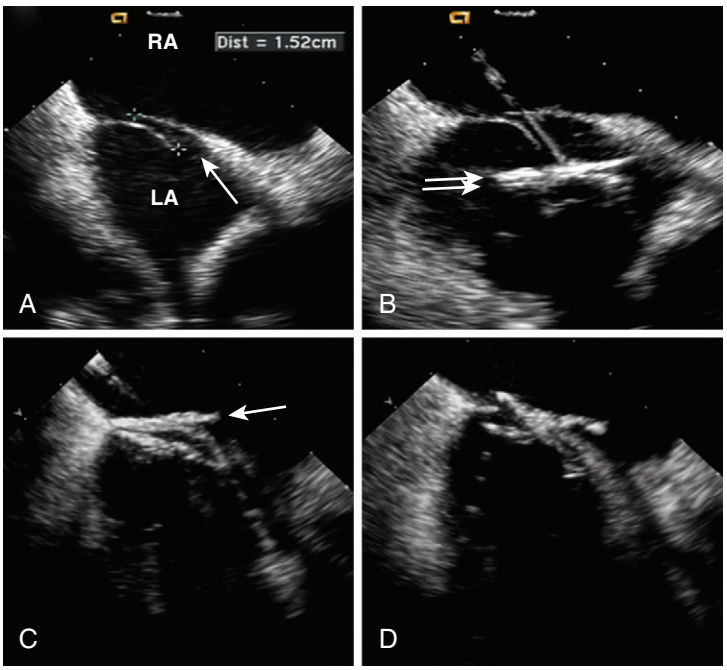

Figure 20-15 Intracardiac echocardiography in a patient with patent foramen ovale (PFO). **A,** Septal view, demonstrating the PFO (*arrow*) and the thin septum primum. **B,** The left atrial disc (*arrow*) deployed in the left atrium. **C,** The right atrial disc (*arrow*) deployed in the right atrium. **D,** The device released, demonstrating good position.

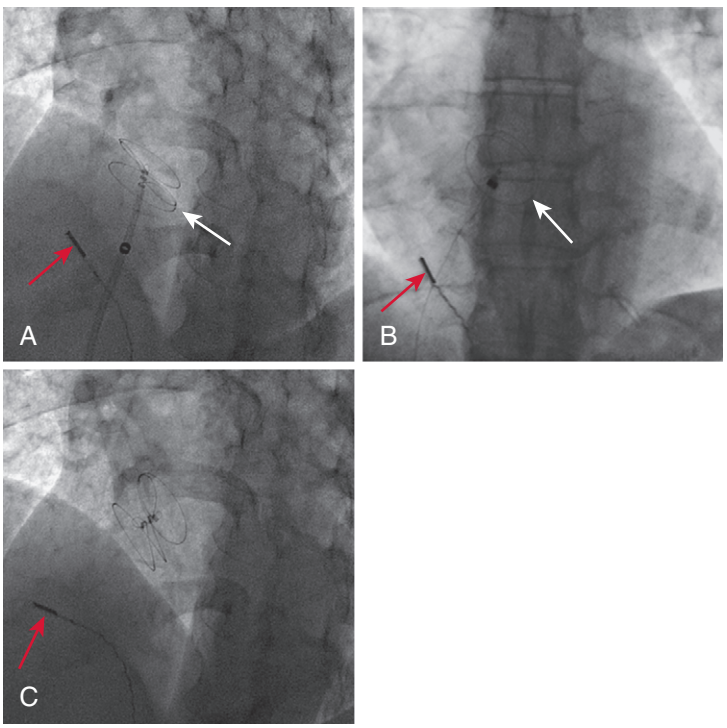

Figure 20-16 Cineangiographic image of the patient whose intracardiac echocardiogram is shown in Figure 20-15. **A,** The left atrial disc (*white arrow*) deployed in the left atrium. **B,** The right atrial disc deployed in the right atrium. **C,** The device released, demonstrating good position. Red arrow shows position of intracardiac echo transducer.

