Best of the EM-CC Literature 2021

Or: What is Old is New Again

1

DMC Detroit Receiving Hospital

DMC Sinai-Grace Hospital

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Conflicts of Interest?

Contracted Research: Teleflex Inc, 410 Medical, Hospi Corp = Vascular access research. Yeah, I know - not very applicable.

2

LIFE IN THE FASTLANE

REBELEM

Critical Care Reviews
Promoting Open Access to Scientific Advancement

PulmCCM

...all the best in pulmonary and critical care

INTENSIVE

HOME | LABS+LYTES | JOURNAL CLUB | ECHO & U/S | ECMO | ICU-IS-SIM | RESOURCES

EMCrit Project

AIRWAY ARCHIVES

PODCAST HELP! MY PATIENT HAS...

pharmacyjoe.com

Who Has The Time?

Well… me, apparently.

3

I've had enough of COVID

We're going to talk about something else.

4

Top EM-CC Articles of 2021?

Well, I think they're pretty good. If nothing else, it's a 20-minute distraction from talking about COVID.

5

OBJECTIVES

After hearing this talk, attendees will:

- **Have reviewed some of the top-rated non-COVID articles in the 2021 emergency medicine critical care literature.**
- **Understand how these studies relate to precedent studies in the EM-CC literature.**

20 Minutes?

Cover all of 2021 in 20 minutes… it may take that long to read the titles.

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#1

Prospective Validation of Canadian TIA Score and Comparison with ABCD2 and ABCD2i for Subsequent Stroke Risk after Transient Ischaemic Attack: Multicentre Prospective Cohort Study.

Perry JJ, Sivilotti MLA, Emond M, et al. *BMJ* (2021); 372: n49. PMID: 33541890

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Prospective validation of Canadian TIA Score and comparison with ABCD2 and ABCD2i for subsequent stroke risk after transient ischaemic attack: multicentre prospective cohort study

Jeffrey J Perry,[1,2] Marco L A Sivilotti,[3] Marcel Émond,[4,5] Ian G Stiell,[1,2] Grant Stotts,[6] Jacques Lee,[7,8] Andrew Worster,[9] Judy Morris,[10] Ka Wai Cheung,[11] Albert Y Jin,[12] Wieslaw J Oczkowski,[13] Demetrios J Sahlas,[13] Heather E Murray,[3] Ariane Mackey,[4,14] Steve Verreault,[4,14] Marie-Christine Camden,[4,14] Samuel Yip,[15] Philip Teal,[15] David J Gladstone,[16] Mark I Boulos,[16] Nicolas Chagnon,[17] Elizabeth Shouldice,[18] Clare Aizema,[6] Tarik Slaoui,[19] Jeanne Teitelbaum,[19] Kasim E Abdulaziz,[2] Marie-Joe Nemnom,[2] George A Wells,[2] Mukul Sharma[13]

thebmj

OBJECTIVE: To validate the previously derived Canadian TIA Score to stratify subsequent stroke risk in a new cohort of emergency department patients with transient ischaemic attack.
SETTING: 13 Canadian emergency departments over five years (2012-2017).
PARTICIPANTS: **7,607** consecutively enrolled adult patients attending the emergency department with transient Ischaemic attack or minor stroke.
MAIN OUTCOME MEASURES: The primary outcome was subsequent stroke or carotid endarterectomy/carotid artery stenting within seven days. The secondary outcome was subsequent stroke within seven days (with or without carotid endarterectomy/carotid artery stenting). Telephone follow-up used the validated Questionnaire for Verifying Stroke Free Status at seven and 90 days. All outcomes were adjudicated by panels of three stroke experts, blinded to the index emergency department visit. Exclusions were symptoms > 24 hrs ("stroke"), decreased GCS from baseline, alternative diagnosis, presented > 7 days after onset, or received Tx for stroke.
RESULTS: Of the 7607 patients, **108** (1.4%) had a subsequent stroke within seven days, **83** (1.1%) had carotid endarterectomy/carotid artery stenting within seven days, and **nine** had both. The Canadian TIA Score stratified the risk of stroke, carotid endarterectomy/ carotid artery stenting, or both within seven days as low (risk ≤0.5%; interval likelihood ratio 0.20, 95% confidence interval 0.09 to 0.44), medium (risk 2.3%; interval likelihood ratio 0.94, 0.85 to 1.04), and high (risk 5.9% interval likelihood ratio 2.56, 2.02 to 3.25) more accurately (AUC 0.70, 95% CI 0.66-0.73) than the ABCD2 (AUC 0.60, 0.55-0.64) or ABCD2i (AUC 0.64, 0.59 to 0.68). Results were similar for subsequent stroke regardless of carotid endarterectomy/carotid artery stenting within seven days.
CONCLUSION: The Canadian TIA Score stratifies patients' seven-day risk for stroke, with or without carotid endarterectomy/carotid artery stenting, and is now ready for clinical use. Incorporating this validated risk estimate into management plans should improve early decision making at the index emergency visit regarding benefits of hospital admission, timing of investigations, and prioritisation of specialist referral.

TIA Scores

"Medium risk" has nothing to do with psychics. You need CTA + 48-hr follow-up.

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Table 1 | Canadian TIA Score

Items	Points
Clinical findings:	
1) First transient ischaemic attack (in lifetime)	2
2) Symptoms ≥10 minutes	2
3) Past history of carotid stenosis	2
4) Already on antiplatelet therapy	3
5) History of gait disturbance	1
6) History of unilateral weakness	1
7) History of vertigo	−3
8) Initial triage diastolic blood pressure ≥110 mm Hg	3
9) Dysarthria or aphasia (history or examination)	1
Investigations in emergency department:	
1) Atrial fibrillation on electrocardiogram	2
2) Infarction (new or old) on computed tomography	1
3) Platelet count ≥400×10^9/L	2
4) Glucose ≥15 mmol/L	3
Total score (−3 to 23):	X

Table 6 Calculate $ABCD^2$ score

$ABCD^2$ score	Points
Age > 60 years	1
BP = 140/90 mmHg at initial evaluation	1
Clinical features of the TIA	
Speech disturbance without weakness, or	1
Unilateral weakness	2
Duration of symptoms	
10–59 min, or	1
>60 min	2
Diabetes mellitus in patient's history	1

Score	AUC
Canadian TIA	0.70
ABCD2i	0.64
ABCD2	0.60

TIA Scores

Receiver Operating Characteristic Curve

AUC is a measure of the accuracy of a quantitative diagnostic test.

