JOURNAL REVIEW AUG 2021

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MILRINONE AS COMPARED WITH DOBUTAMINE IN THE TREATMENT OF CARDIOGENIC SHOCK

NEJM Aug 2021

The two agents have unique mechanisms of action. Milrinone is a phosphodiesterase 3 inhibitor that increases cardiac inotropy, peripheral vasodilation, whereas dobutamine is a synthetic catecholamine that acts as a β_1- and β_2-receptor agonist and improves blood pressure by increasing cardiac output.

Anecdotal data favored milrinone over dobutamine with regard to its effect on atrial arrhythmias, postmyocardial infarction (MI) ischemia, and right ventricular failure, but randomized clinical trials are lacking

- In the DoReMi study, the authors randomized 192 patients admitted to single academic institution with CS
  - 80% SCAI class “C”; Society for Cardiovascular Angiography and Interventions cardiogenic shock classification
  - 68% on vasopressors at randomization;
  - 67% ischemic etiology;
  - 8% with right ventricular dominant shock
- to either blinded milrinone or dobutamine and titrated according to a standardized dosing scale based on clinical judgement.

PRIMARY OUTCOME

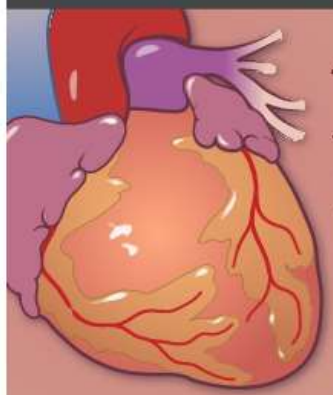
- a composite of
- all-cause in-hospital death
- resuscitated cardiac arrest
- cardiac transplant or mechanical circulatory support
- Nonfatal MI
- TIA or stroke
- renal replacement therapy

it was similar in both groups (49% milrinone vs 54% dobutamine; RR, 0.90, 95% CI, 0.69–1.19; P = .47).

The NEW ENGLAND JOURNAL of MEDICINE

Milrinone vs. Dobutamine in Cardiogenic Shock

DOUBLE-BLIND, RANDOMIZED TRIAL



192

Patients admitted to the cardiac ICU with cardiogenic shock

Milrinone
N=96

Dobutamine
N=96

In-hospital death from any cause, TIA, stroke, or cardiovascular or renal events

49%
47 patients

54%
52 patients

Relative risk, 0.90; 95% CI, 0.69–1.19; P=0.47

No between-group difference was observed in the primary composite outcome or in important secondary outcomes.

R. Mathew et al. 10.1056/NEJMoa2026845

- No difference in the individual components of the primary outcome.
- No differences in prespecified subgroups, including age, etiology of shock, ventricular function, baseline renal function, or baseline vasopressor use.

LIMITATIONS

- Single-center design that may limit external generalizability
- Sample size assumed a large 20% difference in treatment effect. Thus, it is likely underpowered for the primary outcome and in prespecified subgroups.

- This trial might play an essential role in changing our day-by-day practice but remains to be confirmed

RETURN HOSPITAL ADMISSIONS AMONG 1419 COVID-19 PATIENTS DISCHARGED FROM FIVE U.S. EMERGENCY DEPARTMENTS

Academic Emergency Medicine
A GLOBAL JOURNAL OF EMERGENCY CARE

27 August 2020

Department of Emergency Medicine, Center for Emergency Care Policy and Research, Perelman School of Medicine at the University of Pennsylvania

It is not known how often and which patients with COVID-19 return to the hospital following initial evaluation in the ED. To date, prediction models have focused on the risk of critical illness among hospitalized patients. In this study, we describe the incidence/characteristics of return hospital admission within 72 hours for patients with COVID-19 who were discharged from the ED upon initial presentation.

- retrospective cohort study of adult patients with COVID-19 discharged from five distinct hospital EDs within a multihospital health system spanning Pennsylvania and New Jersey March 1 to May 28, 2020
- included in the study cohort if they tested positive for COVID-19 within 7 days before or after the ED encounter
- primary outcome was inpatient admission or observation within 72 hours of the index ED encounter
- Covariates included patient age, sex, and race/ethnicity, hypertension, diabetes, and obesity. chest radiograph findings, in two categories: 1) normal or not performed and 2) indeterminate or abnormal. fever (temperature> 38C), hypoxia (pulse oximetry less than 95% on room air), and tachycardia (pulse rate > 100 beats/min).