Complications

RA and Aortic Perforation. A total of two patients in the worldwide data (none in the United States) had this complication. There was one case report by Trepel *et al.* in a patient who presented with pericardial tamponade. At surgery, erosion of the RA roof and aortic root was noted. Following this report, the company introduced the septal measurements, emphasizing the distance of the free RA wall from the defect/device.

Entrapment of Prominent Eustachian Valve on the Delivery Cable. This caused no problems with device delivery and release but part of the eustachian valve was avulsed. To avoid this, prior to release, advance the sheath to the hub of the right side disc.

Results

During phase I of the U.S. clinical Helix trial for ASD, closure rates were in excess of 95% at 3 to 6 months follow-up. There were no complications related to the device. The length of hospital stay was about 1 day. No episodes of atrial arrhythmias have been reported.

PFO Closure With HELEX Occluder Device

The HELEX device, with its characteristics of flexibility, low profile, and low thrombogenicity, make it an eminently suitable device with which to close the PFO in patients with cryptogenic stroke. The device is suited to all types of PFO except perhaps those associated with a long flaplike tunnel in excess of 8 mm from the RA to LA aspect. The device is being evaluated in a randomized study against continued medical therapy for the prevention of stroke recurrence. The name of the trial is REDUCE. Closure rates approach 100%, and thrombus formation and recurrent cerebrovascular events have been very low.

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21

Interventions for Failing Hemodialysis Access

JOHN A. BITTL

During the past decade, the management of failing hemodialysis accesses has shifted from surgical repair to catheter-based approaches. The advantages of endovascular approaches over surgery include the avoidance of temporary hemodialysis catheters, the preservation of venous segments for future access creation, and the prolongation of total survival time on hemodialysis. This chapter reviews the mechanisms of dialysis access failure and describes the interventional management of failing and thrombosed fistulas and grafts.

Timing of Procedure

An emergency fistulogram should be performed for refractory access-site bleeding after hemodialysis. Emergency angiography and intervention are also indicated for failing or thrombosed hemodialysis accesses in patients with hyperkalemia, volume overload, or refractory hypertension.

Urgent catheter-based treatment is indicated for patients with thrombosed hemodialysis accesses. Delays in treatment more than 24 hours after diagnosis or more than 48 hours after hemodialysis may require temporary catheter placement or increase the risks of complications. Urgent angiography should also be performed for malfunctioning but nonthrombosed dialysis accesses because thrombosis may be imminent.

Contraindications to percutaneous treatment include graft infection, a central right-to-left shunt, or pulmonary hypertension. A relative contraindication to catheter-based therapy is thrombosis of new fistula or graft within 30 days of surgical creation or revision. In this situation, thrombosis has likely arisen from a technical problem or anatomy not amenable to catheter-based therapy.

Hemodialysis Access Anatomy

An autogenous arteriovenous access is surgically created by directly anastomosing a native outflow vein (Fig. 21-1) to a native inflow artery (Fig. 21-2), usually in the form of an end-to-side anastomosis. A prosthetic arteriovenous access is constructed by surgically interposing a segment of polytetrafluoroethylene (PTFE) between a native artery and a native vein in either a straight or looped configuration. Common patterns include the brachial-cephalic configuration in the forearm or the brachial-basilic configuration in the upper arm (Fig. 21-3). For the purposes of this chapter, an autogenous arteriovenous access will be referred to as a *fistula,* a prosthetic arteriovenous access as a *graft,* and when mentioned together, both types will be referred to as *accesses*.

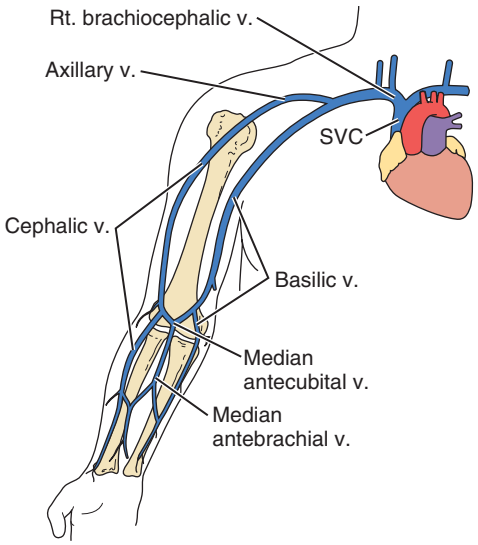

Figure 21-1 Venous anatomy of the upper extremity. *Rt,* right; *SVC,* superior vena cava; *v*, vein. (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3:1–11, with permission from Elsevier.)