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thebmj

Pros

- Large, prospective multicenter cohort study, involving 6 (of 13) sites not involved in the original derivation study, incl. both academic (10) and urban community (3) hospitals
- Clinically-relevant primary outcome (stroke or carotid revascularization < 7 days)
- Subjective data recorded by study physicians, with 7- and 90-day telephone follow-up
- 99.6% subjects completed 7-day follow-up
- **Canadian TIA Score risk-stratified 16.3% of subjects as low-risk (< 1% primary outcome), while neither ABCD2 nor ABCD2i score classified <u>any</u> as low-risk**
- Outcomes were adjudicated by panel of 3 stroke experts, blinded to index ED visit
- Used pre-specified risk thresholds (low risk <1%, medium risk 1 to 5%, and high risk >5%) based on previous surveys of ED physicians and neurologists

Cons

- **Canadian TIA Score is more complicated than ABCD2**
- 20% of eligible patients were not enrolled
- Overall rate of outcome was low, which would <u>overestimate the performance</u> of a clinical decision instrument since it was such a low-risk group
- Composite 1˚ outcome includes procedure (carotid revascularization) = subjective!
- Validation study done by the same group, in the same health system
- Canadian TIA risk score was not compared to clinician gestalt
- **Canadian TIA score AUC 0.70 -> remains POOR discrimination ability**

TIA Scores – Still Poor…

Carotid revascularization was not addressed in ABCD2.

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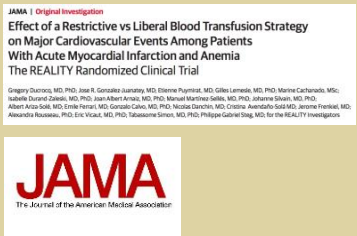
#2

Effect of a Restrictive vs. Liberal Blood Transfusion Strategy on Major Cardiovascular Events Among Patients with Acute Myocardial Infarction and Anemia: The REALITY Randomized Clinical Trial.

Ducrocq G, Gonzalez-Juanatey JR, Puymirat E, et al. *JAMA* (2021); 326(6): 552-560. PMID: 33560322

11


JAMA | Original Investigation

Effect of a Restrictive vs Liberal Blood Transfusion Strategy on Major Cardiovascular Events Among Patients With Acute Myocardial Infarction and Anemia
The REALITY Randomized Clinical Trial

Gregory Ducrocq, MD, PhD; Jose R. Gonzalez-Juanatey, MD; Etienne Puymirat, MD; Gilles Lemesle, MD, PhD; Marine Cachanado, MSc; Isabelle Durand-Zaleski, MD, PhD; Joan Albert Arnaiz, MD, PhD; Manuel Martinez-Sellés, MD, PhD; Johanne Silvain, MD, PhD; Albert Ariza-Solé, MD; Emile Ferrari, MD; Gonzalo Calvo, MD, PhD; Nicolas Danchin, MD; Cristina Avendaño-Solá MD; Jerome Frenkiel, MD; Alexandra Rousseau, PhD; Eric Vicaut, MD, PhD; Tabassome Simon, MD, PhD; Philippe-Gabriel Steg, MD; for the REALITY Investigators

JAMA
The Journal of the American Medical Association

IMPORTANCE: The optimal transfusion strategy in patients with acute myocardial infarction and anemia is unclear.
OBJECTIVE: To determine whether a restrictive transfusion strategy would be clinically noninferior to a liberal strategy.
DESIGN, SETTING, AND PARTICIPANTS: Open-label, noninferiority, randomized trial conducted in 35 hospitals in France and Spain including **668** patients with myocardial infarction and hemoglobin level between 7 and 10 g/dL. Enrollment could be considered at any time during the index admission for myocardial infarction. The first participant was enrolled in March 2016 and the last was enrolled in September 2019. The final 30-day follow-up was accrued in November 2019.
INTERVENTIONS: Patients were randomly assigned to undergo restrictive (transfusion triggered by Hgb ≤ 8; n = 342) or a liberal (transfusion triggered by Hgb ≤ 10 g/dL; n = 324) transfusion strategy.
MAIN OUTCOMES AND MEASURES: The primary clinical outcome was major adverse cardiovascular events (MACE; composite of all-cause death, stroke, recurrent myocardial infarction, or emergency revascularization prompted by ischemia) at 30 days. Noninferiority required that the upper bound of the 1-sided 97.5% CI for the relative risk of the primary outcome be less than 1.25. The secondary outcomes included the individual components of the primary outcome.
RESULTS: Among 668 patients who were randomized, 666 patients (median [interquartile range] age, 77 [69-84] years; 281 [42.2%] women) completed the 30-day follow-up, including 342 in the restrictive transfusion group (122 [35.7%] received transfusion; 342 total units of packed red blood cells transfused) and 324 in the liberal transfusion group (323 [99.7%] received transfusion; 758 total units transfused). At 30 days, MACE occurred in 36 patients (11.0% [95% CI, 7.5%-14.6%]) in the restrictive group and in 45 patients (14.0% [95% CI, 10.0%-17.9%]) in the liberal group (difference, −3.0% [95% CI, −8.4% to 2.4%]). The relative risk of the primary outcome was 0.79 (1-sided 97.5% CI, 0.00-1.19), meeting the prespecified noninferiority criterion. In the restrictive vs liberal group, all-cause death occurred in 5.6% vs 7.7% of patients, recurrent myocardial infarction occurred in 2.1% vs 3.1%, emergency revascularization prompted by ischemia occurred in 1.5% vs 1.9%, and nonfatal ischemic stroke occurred in 0.6% of patients in both groups.
CONCLUSIONS AND RELEVANCE: Among patients with acute myocardial infarction and anemia, a restrictive compared with a liberal transfusion strategy resulted in a noninferior rate of MACE after 30 days. However, the CI included what may be a clinically important harm.

Blood Transfusion

Save that blood for someone else.

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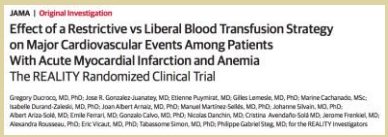
JAMA | Original Investigation

Effect of a Restrictive vs Liberal Blood Transfusion Strategy on Major Cardiovascular Events Among Patients With Acute Myocardial Infarction and Anemia
The REALITY Randomized Clinical Trial

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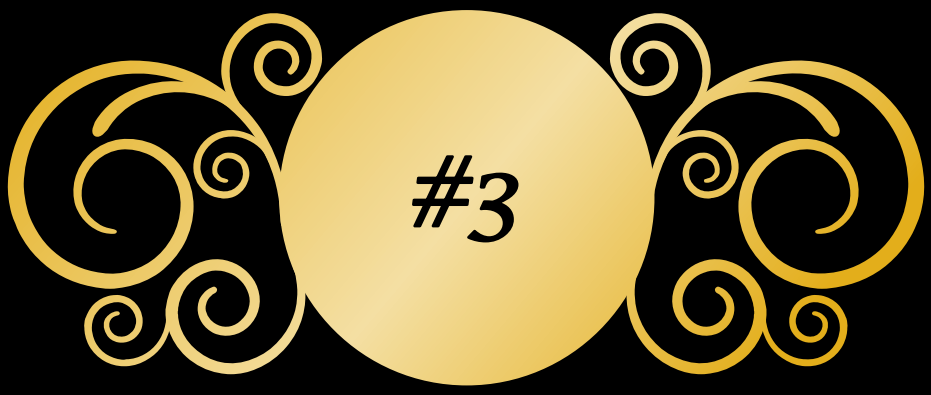
Pros
- Open label, noninferiority, RCT in 35 hospitals in France and Spain
- **Previous transfusion studies have excluded AMI** – this study includes AMI with or without STEMI
- **666 (of 668; 99.7%) subjects had 30-day follow-up**
- Relative risk (RR) 0.79 (97.5% CI 0.00-1.19) – meets non-inferiority threshold (i.e, non-inferiority required 1-sided 97.5% CI < 1.25)
- Baseline characteristics balanced between groups

Cons
- Excluded patients in shock or with "life-threatening bleed" (subjective)
- **MINT study (3500 subjects) is still ongoing** (restrictive vs. liberal transfusion for AMI)
- Unblinded – not clear how this will affect the results
- Small size of study does not permit determination of clinical superiority
- Only examined 30-day outcomes

Blood Transfusion

So… we have to wait for MINT?