- The cohort included 1,419 patients. A total of 66 patients (4.7%) had a return hospital admission within 72 hours An additional 56 (3.9%) patients returned to an ED within 72 hours but were again discharged.
- patients aged > 60 (AOR = 4.6, 95% CI = 2.2 to 9.5) had significantly increased odds of return admission
- patients presenting with hypoxia (AOR = 2.9, 95% CI = 1.2 to 7.2)
- Patients presenting with fever also had higher odds of return admission (AOR = 2.4, 95% CI = 1.3 to 4.5)
- patients with abnormal chest radiograph (AOR = 2.4, 95% CI = 1.5 to 3.7) had higher odds of return admission.

- A total of 117 (8.2%) returned to a hospital for admission within 7 days
- All statistically significant risk factors identified for the primary outcome remained significant.
- Plus: hypertension (AOR = 1.5, 95% CI = 1.1 to 2.0), obesity (AOR = 1.5, 95% CI = 1.1 to 2.0), and age between 41 and 59 years (AOR = 2.1, 95% CI = 1.6 to 2.8).

POINTS

- Even with better evidence to guide disposition, it may not be feasible—or effective—to admit all patients with higher risk upon first presentation. Importantly, return hospital admission does not equate to failure in patient care>> the need for a higher level of care than can be provided at home.
- anticipatory guidance for symptoms that should prompt return.

LIMITATIONS

- patients presenting to the EDs within a single health system
- patients might travel
- some ED visits and return hospital admissions were unrelated to COVID-19
- providers treating patients in this study were not necessarily aware of the COVID-19 status of patients
- do not account for patients who may have died at home.
- did not include the full range of potential risk factors as covariates in the model that may be associated with return hospital admission.
- not include patients with COVID-19 with false-negative tests.

EARLY RHYTHM-CONTROL THERAPY IN PATIENTS WITH ATRIAL FIBRILLATION

The NEW ENGLAND JOURNAL of MEDICINE

October 1, 2020

- (AF) is the most common cardiac arrhythmia.
- Previous trials have not shown superiority of rhythm control with antiarrhythmic drugs over rate control in patients with established AF.
- Rhythm control therapy may be more effective when delivered early.

The primary indication for rhythm control is to reduce AF-related symptoms and improve quality of life. The routine use of a rhythm-control strategy is not universally recommended; an initial rate-control strategy is reasonable for many patients.

OBJECTIVE

- The Early Treatment of AF for Stroke Prevention Trial (EAST-AFNET 4) was designed to test whether a strategy of early rhythm-control therapy that includes AF ablation would be associated with better outcomes in patients with early AF than contemporary, evidence-based usual care.
- International prospective, randomized, investigator-initiated, parallel-group, open, blinded-outcome-assessment.

INTERVENTION

- Patients with AF diagnosed within 1 year were randomized 1:1 to either receive early rhythm control (n = 1,395) or usual care (n = 1,394).
  - Early rhythm control: antiarrhythmic drugs or AF ablation, as well as cardioversion of persistent AF, after randomization.
  - Usual care: initially treated with rate-control therapy without rhythm control. Limited rhythm control to the management of AF-related symptoms.

INCLUSION CRITERIA

Recent-onset AF (≤1 year prior to enrollment)

At least one ECG within recent 12 months that documents AF > 30 s

One of the following:

- Age > 75 years or
- Prior stroke or transient ischemic attack

OR two of the following

- Age > 65 years,
- Female sex,
- Hypertension
- Diabetes mellitus or impaired glucose tolerance
- Severe CAD (prior MI, CABG, or PCI)
- Stable CHF (NYHA II or LVEF < 50%)
- LVH (> 15 mm wall thickness)
- CKD III or IV
- PAD

EXCLUSION CRITERIA

Life expectancy < 1 year

Participation in another clinical trial or previous participation in the EAST trial

Pregnant women or women of childbearing potential not on adequate birth control and breastfeeding women.

Drug abuse.