The selection of a particular permanent hemodialysis access creation is based on the principle of "Fistula First," which is derived from evidence favoring the creation of an autogenous fistula whenever possible before resorting to a PTFE graft. The selection of a specific location is based on the recommended sequence of using the nondominant arm before the dominant arm, the forearm before the upper arm, and the upper extremity before the lower extremity.

Mechanisms of Hemodialysis Access Failure

Although the primary patency of fistulas is low, autogenous fistulas have better long-term patency than prosthetic grafts. After surgical creation, <50% of fistulas mature adequately to support hemodialysis. When fistulas mature adequately, they remain patent for a median of 3 to

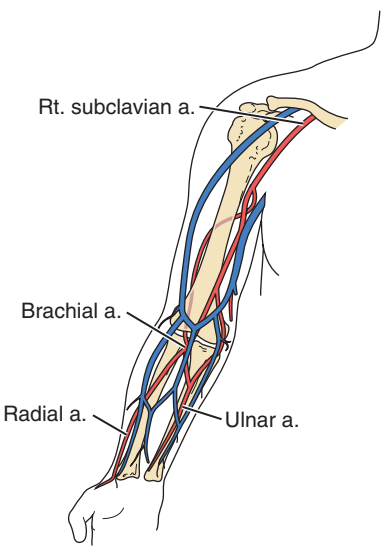

Figure 21-2 Pertinent arterial anatomy of the upper extremity. *a,* artery; *Rt.,* right. (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3:1–11, with permission from Elsevier.)

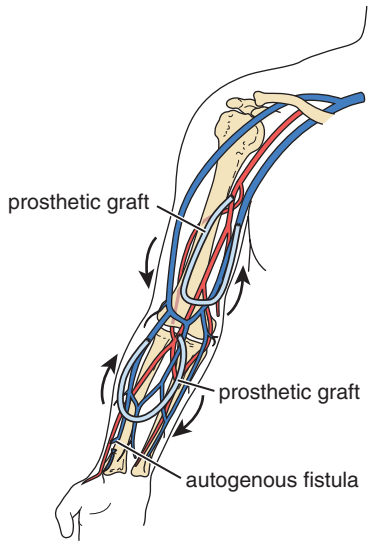

Figure 21-3 Access anatomy of the upper extremity. A radial-cephalic fistula is created by an end-to-side anastomosis between the cephalic vein and the radial artery, with ligation of the distal stump of the cephalic vein. A brachial-cephalic graft in the forearm (*lower arm arrows*) requires the surgical interposition of a polytetrafluoroethylene (PTFE) loop using end-to-side connections. A brachial-basilic graft in the upper arm (*upper arm arrows*) requires the surgical insertion of a PTFE loop using end-to-side connections. (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3:1–11, with permission from Elsevier.)

7 years. The primary patency of PTFE grafts exceeds 80%, but prosthetic accesses remain patent for only 12 to 18 months.

Two failure modes of fistulas and grafts are amenable to interventional treatment (Fig. 21-4). An inflow stenosis in newly placed fistulas may inhibit physiologic hypertrophy and maturation. An outflow stenosis in chronically used fistulas and grafts may cause high pressures and thrombosis. Although 50% of malfunctioning accesses ultimately undergo thrombosis, this is not the primary cause of failure. Instead, shear stress and fibromuscular hyperplasia of the outflow vein causes a progressively worsening stenosis, which then leads to stasis and eventual thrombosis (see Fig. 21-4).

Stenoses can occur anywhere in a dialysis access, but the most common location is the anastomosis between the prosthetic graft and the outflow vein. Although fistulas contain no outflow anastomosis, they are also susceptible to stenosis formation in the outflow vein.