13



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

Dankiewicz J, Cronberg T, Lilja G, et al. *N Engl J Med* (2021); 384: 2283-2294. PMID: 34133859

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Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

J. Dankiewicz, T. Cronberg, G. Lilja, J.C. [redacted] H. Levin, S. Ullén, C. Rylander, M.P. Wise, M. Oddo, A. Cariou, J. [redacted] J. Hovdenes, M. Saxena, H. Kirkegaard, P.J. Young, P. Pelosi, C. Storm, F.S. Taccone, M. Joannidis, C. Callaway, G.M. Eastwood, M.P.G. Morgan, P. Nordberg, D. Erlinge, A.D. Nichol, M.S. Chew, J. Hollenberg, M. Thomas, J. Bewley, K. Sweet, A.M. Grejs, S. Christensen, M. Haenggi, A. Levis, A. Lundin, J. Düring, S. Schmidbauer, T.R. Keeble, G.V. Karamasis, C. Schrag, E. Faessler, O. Smid, M. Otáhal, M. Maggiorini, P.D. Wendel Garcia, P. Jaubert, J.M. Cole, M. Solar, O. Borgquist, C. Leithner, S. Abed-Maillard, L. Navarra, M. Annborn, J. Undén, I. Brunetti, A. Awad, P. McGuigan, R. Bjørkholt Olsen, T. Cassina, P. Vignon, H. Langeland, T. Lange, H. Friberg, and N. Nielsen, for the TTM2 Trial Investigators*

BACKGROUND: Targeted temperature management is recommended for patients after cardiac arrest, but the supporting evidence is of low certainty.
METHODS: In an open-label trial with blinded assessment of outcomes, we randomly assigned **1900** adults with coma who had had an out-of-hospital cardiac arrest of presumed cardiac or unknown cause to undergo targeted hypothermia at 33°C, followed by controlled rewarming, or targeted normothermia with early treatment of fever (body temperature, ≥37.8°C). The primary outcome was death from any cause at 6 months. Secondary outcomes included functional outcome at 6 months as assessed with the modified Rankin scale. Prespecified subgroups were defined according to sex, age, initial cardiac rhythm, time to return of spontaneous circulation, and presence or absence of shock on admission. Prespecified adverse events were pneumonia, sepsis, bleeding, arrhythmia resulting in hemodynamic compromise, and skin complications related to the temperature management device.
RESULTS: A total of 1850 patients were evaluated for the primary outcome. At 6 months, 465 of 925 patients (50%) in the hypothermia group had died, as compared with 446 of 925 (48%) in the normothermia group (relative risk with hypothermia, 1.04; 95% confidence interval [CI], 0.94 to 1.14; P=0.37). Of the 1747 patients in whom the functional outcome was assessed, 488 of 881 (55%) in the hypothermia group had moderately severe disability or worse (modified Rankin scale score ≥4), as compared with 479 of 866 (55%) in the normothermia group (relative risk with hypothermia, 1.00; 95% CI, 0.92 to 1.09). Outcomes were consistent in the prespecified subgroups. Arrhythmia resulting in hemodynamic compromise was more common in the hypothermia group than in the normothermia group (24% vs. 17%, P<0.001). The incidence of other adverse events did not differ significantly between the two groups.
CONCLUSIONS: In patients with coma after out-of-hospital cardiac arrest, targeted hypothermia did not lead to a lower incidence of death by 6 months than targeted normothermia.

Temperature

Straight up, or on the rocks?

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Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

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Download

2002 – Introduced hypothermia @ 33°C

- Bernard SA, et al. Treatment of comatose survivors of out-of-hospital cardiac arrest with induced hypothermia. N Engl J Med. 2002 Feb 21; PMID: 11856794
  - 77 subjects (33°C within 2 hours x 12 hrs vs. normothermia)
- Hypothermia after Cardiac Arrest (HACA) Study Group. Mild therapeutic hypothermia to improve the neurologic outcome after cardiac arrest. N Engl J Med. 2002 Feb; PMID: 11856793
  - 273 subjects (32-34°C x 24 hrs vs. normothermia)

2013 – No Benefit with 33°C over 36°C

- Nielsen N, et al. Targeted temperature management (TTM) at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013 Dec 5; PMID: 24237006.
  - 950 subjects randomized to 33°C or 36°C targeted hypothermia x 28 hours, with gradual rewarming by 0.5 °C / hour to target of 37°C at 36 hours post-ROSC

Brief Hx of Hypothermia

The results have been lukewarm.

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Hypothermia versus Normothermia after Out-of-Hospital Cardiac Arrest

J. Dankiewicz, T. Cronberg, G. Lilja, J. [redacted], H. Levin, S. Ullén, C. Rylander, M.P. Wise, M. Oddo, A. Cariou, J. [redacted], J. Hovdenes, M. Saxena, H. Kirkegaard, P.J. Young, P. Pelosi, C. Storm, F.S. Taccone, M. Joannidis, C. Callaway, G.M. Eastwood, M.P.G. Morgan, P. Nordberg, D. Erlinge, A.D. Nichol, M.S. Chew, J. Hollenberg, M. Thomas, J. Bewley, K. Sweet, A.M. Grejs, S. Christensen, M. Haenggi, A. Levis, A. Lundin, J. Düring, S. Schmidbauer, T.R. Keeble, G.V. Karamasis, C. Schrag, E. Faessler, O. Smid, M. Otáhal, M. Maggiorini, P.D. Wendel Garcia, P. Jaubert, J.M. Cole, M. Solar, O. Borgquist, C. Leithner, S. Abed-Maillard, L. Navarra, M. Annborn, J. Undén, I. Brunetti, A. Awad, P. McGuigan, R. Bjørkholt Olsen, T. Cassina, P. Vignon, H. Langeland, T. Lange, H. Friberg, and N. Nielsen, for the TTM2 Trial Investigators*

Modified Rankin Scale	
0	No symptoms
1	No significant disability. Able to carry out all usual activities, despite some symptoms.
2	Slight disability. Able to look after own affairs without assistance, but unable to carry out all previous activities.
3	Moderate disability. Requires some help, but able to walk unassisted.
4	Moderate severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted.
5	Severe disability. Requires constant nursing care and attention, bedridden, incontinent.
6	Dead