Prior AF ablation or surgical therapy of AF, or previous therapy failure on amiodarone

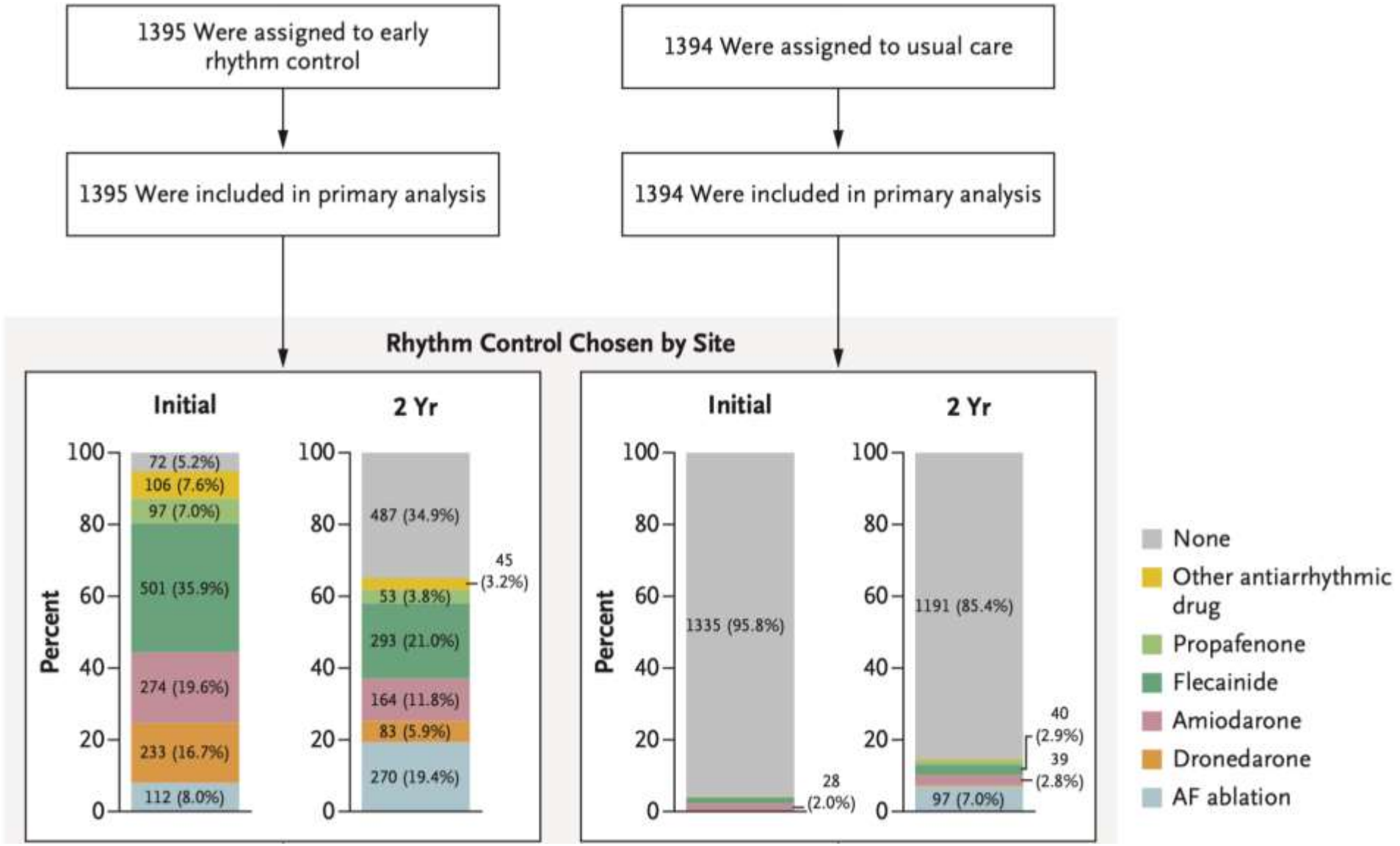
Patients not suitable for rhythm control of AF.