Hemodialysis Access Monitoring, Surveillance, and Testing

Monitoring refers to regular physical examination and the assessment of dialysis adequacy. A well-functioning fistula or graft should have a prominent thrill, loud medium-pitched bruit, and minimal pulsation. A soft bruit suggests the presence of an inflow stenosis,

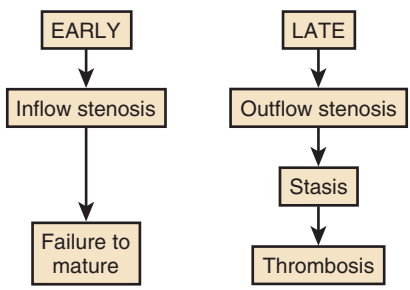

Figure 21-4 Pathogenesis of dialysis access failure. The early appearance of an inflow (anastomotic) stenosis may lead to failure of fistula maturation. The late development of a stenosis in the outflow segment of a fistula or graft is the cause of stasis and access thrombosis. (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3:1–11, with permission from Elsevier.)

whereas a prominent pulsation, short but high-pitched bruit, or aneurysmal dilatation suggests the presence of an outflow stenosis. Marked arm edema suggests the presence of dual venous obstruction (cephalic and basilic) or a subclavian vein stenosis or occlusion.

Surveillance entails the use of noninvasive testing. The finding of rising pressures of >150 mm Hg at a constant flow of 200 mL/min on dialysis suggests the presence of an outflow stenosis. Estimating the recirculation fraction using urea concentrations or clinical parameters such as body weight, volume status, or serum potassium concentration suggests that a malfunctioning access is causing incomplete hemodialysis. The uncertain benefits of preemptive graft intervention have tempered enthusiasm for routine noninvasive surveillance using Doppler ultrasound.

At the time of angiography and intervention, hemodynamic measurements may help to assess procedural success. An inflow stenosis may reduce access pressures to <15 mm Hg and prevent adequate filling. An outflow stenosis may increase access pressures to arterial levels. The ideal systolic pressure of an access should be <50 mm Hg, and the optimal ratio of systolic pressure in the access to systolic systemic pressure should be 0.30 to 0.40.

A significant stenosis is defined by the presence of at least a 50% diameter stenosis. A successful endovascular intervention is defined by the ability to complete at least one dialysis session.

Procedures

The term *fistulogram* refers to the angiographic study of either an autogenous arteriovenous fistula or a prosthetic arteriovenous graft. Before an angiographic procedure is performed, aspirin 325 mg may be given orally. Clopidogrel can be substituted in aspirin-allergic patients. During the treatment of thrombosed accesses, heparin is usually given intravenously in a dose of 5000 units. Lower doses of heparin can be used or heparin can be omitted if the risk of bleeding or perforation is increased. Antibiotic prophylaxis with cephalothin 1 g intravenously is commonly recommended. If an allergy to cephalosporins exists, vancomycin 1 g intravenously can be substituted and given over 1 hour. Warfarin is recommended for secondary prevention of access thrombosis if no stenosis is found.

Thrombosed Accesses

A four-step procedure is recommended.

1. Thrombectomy

Two 6F sheaths are placed within the access: one in the direction of the venous outflow and one in the direction of the arterial inflow (Fig. 21-5). Sheath insertion is carried out by inserting 18-gauge needles into the occluded fistula or graft near the usual entry sites, which are identified by needle tracks and induration. As the thrombosed access is entered, a "pop" may be felt as the needle penetrates the dura. Although no flashback is seen and no blood can be aspirated from a thrombosed access, intravascular entry is confirmed by smooth guidewire advancement under fluoroscopy. It is important to avoid puncturing the back wall of the graft, because an extrinsic hematoma may cause extrinsic compression. It is important to avoid injecting contrast into a thrombosed access, because thrombus may dislodge and embolize. An alternative approach is to begin with a 4F micropuncture set (Cook, Bloomington, IN).