Pros

- High external validity with large sample size (1861) from 61 institutions in 14 countries
  - 5x combined enrollment of [Bernard et al + HACA]
- Enrolled within 3 hours of sustained (> 20 min) ROSC
- **Clear separation of temperatures between groups**
- Thorough post-CA intensive care bundle was applied to both groups
- **Blinded neurologic prognosis assessment (at 96 hours)** for those patients who remained in ICU
- Nearly complete (94%) follow-up, with outcomes assessed via the mRS (a well-recognized, validated and frequently used, scoring system) and <1% missing for the primary outcome
- Outcomes assessed at 1 month, 6 months, and 24 months
- Only statistically significant secondary outcome was arrhythmia causing hemodynamic compromise in hypothermia group (p<0.001)
- **Hypothermia group required more paralytics and longer duration of mechanical ventilation**

Cons

- **Primary outcome was death from any cause** @ 6 months (not neurologic outcome)
- Unclear if can be applied to IHCA patients
- 80% of subjects in both groups were male
- **Excluded unwitnessed CA with initial rhythm of asystole**
  - **90% of all subjects received bystander CPR**
  - **~50% of subjects in both arms survived to 6 months**
- **Both arms had TTM (33℃ vs. <37.8℃), and half of normothermia pts required cooling**
- Hypothermia was achieved at 3 hours post-ROSC – could earlier be better?
- Outcomes may have been affected by conservative neuroprognostication protocol

Temperature

Good luck getting these outcomes in a general ED population.

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#4

Early Head-to-Pelvis Computed Tomography in Out-of-Hospital Circulatory Arrest without Obvious Etiology.

Branch KRH, Strote J, Gunn M, et al. *Acad Emerg Med* (2021); 28: 394-403. PMID: 33606342

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Early head-to-pelvis computed tomography in out-of-hospital circulatory arrest without obvious etiology

Kelley R. H. Branch MD, MSc[1] | Jared Strote MD, MPH[2] | Martin Gunn MD[3] | Charles Maynard PhD[4] | Peter J. Kudenchuk MD[1] | Robin Brusen MD[5] | Bradley J. Petek MD[6] | Michael R. Sayre MD[2] | Rachael Edwards MD[3] | David Carlbom MD, MPH[7] | Catherine R. Counts PhD[2] | Jeffrey L. Probstfield MD[1] | Medley O. Gatewood MD[2]

Academic Emergency Medicine

OBJECTIVES: Patients resuscitated from an out-of-hospital circulatory arrest (OHCA) commonly present without an obvious etiology. We assessed the diagnostic capability and safety of early head-to-pelvis computed tomography (CT) imaging in such patients.

METHODS: From November 2015 to February 2018, we enrolled **104** patients resuscitated from OHCA without obvious cause (idiopathic OHCA) to an early sudden-death CT (SDCT) scan protocol within 6 h of hospital arrival. The SDCT protocol included a noncontrast CT head, an electrocardiogram-gated cardiac and thoracic CT angiogram, and a nongated venous-phase abdominopelvic CT angiogram. Patients needing urgent cardiac catheterization or hemodynamically unable to tolerate SDCT were excluded. Cardiac CT analyses were blinded, but other SDCT findings were clinically available. Primary endpoints were the number of OHCA causes identified by SDCT compared to the adjudicated cause and critical diagnoses identified by SDCT, including resuscitation complications. Safety endpoints were acute kidney injury (AKI) and inappropriate treatments based on SDCT findings. Acute coronary syndrome was the presumed etiology if any major coronary artery had a >50% stenosis without another OHCA cause.

RESULTS: SDCT scans occurred within 1.9 ± 1.0 h of hospital arrival and identified 39% (41/104) of all OHCA causes and 95% (39/41) of causes potentially identifiable by SDCT. Critical findings were identified by SDCT in 98% (43/44) of patients that included potentially life-threatening resuscitation complications of liver or spleen laceration (n = 6); pneumothorax or thoracic organ laceration (n = 8); and mediastinal, pericardial, or vascular hemorrhage (n = 3). SDCT exclusively **identified 13 (13%) OHCA causes that would otherwise not be identified without SDCT imaging**. No inappropriate treatments resulted from SDCT findings. Acute kidney injury was common (28%) but only one (1%) patient required new dialysis.

CONCLUSIONS: This observational cohort study suggests that early SDCT scanning is safe, can expedite the diagnosis of potential causes, and can meaningfully change clinical management after idiopathic OHCA.

Scanning CA

Scan 'em all, and let Radiology sort 'em out.

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Early head-to-pelvis computed tomography in out-of-hospital circulatory arrest without obvious etiology

Kelley R. H. Branch MD, MSc[1] | Jared Strote MD, MPH[2] | Martin Gunn MD[3] | Charles Maynard PhD[4] | Peter J. Kudenchuk MD[1] | Robin Brusen MD[5] | Bradley J. Petek MD[6] | Michael R. Sayre MD[2] | Rachael Edwards MD[3] | David Carlbom MD, MPH[7] | Catherine R. Counts PhD[2] | Jeffrey L. Probstfield MD[1] | Medley O. Gatewood MD[2]

Academic Emergency Medicine

Pros

- Prospective, observational cohort study
- **Novel "sudden-death" CT (SDCT) protocol** (<6 hours post-arrival) including non-contrast CT head, electrocardiogram-gated cardiac and thoracic CTA, and non-gated venous-phase abdominopelvic CTA
- Can identify complications of CPR as well
- **In 13% of cases, determined cause of arrest that would not have been identified without CT**
- Identified 39% of all causes of OHCA
- Identified 95% of all causes deemed "potentially identifiable" by CT
- The only safety event was AKI (28%), although only 1 patient required dialysis.
  - Transient renal dysfunction is common after OHCA (40-50%)

Cons

- **Enrolled only "idiopathic" OHCA, without "obvious" cause**
  - Maybe the "obvious" cases weren't obvious?
  - ACS was the presumed etiology if any major coronary artery had a >50% stenosis without another OHCA cause
- Excluded patients who required emergent cardiac catheterization or were too hemodynamically unstable for SDCT
- No control group to compare AKI outcomes

Scanning CA

The new standard of care for post-ROSC diagnosis?

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#5

Effect of Intravenous Fluid Treatment with a Balanced Solution vs. 0.9% Saline Solution in Mortality in Critically-Ill Patients.: The BaSICS Randomized Clinical Trial.

Zampieri FG, Machado FR, Biondi RS, et al. *JAMA*. 2021; 326(9): 818-829. PMID: 34375394

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Effect of Intravenous Fluid Treatment With a Balanced Solution vs 0.9% Saline Solution on Mortality in Critically Ill Patients
The BaSICS Randomized Clinical Trial

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JAMA
The Journal of the American Medical Association

