Recent
Relevant
Reliable
Unbiased

BEEM Report

June 2023

Paris BEEM

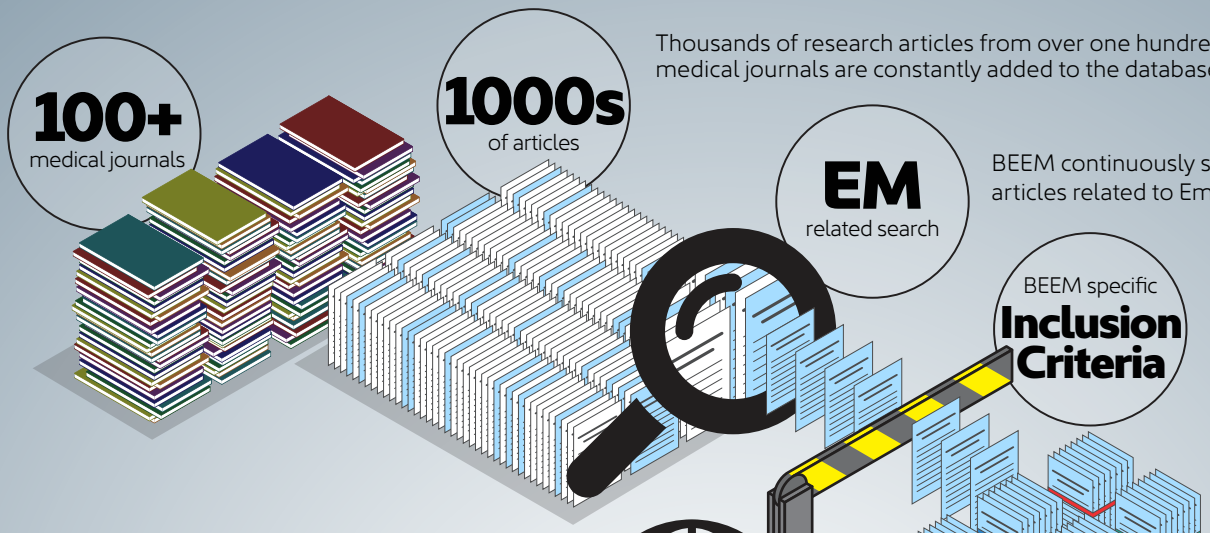
Better Outcomes Require
Tthe Best Evidence

Number Needed to Read 1 NNR

BEEM.ca
Best Evidence in Emergency Medicine

The BEEM Process

Identifying the Best Evidence



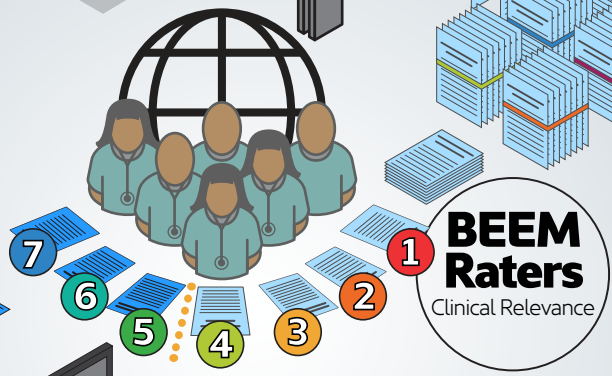
Thousands of research articles from over one hundred medical journals are constantly added to the database.

EM
related search

BEEM continuously scans for the latest articles related to Emergency Medicine.

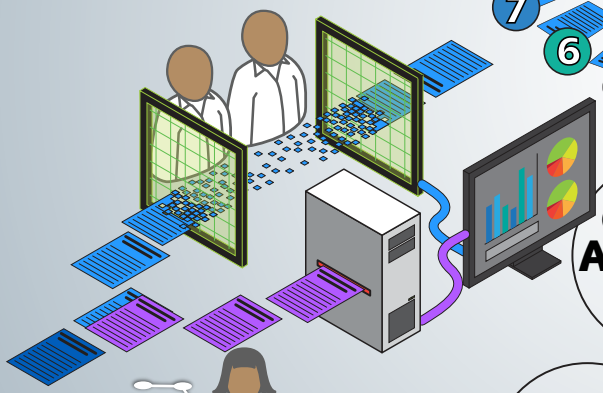
BEEM specific
Inclusion Criteria

Articles meeting the inclusion criteria are sorted by discipline and study design.