Although the method is called the "cross-sheath" technique, the tips of the sheaths face each other but do not actually overlap (Fig. 21-5). Two 150-cm 0.018-inch V-18 hydrophilic control wires

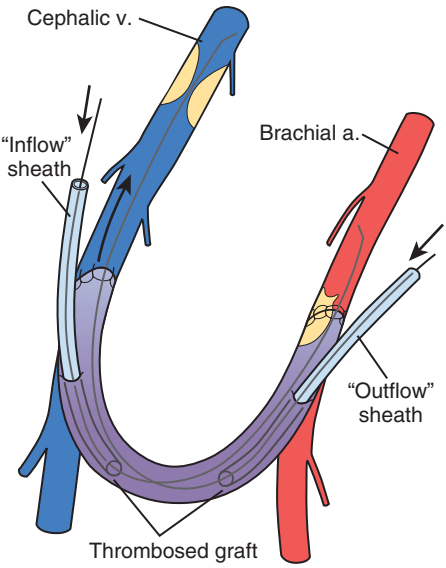

Figure 21-5 Cross-sheath method. A 6F sheath is inserted into the access near the arterial inflow anastomosis and directed into the direction of the outflow, and a 6F sheath is inserted into the access near the venous outflow in the direction of the inflow. Guidewires are advanced in the direction of the inflow and outflow under fluoroscopic guidance. No contrast is injected into a thrombosed access. *a,* artery; *v,* vein. (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3:1–11, with permission from Elsevier.)

(Boston Scientific Medi-Tech, Miami, FL) are advanced through the sheaths under fluoroscopic guidance without contrast injections, one in the outflow direction and one in the inflow direction. If it is difficult to identify or advance the wire beyond the outflow stenosis or to enter the inflow artery, a 65-cm 5F multipurpose A1 catheter (Cordis, Miami Lakes, FL) can be inserted for additional maneuverability. The resistant stenosis can usually be penetrated with a 0.035-inch hydrophilic curved wire and replaced with a 0.018-inch guidewire for thrombectomy.

Several thrombectomy devices are available, including the AngioJet AVX rheolytic thrombectomy catheter (Possis Medical, Minneapolis, MN), pulse-spray infusion catheters (Cook, Bloomington, IN), pulse-spray side-slit catheters (AngioDynamics, Glens Falls, NY), the Amplatz Thrombectomy Device (Microvena, White Bear Lake, MN), the Arrow-Trerotola Percutaneous Thrombectomy Device (Arrow International, Reading, PA), and the Gelbfish Endo-Vac device (Neovascular Technologies, New York, NY).

Thrombectomy is carried out first in the outflow direction (Fig. 21-6) and then in the inflow direction (Fig. 21-7). When the blunt edge of the opposing sheath blocks advancement of the rheolytic thrombectomy catheter, transient insertion of the sheath dilator in the opposing sheath may present a smoother transition for passage of the thrombectomy catheter.

After successful thrombectomy restores flow, the access sheaths are flushed with heparinized saline, and angiography can be safely performed to delineate the outflow stenosis.

2. Angioplasty

Venous angioplasty of the culprit outflow stenosis entails the use of 4- to 10-mm balloons (Fig. 21-8). The venous stenoses tend to be fibrotic, may be resistant to dilatation, and occasionally require pressures >20 atm. High-pressure, noncompliant balloons with rated burst pressures of 20 to 24 atm can be used (Conquest or Dorado, Bard Peripheral Vascular, Tempe, AZ). Cutting balloons can be used when high-pressure balloons are unsuccessful (Boston Scientific), but the use of peripheral cutting balloons in one study was associated with an increased risk of rupture. Stents are usually reserved for severe recoil, venous perforations, or stenoses in surgically inaccessible veins, but the use of stent grafts will likely increase in an effort to reduce restenosis.

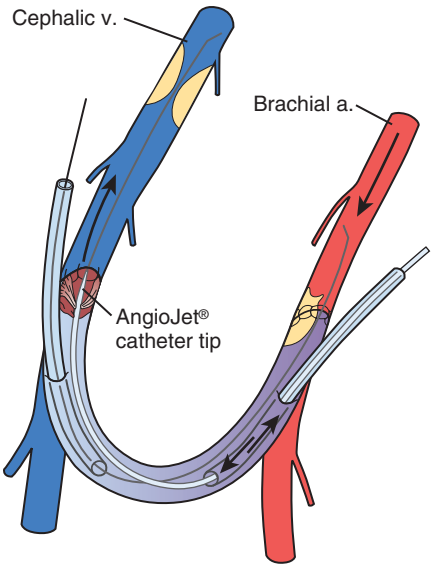

Figure 21-6 Rheolytic thrombectomy of venous outflow. *a,* artery; *v,* vein. (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3:1–11, with permission from Elsevier.)