IMPORTANCE: Intravenous fluids are used for almost all intensive care unit (ICU) patients. Clinical and laboratory studies have questioned whether specific fluid types result in improved outcomes, including mortality and acute kidney injury.
OBJECTIVE: To determine the effect of a balanced solution vs. saline solution (0.9% sodium chloride) on 90-day survival in critically ill patients.
DESIGN, SETTING, AND PARTICIPANTS: Double-blind, factorial, randomized clinical trial conducted at 75 ICUs in Brazil. Patients who were admitted to the ICU with at least 1 risk factor for worse outcomes, who required at least 1 fluid expansion, and who were expected to remain in the ICU for more than 24 hours were randomized between May 29, 2017, and March 2, 2020; follow-up concluded on October 29, 2020. Patients were randomized to 2 different fluid types (a balanced solution vs saline solution reported in this article) and 2 different infusion rates (reported separately).
INTERVENTIONS: Patients were randomly assigned 1:1 to receive either a balanced solution (n = 5522) or 0.9%saline solution (n = 5530) for all intravenous fluids.
MAIN OUTCOMES AND MEASURES: The primary outcome was 90-day survival.
RESULTS: Among 11,052 patients who were randomized, **10,520** (95.2%) were available for the analysis (mean age, 61.1 [SD, 17] years; 44.2% were women). There was no significant interaction between the 2 interventions (fluid type and infusion speed; P = .98). Planned surgical admissions represented 48.4% of all patients. Of all the patients, 60.6% had hypotension or vasopressor use and 44.3% required mechanical ventilation at enrollment. Patients in both groups received a median of 1.5 L of fluid during the first day after enrollment. By day 90, 1381 of 5230 patients (26.4%) assigned to a balanced solution died vs 1439 of 5290 patients (27.2%) assigned to saline solution (adjusted hazard ratio, 0.97 [95% CI, 0.90-1.05]; P = .47). There were no unexpected treatment related severe adverse events in either group.
CONCLUSION AND RELEVANCE: Among critically ill patients requiring fluid challenges, **use of a balanced solution compared with 0.9% saline solution did not significantly reduce 90-day mortality**. The findings do not support the use of this balanced solution.

Balance

Apparently saline is balanced enough?

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Effect of Intravenous Fluid Treatment With a Balanced Solution vs 0.9% Saline Solution on Mortality in Critically Ill Patients
The BaSICS Randomized Clinical Trial


JAMA
The Journal of the American Medical Association

2015 – 0.9% Saline vs. Plasma-Lyte 148

- Young P et al. Effect of a buffered crystalloid solution vs saline on acute kidney injury among patients in the intensive care unit: The **SPLIT** randomized clinical trial. JAMA 2015 Oct 27; 314(16):170-1710. PMID: 26444692.
  - 2278 subjects enrolled at 4 ICUs in New Zealand
  - Most subjects received < 2 Liters IVF
  - **No difference in primary outcome (AKI) or mortality**
  - >70% pts came from OR (only 15% from ED, 4% with sepsis)

2018 - 0.9% Saline vs. Plasma-Lyte 148 or Lactated Ringer's

- Self WH, et al. Balanced crystalloids versus saline in noncritically ill adults. N Engl J Med 2018 Mar 1;378:819-828. PMID: 29485926.
  - Saline against Lactated Ringer's or Plasma-Lyte in the Emergency Department (**SALT-ED**) Trial
  - Single-center, 13,347 subjects enrolled in the ED, median volume of 1079 mL
  - No difference in hospital-free days between groups
- Semler MW, et al. Balanced crystalloids versus saline in critically ill adults. N Engl J Med 2018 Mar 1;378:829-839. PMID: 29485925.
  - Isotonic Solutions and Major Adverse Renal Events Trial (**SMART**)
  - Single-center, 15,802 subjects enrolled in the ICU, median volume of 1,020 mL IVF
- Both trials used combined primary outcome of Major Adverse Kidney Event in 30 days (**MAKE30**)
  - **Composite outcome of death from any cause, new renal-replacement therapy or persistent renal dysfunction was higher with saline** in critically ill patients
  - The greatest benefit of balanced crystalloids in this trial was seen in the subset of patients with sepsis (Mortality 29.4% vs 25.2%; NNT = 24)

Plasma-Lyte?

May not prevent death, but your kidneys will like it.

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Effect of Intravenous Fluid Treatment With a Balanced Solution vs 0.9% Saline Solution on Mortality in Critically Ill Patients
The BaSICS Randomized Clinical Trial

Pros

- Large, multicenter RCT
- **Asks a clinically important question (i.e., 90-day survival)**
  - Previous studies used combined outcome (MAKE30 = death or kidney injury)
- Baseline features well-balanced between groups
- Most fluid challenges were performed in the assigned rate on measured days (e.g., >90% of all fluid challenges on day 1 done at the assigned infusion rate)
- Provides evidence that among critically ill patients requiring fluid challenges, neither the type of fluid nor the rate of fluid administration (333mL/hr vs 999mL/hr) improve 90-day mortality

Cons

- Assessment of fluid infusion was unblinded (i.e., patients and physicians were aware of the groups to which they were allocated)
- **Large portion of patients received a fluid bolus prior to ICU admission.**
- **Overall, patients received relatively small amounts of fluid**
- Slower infusion rate was defined arbitrarily at 333 mL/hr (not evidence-based)
- Secondary endpoints were not adjusted for multiple comparisons and are therefore only hypothesis-generating
- The reason for fluid bolus challenges was not recorded
- No recording of immediate effects of fluid challenges on hemodynamic parameters
- **No evidence on how the volume of fluid given may influence outcomes**

Balanced?

Use what you like. Until the next study comes out.

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#6

Dexmedetomidine or Propofol for Sedation in Mechanically Ventilated Adults with Sepsis.

Hughes CG, Mailloux PT, Devlin JW, et al. *N Engl J Med* (2021) 384: 1424-1436. PMID: 33528922

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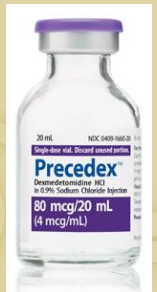
Dexmedetomidine or Propofol for Sedation in Mechanically Ventilated Adults with Sepsis

C.G. Hughes, P.T. Mailloux, J.W. Devlin, J.T. Swan, R.D. Sanders, A. Anzueto, J.C. Jackson, A.S. Hoskins, B.T. Pun, O.M. Orun, R. Raman, J.L. Stollings, A.L. Kiehl, M.S. Duprey, L.N. Bui, H.R. O'Neal, Jr., A. Snyder, M.A. Gropper, K.K. Guntupalli, G.J. Stashenko, M.B. Patel, N.E. Brummel, T.D. Girard, R.S. Dittus, G.R. Bernard, E.W. Ely, and P.P. Pandharipande, for the MENDS2 Study Investigators*



BACKGROUND: Guidelines currently recommend targeting light sedation with dexmedetomidine or propofol for adults receiving mechanical ventilation. Differences exist between these sedatives in arousability, immunity, and inflammation. Whether they affect outcomes differentially in mechanically ventilated adults with sepsis undergoing light sedation is unknown.

METHODS: In a multicenter, double-blind trial, we randomly assigned mechanically ventilated adults with sepsis to receive dexmedetomidine (0.2 to 1.5 µg per kilogram of body weight per hour) or propofol (5 to 50 µg per kilogram per minute), with doses adjusted by bedside nurses to achieve target sedation goals set by clinicians according to the Richmond Agitation–Sedation Scale (RASS, on which scores range from −5 [unresponsive] to +4 [combative]). The primary end point was days alive without delirium or coma during the 14-day intervention period. Secondary end points were ventilator-free days at 28 days, death at 90 days, and age-adjusted total score on the Telephone Interview for Cognitive Status questionnaire (TICS-T; scores range from 0 to 100, with a mean of 50Å}10 and lower scores indicating worse cognition) at 6 months.