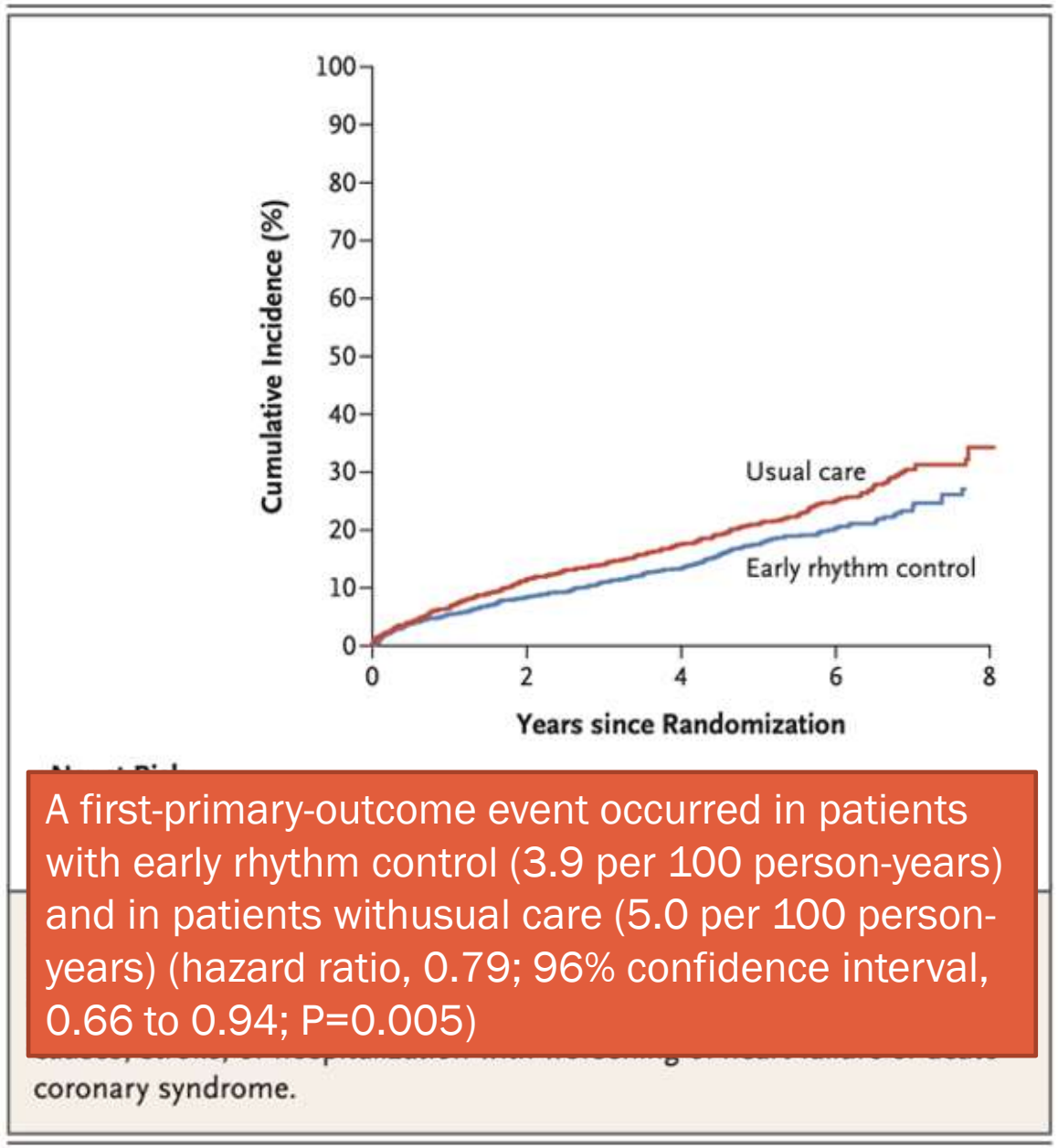
Severe mitral valve stenosis/prosthetic mitral valve

Hepatic dysfunction, thyroid dysfunction, severe renal dysfunction

OUTCOMES

PRIMARY	Composite of: ➢ death from cardiovascular causes ➢ stroke (ischemic or hemorrhagic) ➢ hospitalization with worsening HF, or ACS Number of nights spent in the hospital/year
SECONDARY	➢ Each component of primary outcome ➢ Symptoms (palpitations, fatigue, dizziness, dyspnea, chest pain, anxiety) ➢ LV function ➢ Quality of life
SAFETY	Composite of: ➢ death ➢ stroke ➢ serious adverse events related to rhythm-control therapy