3. Fogarty Thrombectomy

Fogarty thrombectomy using an over-the-wire 4F Thru-Lumen Embolectomy Catheter (Edwards Lifesciences, Irvine, CA) is recommended in almost all cases to extract resistant thrombus at the arterial inflow (Fig. 21-9). The catheter must be withdrawn forcefully to dislodge the resistant thrombus. Persistent thrombosis is most successfully treated with repeat Fogarty thrombectomy of the inflow. If this fails and the access continues to have low pressure, balloon angioplasty of the arterial inflow anastomosis with a 6-mm dilatation catheter can be tried. An approach of last resort is to perform balloon angioplasty along the entire length of the access.

4. Central Venography

Venography of the entire venous outflow and central veins is necessary to rule out the presence of a central stenosis. Treatment of incidental central vein stenoses remains controversial. Angioplasty or

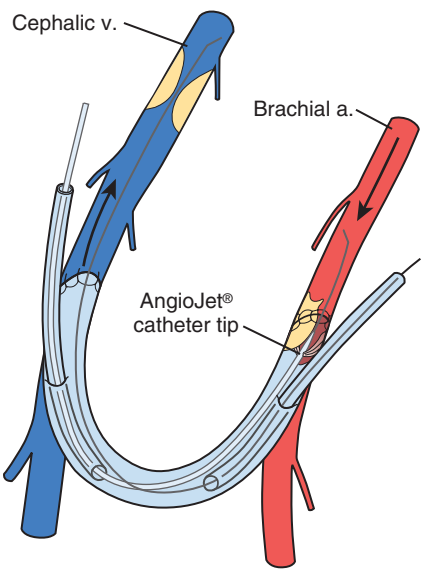

Figure 21-7 Rheolytic thrombectomy of arterial inflow. *a,* artery; *v,* vein. (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3:1–11, with permission from Elsevier.)

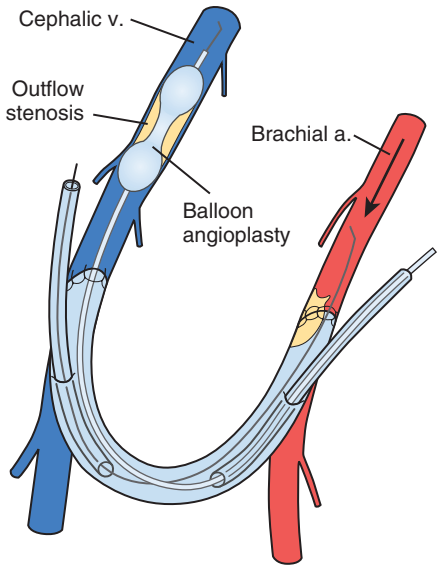

Figure 21-8 Balloon dilatation of outflow stenosis. The outflow stenosis is commonly found at or near the venous outflow anastomosis but can be encountered anywhere in the peripheral vein. *a,* artery; *v,* vein. (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3: 1–11, with permission from Elsevier.)

stenting of asymptomatic stenoses may be associated with more rapid stenosis progression and escalation of lesions compared with the strategy of watchful waiting. If treatment of a central-vein stenosis is recommended, it requires large-diameter such the XXL(Boston Scientific Medi-Tech, Natick, MA), Atlas(Bard, Tempe, AZ), or SMART Control stent (Cordis, Miami, FL) up to 14 mm in diameter.

Nonthrombosed Accesses

For nonthrombosed fistulas and grafts, an abbreviated endovascular approach is used. A diagnostic fistulogram can usually be obtained through a 4F micropuncture catheter placed in either direction. The catheter should be directed toward the inflow if the fistula is hypoplastic. The catheter should be directed toward the outflow if the access has been chronically used for hemodialysis and demonstrates signs of increased pressure.