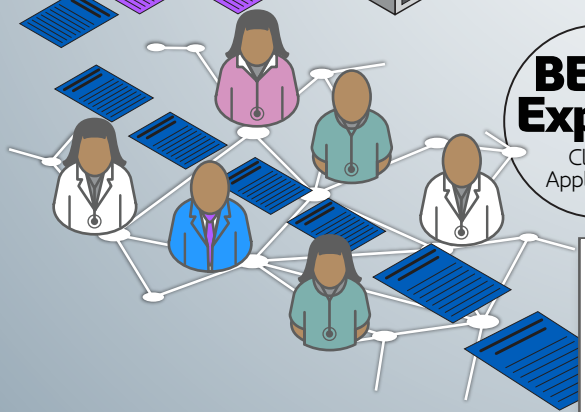
BEEM Raters
Clinical Relevance

Using only their titles and conclusions, articles are rated for their relevance to clinical practice by BEEM's international network of Emergency Physicians. Articles with a median score of 5 or better are selected for Critical Appraisal.



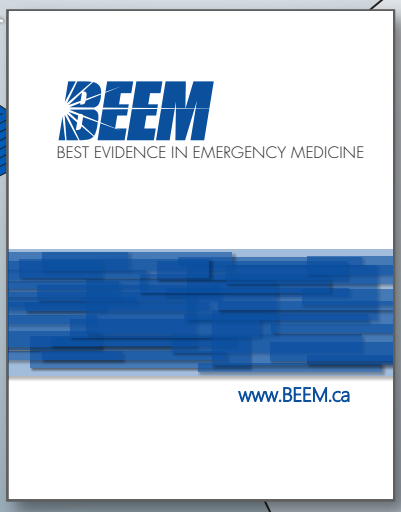
Critical Appraisal
Validity

Our in-house team of clinical epidemiologists appraises each article to identify errors and sources of bias and determine the validity of each study's results.



BEEM Experts
Clinical Applicability

Articles and critical appraisals are sent to select physicians with relevant subspecialty expertise for consensus on clinical applicability.



BEEM Manual & Events

- ☑ Recent
- ☑ Relevant
- ☑ Reliable
- ☑ Unbiased

The best evidence-based guidance for clinical practice in Emergency Medicine

Best Evidence in Emergency Medicine (BEEM)

About BEEM

Founded in 2004, Best Evidence in Emergency Medicine (BEEM) is an international knowledge translation project and collaboration of academic emergency physician researchers and educators from around the world. The objective of BEEM is to find and appraise emergency medicine-related studies of the highest levels of evidence that have the most impact on emergency medicine clinical practice to provide emergency medicine practitioners with the best clinical evidence to optimize patient care.

The BEEM Process

BEEM conducts continuous multiple source searches of 1,000s of articles from more than 100 medical journals for research studies and clinical practice guidelines related to emergency medicine. Articles meeting the BEEM selection criteria (noted further below) are sent to BEEM Raters, a group of Emergency Physicians from around the world that assess each study on its clinical relevance using the validated and reliable BEEM Rater Score. BEEM's team of experts in health research methodology and biostatistics appraise the studies with the highest BEEM Rater scores, producing the highest quality and most reliable critical appraisals. In addition, emergency medicine experts from around the world are invited to write the BEEM Bottom Line, a summary of the impact of the original research study on emergency medicine practice.

The BEEM critical appraisal process allows for the most comprehensive article review. Because BEEM's editorial staff and authors have no ties to industry or conflicts of interest that bias them in their assessments, BEEM has no obligation to favorably appraise any article based on the sponsor, the author, or the primary journal. This results in the most recent, relevant, reliable, and unbiased single source of practice-changing clinical evidence for emergency physicians.

BEEM Article Selection Criteria

Therapy Study: randomized controlled trials of human patients, systematic reviews of randomized controlled trials of human patients, and clinical practice guidelines based on systematic reviews

Harm Study: randomized controlled trials of human patients, systematic reviews of randomized controlled trials of human patients, prospective cohort studies, and case control studies

Diagnostic Study: level five and demonstration of patient outcome efficacy

Clinical Practice Guidelines: based on systematic reviews

Clinical Decision/Prediction Rules: minimum level two (i.e., rules that can be used in various settings with confidence with accuracy)

Dear BEEM Attendee,

BEEM is a well-established conference that is designed to provide you with the highest levels of evidence for high impact articles related to the practice of Emergency Medicine. The sessions are categorized in different areas to cover a breadth of papers that include trauma, critical care, pediatrics, infectious diseases and cardiology to name a few. Each article is reviewed using the BEEM critical appraisal methodology to equip you with an unbiased critique.

During the conference, you will learn from experts in the field of Emergency Medicine and critical appraisal / methodology. You will have multiple opportunities to interact with the other participants as well as faculty. Please feel free to ask them any questions you have.