1395 Were assigned to early rhythm control
1394 Were assigned to usual care
1395 Were included in primary analysis
1394 Were included in primary analysis
Rhythm Control Chosen by Site
Initial
2 Yr
Percent
100
80
60
40
20
0
72 (5.2%)
106 (7.6%)
97 (7.0%)
501 (35.9%)
274 (19.6%)
233 (16.7%)
112 (8.0%)
487 (34.9%)
45 (3.2%)
53 (3.8%)
293 (21.0%)
164 (11.8%)
83 (5.9%)
270 (19.4%)
1335 (95.8%)
28 (2.0%)
1191 (85.4%)
40 (2.9%)
39 (2.8%)
97 (7.0%)
None
Other antiarrhythmic drug
Propafenone
Flecainide
Amiodarone
Dronedarone
AF ablation



A first-primary-outcome event occurred in patients with early rhythm control (3.9 per 100 person-years) and in patients withusual care (5.0 per 100 person-years) (hazard ratio, 0.79; 96% confidence interval, 0.66 to 0.94; P=0.005)

coronary syndrome.

Second primary outcome event (number of nights spent in the hospital) not significantly different between both groups.

- No significant difference between rhythm control and usual care with regards to:Symptoms
- LV function
- Cognitive function

CONCLUSION

- Early-rhythm control therapy in patients with early AF and CV conditions was associated with a lower risk of death from cardiovascular causes, stroke, or hospitalization for heart failure or acute coronary syndrome than usual care over a follow-up time of more than 5 years, without affecting the number of nights spent in the hospital.

LIMITATIONS

- Only enrolled patients with early AF, and thus the results may not be generalizable to patients in whom early rhythm-control therapy that includes AF ablation is initiated later.
- All enrolled patients deemed eligible for either rate-control or rhythm-control therapy, which probably excluded the most symptomatic patients.
- Did not collect detailed information on recurrent AF in both groups, so data on percentages of patients with sinus rhythm are not comparable to data on recurrent AF from other rhythm-control trials.

A QUANTITATIVE EVALUATION OF AEROSOL GENERATION DURING TRACHEAL INTUBATION AND EXTUBATION

Anaesthesia
Peri-operative medicine, critical care and pain
Association of Anaesthetists