When a stenosis is identified, angioplasty can be carried out through the 4F micropuncture sheath using a coronary balloon (Maverick, Boston Scientific, Natick, MA) or through 4F or 5F sheaths using peripheral monorail balloons (Sterling, Boston Scientific Medi-Tech, Miami, FL). If ultra-high-pressure balloons are needed, larger sheaths may be required. An uncommon cause of low fistula or graft

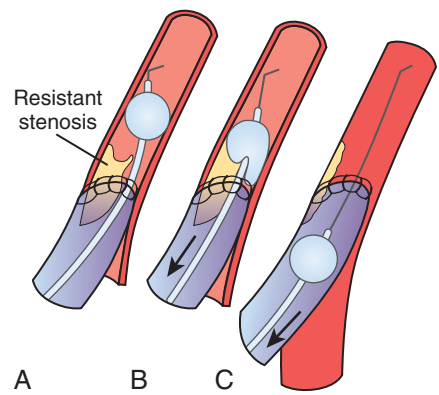

Figure 21-9 Fogarty embolectomy. The balloon catheter is inflated (*A*), pulled back to the thrombus (*B*), and forcefully withdrawn to mechanically dislodge the resistant inflow stenosis (*C*). (Reprinted from Bittl JA. Catheter interventions for hemodialysis fistulas and grafts. *JACC Cardiovasc Interv* 2010;3:1–11, with permission from Elsevier.)

pressure is a stenosis within the native inflow artery. When a patient has an occluded radial artery and has a fistula perfused via the ulnar artery and palmar arch, retrograde advancement of a coronary angioplasty balloon may be required.

Patients can be referred immediately for hemodialysis or discharged to home within 30 minutes of completion of the procedure. Sutures placed for hemostasis should be removed in 24 to 48 hours.

Success Rates and Complications

The acute success rate for endovascular treatment depends on access type and the mechanism of failure. The published success rates for thrombosed fistulas range from 78% to 87%, and the success rates for thrombosed grafts range from 93% to 96%. A high proportion of unsuccessful procedures may involve hypoplastic fistulas that failed to mature, of which only about 50% are ultimately able to be used for hemodialysis.

Long-term patency after endovascular treatment also depends on access type and the presence of thrombosis. Six-month patency rates after endovascular treatment range from 61% to 66%, and the 1-year patency rates range from 38% to 41%. Fistulas have longer median patencies than grafts unless thrombosis has occurred, in which case the median patencies are approximately 3 months for both types of accesses.

Complications from endovascular treatment of dialysis access failure are rare but usually mild and controllable. Hematomas can be categorized as minor and non-flow limiting, large and flow limiting, or massive and associated with pulsatile extravasation or free perforation. Free-flowing rupture usually requires firm compression and placement of a VIABAHN endoprosthesis (WL Gore & Associates, Flagstaff, AZ), Fluency Plus Tracheobronchial StentGraft (Bard Peripheral Vascular), or polyethylene teryltolate-covered stent (WallGraft, Boston Scientific, Natick, MA) after upsizing to an 11F sheath. Pinhole perforations can usually be controlled by manual compression alone or with suture placement. Venous ruptures have occurred in about 0.9% of hemodialysis interventions.

Other complications include catheter or device breakage requiring retrieval with snares. Arterial embolization requires Fogarty thrombectomy or surgical treatment. Pulmonary embolism is rare after endovascular treatment of thrombosed accesses. No scintigraphic evidence of pulmonary embolism was seen in one systematic evaluation after various catheter-based approaches to treat thrombosed dialysis accesses.

Several experimental methods are under investigation to enhance the long-term patency of arteriovenous grafts by targeting intimal hyperplasia in the venous outflow. External beam radiation has been tried, but in a small series of patients this method was unable to reduce the likelihood of repeat restenosis. The concept of endothelial cell seeding of PTFE grafts has also been investigated, but this paradoxically increased neointimal hyperplasia at the outflow anastomosis.

Suggested Readings

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