RESULTS: Of 432 patients who underwent randomization, **422** were assigned to receive a trial drug and were included in the analyses — 214 patients received dexmedetomidine at a median dose of 0.27 µg per kilogram per hour, and 208 received propofol at a median dose of 10.21 µg per kilogram per minute. The median duration of receipt of the trial drugs was 3.0 days (interquartile range, 2.0 to 6.0), and the median RASS score was −2.0 (interquartile range, −3.0 to −1.0). We found no difference between dexmedetomidine and propofol in the number of days alive without delirium or coma (adjusted median, 10.7 vs. 10.8 days; odds ratio, 0.96; 95% confidence interval [CI], 0.74 to 1.26), ventilator-free days (adjusted median, 23.7 vs. 24.0 days; odds ratio, 0.98; 95% CI, 0.63 to 1.51), death at 90 days (38% vs. 39%; hazard ratio, 1.06; 95% CI, 0.74 to 1.52), or TICS-T score at 6 months (adjusted median score, 40.9 vs. 41.4; odds ratio, 0.94; 95% CI, 0.66 to 1.33). Safety end points were similar in the two groups.

CONCLUSIONS: Among mechanically ventilated adults with sepsis who were being treated with recommended light-sedation approaches, outcomes in patients who received dexmedetomidine did not differ from outcomes in those who received propofol.

Sedation

Perhaps we have finally stopped comparing Precedex to benzos?

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Dexmedetomidine or Propofol for Sedation in Mechanically Ventilated Adults with Sepsis

C.G. Hughes, P.T. Mailloux, J.W. Devlin, J.T. Swan, R.D. Sanders, A. Anzueto, J.C. Jackson, A.S. Hoskins, B.T. Pun, O.M. Orun, R. Raman, J.L. Stollings, A.L. Kiehl, M.S. Duprey, L.N. Bui, H.R. O'Neal, Jr., A. Snyder, M.A. Gropper, K.K. Guntupalli, G.J. Stashenko, M.B. Patel, N.E. Brummel, T.D. Girard, R.S. Dittus, G.R. Bernard, E.W. Ely, and P.P. Pandharipande, for the MENDS2 Study Investigators*

2007 – MENDS Trial

- Pandharipande PP, et al. Effect of sedation with dexmedetomidine vs. lorazepam on acute brain dysfunction in mechanically ventilated patients. The MENDS randomized controlled trial. JAMA. 2007 Dec 12;298(22):2644-2653. PMID: 18073360.
  - Sedation with dexmedetomidine was associated with more days alive without delirium or coma than lorazepam, as well as decreased 28-day mortality.
  - Dexmedetomidine is an α-2 agonist that causes sedation and may promote biomimetic sleep, have anti-inflammatory effects, and help clear bacterial infection.

2012 – MIDEX-PRODEX Trials

- Jakob SM, et al. Dexmedetomidine vs. midazolam or propofol for sedation during prolonged mechanical ventilation. Two randomized controlled trials. JAMA. 2012 Mar 12;307(11):1151-1160. PMID: 22436955.
  - Each trial randomized about 500 pts
  - Compared dexmedetomidine (0.2-1.4 mcg/kg/hr) to midazolam (0.03-0.2 mg/kg/hr) (MIDEX) and propofol (0.3-4.0 mg/kg/hr) (PRODEX).
  - Found that dexmedetomidine is non-inferior to midazolam and propofol for long-term mild to moderate sedation and may reduce time to extubation.

2021 – MENDS2 Trial

- "Among critically ill adults with sepsis who were receiving mechanical ventilation and for whom recommended light-sedation approaches were used, dexmedetomidine did not lead to better outcomes than propofol with respect to days alive without acute brain dysfunction, ventilator-free days, death at 90 days, or cognition at 6 months."

Sedation

Is Precedex the miracle drug for sepsis?

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Dexmedetomidine or Propofol for Sedation in Mechanically Ventilated Adults with Sepsis

C.G. Hughes, P.T. Mailloux, J.W. Devlin, J.T. Swan, R.D. Sanders, A. Anzueto, J.C. Jackson, A.S. Hoskins, B.T. Pun, O.M. Orun, R. Raman, J.L. Stollings, A.L. Kiehl, M.S. Duprey, L.N. Bui, H.R. O'Neal, Jr., A. Snyder, M.A. Gropper, K.K. Guntupalli, G.J. Stashenko, M.B. Patel, N.E. Brummel, T.D. Girard, R.S. Dittus, G.R. Bernard, E.W. Ely, and P.P. Pandharipande, for the MENDS2 Study Investigators*

Pros

- Multicenter (13 sites), RCT
- Important clinical question (i.e., days alive without delirium / coma)
  - 20% of sepsis pts worldwide (e.g., 4 million / yr) ventilated
- **Logical extension of the MENDS trial, where sepsis subgroup appeared to benefit from dexmedetomidine**
- Contributes to the body of knowledge suggesting that dexmedetomidine is safe in sepsis
- All patients were included in the modified intention-to-treat analysis for the primary outcome with minimal imputation for missing data
- Clinically important cognitive dysfunction occurred in ~25% of patients in each group at 6 months

Cons

- Not blinded to bedside RNs, with unmasking of trial drug reported in 14% of cases. May have introduced bias, but unclear in which direction
- **Higher incidence of delirium at enrollment in the propofol group**, which may bias away from the null hypothesis
- **>90% of eligible patients excluded**, many due to physician / relative declining participation, limiting external validity and suggesting loss of equipoise
- Slow enrollment over several years (2013-2018) may be susceptible to secular trend, necessitated downward adjustment (530 -> 420) to the sample size, although statistical power was maintained

Sepsis Sedation

I don't use Precedex anyway.

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#7

Effect of Vasopressin and Methylprednisolone vs. Placebo on Return of Spontaneous Circulation in Patients with In-Hospital Cardiac Arrest: A Randomized Clinical Trial.

Andersen LW, Isbye D, Kjaergaard J, et al. *JAMA*. 2021; 326(16): 1586-1594. PMID: 34587236

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Effect of Vasopressin and Methylprednisolone vs Placebo on Return of Spontaneous Circulation in Patients With In-Hospital Cardiac Arrest
A Randomized Clinical Trial

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JAMA
The Journal of the American Medical Association