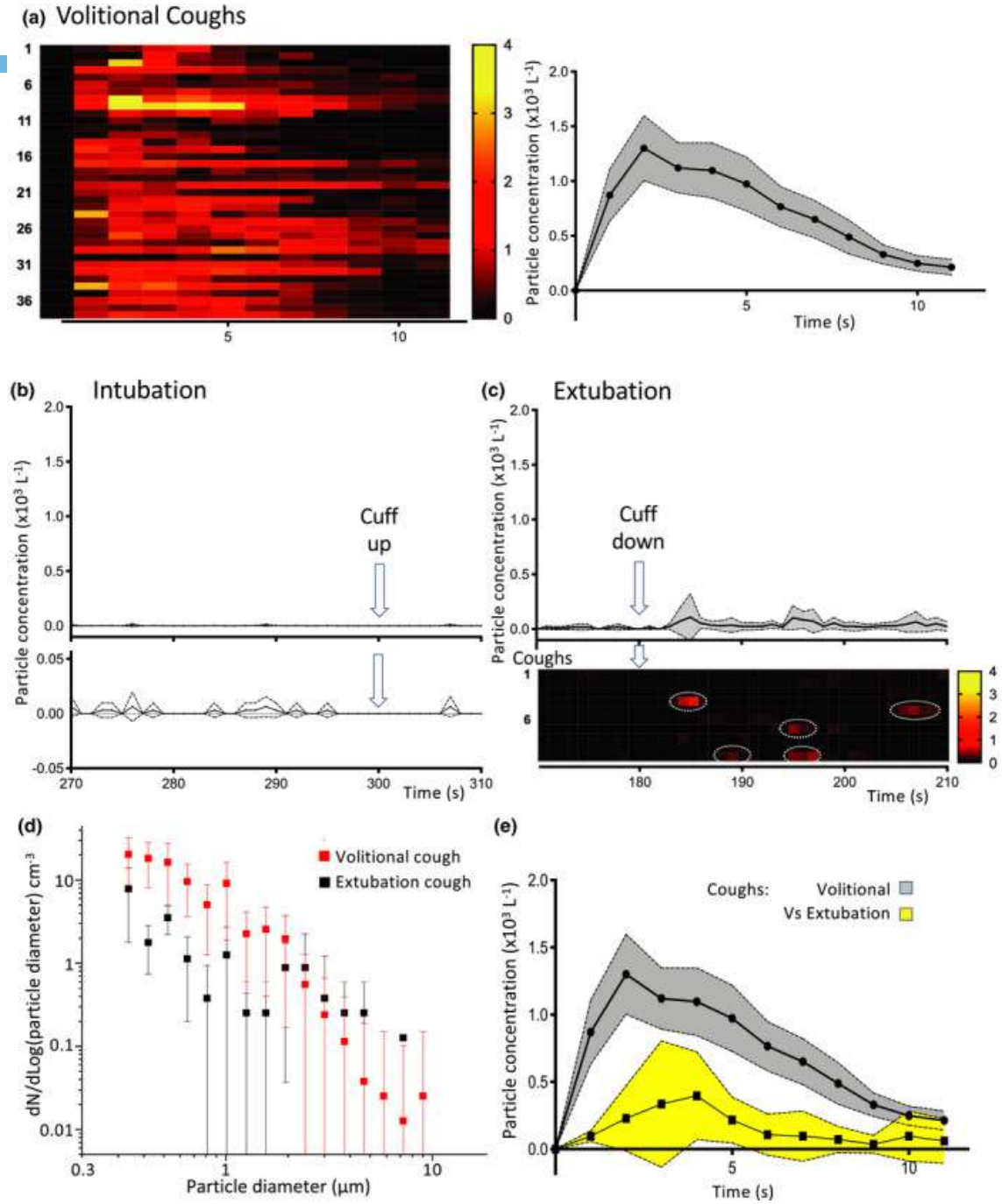
Anaesthesia. 2020 Oct 22

There is currently a lack of quantitative evidence on the number and size of airborne particles produced during aerosol-generating procedures to inform risk assessments.

To address this evidence gap, we conducted real-time, high-resolution environmental monitoring in ultraclean ventilation operating theatres during tracheal intubation and extubation sequences

METHOD

- Recordings were made of 19 intubations and 14 extubations.
- Thirty-eight volitional coughs were sampled at 0.5-m distance.
- Extubation produced a mean (SD) concentration of aerosolised particles of 21 (18) l^{-1} which was 35-fold lower than that seen during a volitional cough ($p < 0.0001$) but 15-fold greater than that seen during intubation ($p = 0.0004$).

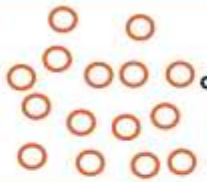


A quantitative evaluation of aerosol generation during tracheal intubation and extubation

Both tracheal intubation and extubation produce less aerosol than voluntary coughing.

For the sequence of tracheal intubation, the concentration of aerosol generated is several orders of magnitude less than a single cough.

There were no increases in aerosolised particles above the patient's face during anaesthesia, face-mask ventilation and airway suctioning.



During tracheal extubation, aerosol concentration was greater than for intubation, but substantially less than a single cough.

A cough event was noted clinically in 50% of extubations and this was frequently detected as an aerosol spike.

Extubation cough aerosol was transient and only detectable for approximately 5 seconds.

There were reduced particle numbers detected behind the patient's head compared to above their airway.

The process of elective tracheal intubation produces a barely recordable increase in aerosol

Our results are at odds with previous retrospective evidence that was used to designate tracheal intubation as an aerosol-generating procedure.

These results should help inform future airborne prevention PPE guidelines by providing evidence on the relative risk of aerosol

LIMITATIONS

- small number of observations, without control.
- The reference coughs were from a single subject
- The measurements were taken during anaesthesia for patients receiving urgent orthopaedic and neurosurgical interventions and may not be generalisable to intubations in a critical care/emergency setting that may be conducted in extremis.
- unable to make any conclusion about the risk of actual SARS-CoV-2 transmission as aerosol generation is still only a presumed risk-factor and particle number concentration is a plausible but unproven surrogate measure of that infection risk

POINTS

- the findings suggest that designating all tracheal intubations and extubations as AGPs of greater risk than patients' coughing is inaccurate.
- Because designating any procedure an AGP has profound implications for both healthcare practices and personal protective equipment use, it seems highly appropriate, and cost-effective for society, that similar quantitative analyses be undertaken to assess the relative risks associated with all procedures now designated as AGPs.