Sincerely,

Dr. Rahim Valani
Chair, BEEM

Dr. Marcel Emond
Co-Chair, Paris BEEM

Best Evidence in Emergency Medecine (BEEM)

Table of Contents

CARDIO-RESPIRATORY

Research Question

What is the diagnostic accuracy of syncope risk scores for serious outcomes?

BEEM Bottom Line

Why is this study important? Risk stratifying patients with ED syncope for serious outcomes is an important task, to avoid low-value hospitalizations and resource expenditures.

What, if any, threats to validity are most likely to have an impact on the results and how? High admission rates in certain countries may have influenced some of the components of the composite outcomes, contributing to potential ascertainment and incorporation bias.

How do the key results compare with the current evidence? This large international study confirms prior smaller validation studies conducted in other countries with younger patient cohorts (Canada, Italy, Australia).

How should this study impact the care of ED patients? Implementation of CSRS can help to identify (very) low risk syncope patients who can be discharged safely from the ED.

Study Summary

Article	Zimmermann T, du Fay de Lavallaz J, Nestelberger T, *et al.* International Validation of the Canadian Syncope Risk Score: A Cohort Study. Ann Intern Med. 2022 Jun; 175(6):783-794. doi: 10.7326/M21-2313. Epub 2022 Apr 26.
Design	Prospective cohort study to validate syncope risk scores. 14 hospitals in 8 countries. ClinicalTrials.gov: NCT01548352
Population	*Included:* ED adults 40+ yo with syncope within 12hrs. *Excluded:* Patients with non-syncopal loss of consciousness (eg. seizure, intoxication, fall, presyncope, stroke).
Predictor Variables	Syncope risk scores (Canadian, OESIL)
Comparison	N/A.
Outcomes	*Primary:* Composite serious outcome (30day) = death, life-threatening arrhythmia, MI, serious structural heart disease, aortic dissection, pulmonary embolism, severe pulmonary hypertension, severe hemorrhage, or any other serious cause/procedural intervention for syncope. *Secondary:* Composite non-procedural outcome = clinical outcomes above without procedural interventions. Both outcomes up to 720days follow-up. *Subgroups*: (Very) Low Risk = CSRS <0, OESIL 0-1; Med Risk = CSRS 1-3, OESIL 2; (Very) High Risk CSRS 4+, OESIL 3-4
Key Results	2283 patients analyzed. Mean age 68yo, 42% women, 19% had coronary artery disease. 54% hospitalized, 46% discharged from ED. *Primary outcome 7.2% (n=165), secondary outcome 3.1% (n=70).* Primary outcome AUC: CSRS 0.85 (95%CI 0.83-0.88), OESIL 0.74 (0.71-0.78); p<0.001 Sens CSRS (Very Low Risk): 0.91 (0.85-0.95), (Very High Risk): 0.45 (0.37-0.53) OESIL (Very LR): 0.82 (0.75-0.87), (Very HR): 0.59 (0.37-0.66) Spec CSRS (VLR): 0.65 (0.64-0.67), (VHR) 0.92 (0.91-0.93), OESIL (VLR): 0.51 (0.49-0.53), (VHR) 0.78 (0.76-0.80) CSRS (VLR): LR+ 2.6, LR- 0.14; (VHR) LR+ 5.63, LR- 0.60 OESIL (VLR): LR+ 1.67, LR- 0.35; (VHR) LR+ 2.68, VR- 0.53 Secondary outcome AUC: CSRC 0.80 (0.75-0.84), OESIL 0.69 (0.64-0.75); p<0.001 CSRS triaged 60.8% (n=1388) towards very low risk; 30d primary outcome 1.1% (15/1388), 30d secondary outcome 1.1% (15/1388). OESIL triaged 48.4% (n=1104) towards low risk; 30d primary outcome 2.7% (30/1104), 30d secondary outcome 2.7% (30/1104). Outcomes 720days (95.2% patients): 20.7% had primary comp outcome, 13.9% sec comp outcome. Event rates higher in VHR/HR/Med risk vs LR/VLR groups.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were representative of those with the problem.	✓	✓
2. The patients were enrolled consecutively or in a way to ensure a representative sample.	✓	✓
3. All patients underwent the same clinical evaluation.	✓	✓
4. All important predictor variables were included in the clinical evaluation and explicitly defined.	✓	✓
5. Clinicians interpreted the predictor variables and scored prospectively and blinded to the outcome.	✓	✓
6. Clinicians interpreted the predictor variables and scored the rule reliably and accurately.	?	?
7. All outcome variables were included in the clinical evaluation and explicitly defined.	✓	✓
8. All patient-important outcomes were considered.	✓	✓
9. The follow-up was complete.	✓	✓
10. The point estimates and respective precisions are clinically significant.	✓	✓

A1 = S. Upadhye A2 = A. Worster

Clinical Appraisal faculty

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Professor Emeritus, Emergency Medicine/Health Research Methods, Evidence & Impact (HEI), McMaster University

Funding and conflicts of interest

Funding Swiss National Science Foundation & Swiss Heart Foundation (and others). No role in any phase of the study.