IMPORTANCE: Previous trials have suggested that vasopressin and methylprednisolone administered during in-hospital cardiac arrest might improve outcomes.
OBJECTIVE: To determine whether the combination of vasopressin and methylprednisolone administered during in-hospital cardiac arrest improves return of spontaneous circulation.
DESIGN, SETTING, AND PARTICIPANTS: Multicenter, randomized, double-blind, placebo-controlled trial conducted at 10 hospitals in Denmark. A total of **512** adult patients with in-hospital cardiac arrest were included between October 15, 2018, and January 21, 2021. The last 90-day follow-up was on April 21, 2021.
INTERVENTION: Patients were randomized to receive a combination of vasopressin and methylprednisolone (n = 245) or placebo (n = 267). The first dose of vasopressin (20 IU) and methylprednisolone (40mg), or corresponding placebo, was administered after the first dose of epinephrine. Additional doses of vasopressin or corresponding placebo were administered after each additional dose of epinephrine for a maximum of 4 doses.
MAIN OUTCOMES AND MEASURES: The primary outcome was return of spontaneous circulation. Secondary outcomes included survival and favorable neurologic outcome at 30 days (CPC score of 1 or 2).
RESULTS: Among 512 patients who were randomized, 501 met all inclusion and no exclusion criteria and were included in the analysis (mean [SD] age, 71 [13] years; 322 men [64%]). One hundred of 237 patients (42%) in the vasopressin and methylprednisolone group and 86 of 264 patients (33%) in the placebo group achieved return of spontaneous circulation (risk ratio, 1.30 [95%CI, 1.03-1.63]; risk difference, 9.6%[95%CI, 1.1%-18.0%]; P = .03). At 30 days, 23 patients (9.7%) in the intervention group and 31 patients (12%) in the placebo group were alive (risk ratio, 0.83 [95%CI, 0.50-1.37]; risk difference: −2.0%[95%CI, −7.5%to 3.5%]; P = .48). A favorable neurologic outcome was observed in 18 patients (7.6%) in the intervention group and 20 patients (7.6%) in the placebo group at 30 days (risk ratio, 1.00 [95%CI, 0.55-1.83]; risk difference, 0.0%[95%CI, −4.7%to 4.9%]; P > .99). In patients with return of spontaneous circulation, hyperglycemia occurred in 77 (77%) in the intervention group and 63 (73%) in the placebo group. Hypernatremia occurred in 28 (28%) and 27 (31%), in the intervention and placebo groups, respectively.
CONCLUSIONS AND RELEVANCE: Among patients with in-hospital cardiac arrest, administration of vasopressin and methylprednisolone, compared with placebo, significantly increased the likelihood of return of spontaneous circulation. However, there is uncertainty whether this treatment results in benefit or harm for long-term survival.

Steroids?

Increased likelihood of ROSC with VAM-IHCA. What else you got?

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ΓΕΝΙΚΟ ΝΟΣΟΚΟΜΕΙΟ ΑΘΗΝΩΝ
Ο ΕΥΑΓΓΕΛΙΣΜΟΣ

2009-2013 ([Vasopressin + Steroids] vs. placebo) @ Evaggalismos General Hospital

- Mentzelopoulos SD, Zakynthinos SG, Tzoufi M, et al. Vasopressin, epinephrine, and corticosteroids for in-hospital cardiac arrest. *Arch Intern Med*. 2009;169(1):15-24. PMID: 19139319.
  - **100** IHCA subjects randomized to placebo vs. 20 IU vasopressin after each Epi cycle (x first 5) + 40 mg Methylprednisolone (x1 dose). Post-ROSC shock treated with 300 mg Hydrocortisone QD.
  - Intervention a/w more frequent sustained (> 15 min) ROSC (39 of 48 patients [81%] vs 27 of 52 [52%]; *P* = .003) and improved survival to hospital discharge (9 [19%] vs 2 [4%]; *P* = .02). Study group patients with postresuscitation shock had improved survival to hospital discharge (8 of 27 patients [30%] vs 0 of 15 [0%]; *P* = .02), improved hemodynamics and central venous oxygen saturation, and more organ failure–free days. Adverse events were similar in the 2 groups.
- Mentzelopoulos SD, Malachias S, Chamos C, et al. Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest: a randomized clinical trial. *JAMA*. 2013;310(3):270-279. PMID: 23860985.
  - **268** IHCA subjects, with same protocol as 2009 study.
  - Primary outcomes redefined as sustained ROSC (20 min), and survival to hospital discharge with Cerebral Performance Category (CPC) 1 or 2.
  - Intervention group had higher probability for ROSC >20 minutes (109/130 [83.9%] vs 91/138 [65.9%]; odds ratio [OR], 2.98; 95% CI, 1.39-6.40; *P* = .005) and survival to hospital discharge with CPC score of 1 or 2 (18/130 [13.9%] vs 7/138 [5.1%]; OR, 3.28; 95% CI, 1.17-9.20; *P* = .02). Intervention patients with postresuscitation shock had higher probability for survival to hospital discharge with CPC scores of 1 or 2 (16/76 [21.1%] vs 6/73 [8.2%]; OR, 3.74; 95% CI, 1.20-11.62; *P* = .02), improved hemodynamics and central venous oxygen saturation, and less organ dysfunction. Adverse event rates were similar in the 2 groups.

Methylprednisolone

Because Europeans are really into steroids.

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Effect of Vasopressin and Methylprednisolone vs Placebo on Return of Spontaneous Circulation in Patients With In-Hospital Cardiac Arrest
A Randomized Clinical Trial

Lars W. Andersen, MD, MPH, PhD, DMSc; Dan Isbye, MD, PhD; Jesper Kjaergaard, MD, PhD, DMSc; Camilla M. Kristensen, BS; Søren Darling, MD; Sime T. Zwisler, MD, PhD; Stine Fisker, CRNA; Jens Christian Schmidt, MD; Hans Kirkegaard, MD, PhD, DMSc; Download MD, PhD; Jørgen R. G. Rosau, MD; Jacob M. Larsen, MD, PhD; Bodil S. Rasmussen, MD, PhD; Signe Riddersholm, MD, PhD; Kasper Iversen, MD, DMSc; Martin Schultz, MD, PhD; Jakob L. Nielsen, CRNA; Bo Lafgren, MD, PhD; Kasper G. Lauridsen, MD, PhD; Christoffer Sølling, MD, PhD; Kim Pælestik, MD; Anders G. Kjærgaard, MD, PhD; Dorte Due-Rasmussen, MD; Fredrik Folke, MD, PhD; Mette G. Charlot, MD, PhD; Rikke Malene H. G. Jepsen, MD, PhD; Sebastian Wiberg, MD, PhD; Michael Dorrins, MD; Tobias Kurth, MD, PhD; Maria Høybye, BS; Birthe Snidberg, RN; Mathias J. Holmberg, MD, MPH, PhD; Asger Granfeldt, MD, PhD, DMSc

JAMA
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Pros

- Multicenter, randomized, double-blind, placebo-controlled trial
- No subjects lost to follow-up
- **90% had initial non-shockable rhythm**
- Groups well-balanced at baseline in terms of PMHx and cardiac arrest characteristics
- **More patients in this trial (501) compared to the two previous studies combined (368)**
- Pre-specified secondary and safety outcomes
- Independent data monitoring committee oversaw trial

Cons

- Vasopressin no longer first-line according to 2015 ACLS protocol recommendations.
- **Trial powered for ROSC, not patient-centered outcomes (survival, CPC)**
- Higher rate of ECMO in placebo (30%) vs. intervention (14%)
- **Data is for IHCA, with rapid time to compressions / drugs** (may not be true for OHCA):
  - Median time from cardiac arrest to epinephrine = 5min
  - Median time from cardiac arrest to trial drug = 8min
- **Fewer patients alive at 30 days (23 patients (9.7%) in the intervention group** vs. 31 patients (12%) in the placebo group, with risk ratio 0.83 [95% CI, 0.50-1.37]; risk difference: -2.0% [95% CI, -7.5% to 3.5%]; P = .48).
- **Same incidence of favorable neurologic outcome** observed in 18 patients (7.6%) in the intervention group and 20 patients (7.6%) in the placebo group at 30 days (risk ratio, 1.00 [95% CI, 0.55-1.83]; risk difference, 0.0% [95% CI, -4.7% to 4.9%]; P > .99).