HYPOTHERMIA VERSUS NORMOTHERMIA AFTER OUT-OF-HOSPITAL CARDIAC ARREST

The NEW ENGLAND JOURNAL of MEDICINE

June 17, 2021

Fever has been thought to be a risk factor for hypoxic-ischemic brain damage in patients post-cardiac arrest. Relatively small trials from the early 2000s showed significant mortality and functional benefits from targeted temperature management to 33℃ after return of spontaneous circulation (ROSC) in patients with shockable rhythms.

2013 TTM1 trial that showed similar outcomes in their hypothermia (33℃) and forced normothermia (36℃) groups

2019, a trial demonstrated a significant improvement in neurologic outcome but not mortality at 90 days in their hypothermia (33℃) arm after non-shockable arrest

OBJECTIVE

- Randomized trial to assess the beneficial and harmful effects of hypothermia vs normothermia and early treatment of fever in comatose patients after out-of-hospital cardiac arrest

METHOD

- **DESIGN**
- Open label-trial with blinded assessment of outcomes
- **INCLUSION CRITERIA**
- ≥ 18 years of age
- Admitted after out-of-hospital arrest from cardiac or unknown cause
  - Both shockable and non-shockable rhythms
- > 20 minutes of spontaneous circulation after resuscitation
- Unconscious, unable to obey verbal commands, and no verbal response to pain

INTERVENTION

- Hypothermia group
  - Cooled with surface or intravascular device to 33℃ for 28 hours followed by gradual rewarming to 37℃ over 12 hours.
- Normothermia
  - Maintained a temperature of 37.5℃ or less.
  - Cooled with a surface or intravascular device for temperatures greater than 37.8℃

OUTCOMES

Primary

- Death from any cause at 6 months

Secondary

- Functional outcome at 6 months based on Rankin Score
- Days alive and out of hospital until day 180
- Health-related quality of life
- Rate of adverse events

RESULTS

- A total of 1850 patients were evaluated for the primary outcome
- **Primary Outcome**
- There was no statistically significant difference in mortality at 6 months between the hypothermia and normothermia group (50% vs 48% respectively, relative risk (RR) with hypothermia of 1.04, p = 0.37)
- The effect of the temperature intervention on death at 6 months was consistent across subgroups, including shockable and non-shockable rhythms.
- **Selected Secondary Outcomes**
- There was no statistically significant difference in the functional outcome between the two groups. (55% in both groups with “poor” functional outcomes. RR with hypothermia = 1.00)
- The hypothermia group had increased risk of arrhythmia resulting in hemodynamic compromise compared to normothermia (24% vs 17%, p < 0.001)

The NEW ENGLAND JOURNAL of MEDICINE

Hypothermia vs. Normothermia after Out-of-Hospital Cardiac Arrest

OPEN-LABEL TRIAL WITH BLINDED OUTCOME ASSESSMENT

1850
Comatose adults after out-of-hospital cardiac arrest

	Hypothermia (target body temperature, 33°C) N=925	Normothermia (target body temperature, ≤37.5°C) N=925
Death from any cause at 6 mo	50%	48%
	RR, 1.04; 95% CI, 0.94 to 1.14; P=0.37	
Modified Rankin scale score ≥4 at 6 mo	55%	55%
	RR, 1.00; 95% CI, 0.92 to 1.09	
Arrhythmia with hemodynamic compromise	24%	17%

Hypothermia did not lead to a lower 6-mo incidence of death than normothermia.

J. Dankiewicz et al. 10.1056/NEJMoa2100591

LIMITATIONS

- No non-temperature regulated group
- ICU staff members were aware of assigned target temperature
- Use of a cooling device was used in 43% of the normothermic group patients (an uncommon type of fever control)
- ⅕ of patients were also involved in TAME trial (targeted mild hypercapnia after resuscitated cardiac arrest)

POINTS

- Historical evidence for the effectiveness of hypothermia to 33℃ post-arrest has been inconsistent at best.
- The new TTM2 trial demonstrates a low likelihood of meaningful clinical or mortality improvement with TTM. In fact, cooling to 33℃ may be harmful in some cases - more often requiring paralytics, increased risk of unstable arrhythmia, and longer average time on the vent.[5]
- While preventing fever in post-ROSC patients may be beneficial, aggressive cooling to 33℃ seems unlikely to provide benefit, regardless of initial rhythm, contradicting previously touted studies.


Any question?