Steroids for IHCA

Yeah sure… but I work in the ED.

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#8

Prevalence of Pulmonary Embolism Among Patients with COPD Hospitalized with Acutely Worsening Respiratory Symptoms.

Couturaud F, Bertoletti L, Pastre J, et al. *JAMA*. 2021; 325(1): 59-68. PMID: 33399840

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Prevalence of Pulmonary Embolism Among Patients With COPD Hospitalized With Acutely Worsening Respiratory Symptoms

Francis Couturaud, MD, PhD; Laurent Bertoletti, MD, PhD; Jean Pastre, MD; Pierre-Marie Roy, MD, PhD; Raphael Le Mao, MD; Frédéric Gagnadoux, MD, PhD; Nicolas Paleiron, MD, MS; Jeannot Schmidt, MD; Olivier Sanchez, MD, PhD; Elodie De Magalhaes, MD; Mariam Kamara, MD, MS; Clément Hoffmann, MD; Luc Bressollette, MD, PhD; Michel Nonent, MD, PhD; Cécile Tromeur, MD, PhD; Pierre-Yves Salaun, MD, PhD; Sophie Barillot, MS; Florence Gatineau, MS; Patrick Mismetti, MD, PhD; Philippe Girard, MD; Karine Lacut, MD, PhD; Catherine A. Lemarié, PhD; Guy Meyer, MD; Christophe Leroyer, MD, PhD; for the PEP Investigators

JAMA
The Journal of the American Medical Association

IMPORTANCE: The prevalence of pulmonary embolism in patients with chronic obstructive pulmonary disease (COPD) and acutely worsening respiratory symptoms remains uncertain. **OBJECTIVE**: To determine the prevalence of pulmonary embolism in patients with COPD admitted to the hospital for acutely worsening respiratory symptoms.
DESIGN, SETTING, AND PARTICIPANTS: Multicenter cross-sectional study with prospective follow-up conducted in 7 French hospitals. A predefined pulmonary embolism diagnostic algorithm based on Geneva score, D-dimer levels, and spiral computed tomographic pulmonary angiography plus leg compression ultrasound was applied within 48 hours of admission; all patients had 3-month follow-up. Patients were recruited from January 2014 to May 2017 and the final date of follow-up was August 22, 2017.
EXPOSURES: Acutely worsening respiratory symptoms in patients with COPD.
MAIN OUTCOMES AND MEASURES: The primary outcome was PE diagnosed within 48 hours of admission. Key secondary outcome was pulmonary embolism during a 3-month follow-up among patients deemed not to have venous thromboembolism at admission and who did not receive anticoagulant treatment. Other outcomes were venous thromboembolism (pulmonary embolism and/or deep vein thrombosis) at admission and during follow-up, and 3-month mortality, whether venous thromboembolism was clinically suspected or not.
RESULTS: Among **740** included patients (mean age, 68.2 years [SD, 10.9 years]; 274 women [37.0%]), pulmonary embolism was confirmed within 48 hours of admission in 44 patients (5.9%; 95% CI, 4.5%-7.9%). Among the 670 patients deemed not to have venous thromboembolism at admission and who did not receive anticoagulation, pulmonary embolism occurred in 5 patients (0.7%; 95% CI, 0.3%-1.7%) during follow-up, including 3 deaths related to pulmonary embolism. The overall 3-month mortality rate was 6.8% (50 of 740; 95% CI, 5.2%-8.8%). The proportion of patients who died during follow-up was higher among those with venous thromboembolism at admission than the proportion of those without it at admission (14 [25.9%] of 54 patients vs 36 [5.2%] of 686; risk difference, 20.7%, 95% CI, 10.7%-33.8%; P < .001). The prevalence of venous thromboembolism was 11.7% (95% CI, 8.6%-15.9%) among patients in whom pulmonary embolism was suspected (n = 299) and was 4.3% (95% CI, 2.8%-6.6%) among those in whom pulmonary embolism was not suspected (n = 441).
CONCLUSIONS AND RELEVANCE: Among patients with COPD admitted to the hospital with an acute worsening of respiratory symptoms, PE was detected in 5.9% of patients using a predefined diagnostic algorithm. Further research is needed to understand the possible role of systematic screening for pulmonary embolism in this patient population.

PE in COPD

Apparently, Albuterol is not a thrombolytic.

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Revised Geneva Score for PE

Predictive variables	Revised Geneva score	Simplified Revised Geneva score
Age >65 years	1	1
Active malignancy (or considered cure <1 year)	2	1
Recent surgery or fracture of the lower limbs within 1 month	2	1
Previous PE or DVT	3	1
Haemoptysis	2	1
Unilateral lower limb pain	3	1
Tenderness on lower limb deep venous palpation and unilateral oedema	4	1
Heart rate		
75–94 bpm	3	1
≥95 bpm	5	2

Pros

- Multicenter study of 740 adult patients with COPD admitted with worsening dyspnea, cough, or sputum production
- Raises awareness of the potential for PE in patients presumed to be admitted for COPD
- **Largest study to date on this topic**, although the 6% overall prevalence of PE was lower than that of several previous studies (e.g., 19.9% in systematic review, PMID: 18812453).
- **Revised Geneva score–based algorithm detected almost all cases** and appears to be superior to clinician judgment alone, although the few missed cases resulted in poor outcomes
  - Patients with high clinical probability of PE (i.e., revised Geneva score ≥11) proceeded directly to CTPA and leg US; those with low or intermediate probability (i.e., revised Geneva score <11) received d-dimer tests

Cons

- **Remains unclear whether PEs may be incidental finding**, rather than cause of COPD exacerbation / hospital admission
- Does not provide guidance for clinically distinguishing COPD exacerbation from PE (i.e., requires imaging)
- **Lacked control group** of patients admitted for respiratory symptoms without COPD diagnosis
- Protocol violations in which 17.6% of patients not suspected of having a PE within 48 hours of admission didn't complete the diagnostic algorithm, usually because leg US wasn't available
- Unclear if d-dimer level thresholds for PE screening may be different in COPD patients than among the general ED population

The Great Masquerader

Anchors away! How do you know it's really COPD?

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- Consider using the Canadian TIA score, rather than ABCD2(i)
- Transfusion for AMI with Hgb < 10 may not add benefit
- Avoidance of hyperthermia (≥ 37.8°C) may be good enough for OHCA, rather than targeted hypothermia
- Consider CT evaluation for idiopathic OHCA (maybe)
- 0.9% saline is probably just as good as "balanced" crystalloid solution for critically ill patients
- Propofol and Precedex are likely equivalent for intubated sepsis sedation
- Consider vasopressin + steroids for IHCA, but unlikely to contribute to improved patient-centered outcomes (especially for OHCA)
- Consider PE in your decompensated COPD patients

Conclusions

There IS a point to all of this.

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