Conflict of interest Online reporting; some authors had public grants, some industry disclosures.

Potential threats to viability

Chance *Type I & II errors?* No sample size calculation *a priori* (no methodology to justify such). ED workups at discretion of ED physician; may not have completed all rule variables assessments?

Selection bias *Is the sampling method representative of the target population; are the groups balanced?*

Measurement bias N/A

Analysis bias *Are the results data- or hypothesis-driven? Is the model over fitted and not applicable?*

Confounding *Residual confounding as with all observational studies because of unknown prognostic factors that cannot be controlled for; Independent factors affecting the outcome; clinicians to comment.* High variation in admission rates across all countries (54%; Canada 14% to USA 80%) with higher rates of monitoring/investigations/interventions for composite outcomes (risk of ascertainment and incorporation bias).

Administrative details

Key words Emergency department, risk scores, syncope

Reference(s)

Research Question

What is the shortest effective duration of antibiotics for acute exacerbations of chronic obstructive pulmonary disease (AECOPD)?

BEEM Bottom Line

Why is this study important? COPD is the 5th leading cause of mortality worldwide and, although bacterial infections account for 50% of acute exacerbations (AECOPD), antibiotics (ABX) are prescribed for up to 90% of cases with resulting adverse reactions and antimicrobial resistance. This review sought to determine if shorter ABX treatment duration might be as effective and yield fewer adverse effects.

What, if any, threats to validity are most likely to have an impact on the results and how? A limited search using electronic databases and hand-searches has the risk of missing potentially important information. Use of different ABX in different duration studies may limit generalizability of comparisons.

How do the key results compare with the current evidence? The latest GOLD and ERS/ATS guidelines support the use of ABX for AECOPD, but the optimal duration is heretofore unclear. This review suggests that 5 days is sufficient.

How should this study impact the care of ED patients? For patients with spirometrically-confirmed COPD and acute exacerbations, a short-course of antibiotics (5d) is as efficacious as longer courses (7-10d).

Study Summary

Article	Llor C, Moragas A, Miravitlles M, Mesquita P, Cordoba G. Are short courses of antibiotic therapy as effective as standard courses for COPD exacerbations? A systematic review and meta-analysis. Pulm Pharmacol Ther. 2022 Feb;72:102111. doi: 10.1016/j.pupt.2022.102111.
Design	Systematic review/meta-analysis. PROSPERO reference number: CRD42019124894.
Population	*Included:* RCTs of adults 40+yo, smoker or ex-smokers >10pkyrs, with spirometrically confirmed COPD (GOLD criteria) *Excluded:* Patients with suspected exacerbations of asthma, acute/chronic bronchitis, CAP or bronchiectasis.
Intervention	Short course of antibiotics (Abx) for 5 days or less.
Comparison	Standard course of Abx (6 days or more).
Outcomes	1) End-of-therapy clinical cure (clinical success within 2wks of Abx completion). 2) Bacterial eradication: negative throat swab culture within 2 wks of Abx completion 3) Adverse events: diarrhea, GI upset, rash
Key Results	Eight studies included, 3670 patients (1828 short course, 1842 std course) 1) End-of-Rx clinical cure (7 studies, 2826pts; Fig 3): No significant differences OR 1.14 (95%CI 0.91-1.44); I^2=0. Short course amoxicillin or clarithromycin slightly less Rx success compared to fluroquiolones (NSS). 2) Bacterial eradication (6 studies, 1832pts; Fig 4): No significant differences OR 1.16 (0.91-1.48); I^2=11%. 3) Adverse events (7 studies, 3610pts; Fig 5): No significant differences OR 0.83 (0.61-1.13); I^2=55%.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Medline, Cochrane databases only; reference lists of selected studies.**	X	X
3. The search for studies was unbiased and reproducible. **Independent duplicate searches**	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible. **Cochrane RoB**	✓	✓
7. The quality of the primary studies is high. **Most studies (except 1) were at mostly low RoB (Figure 2)**	✓	✓
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	?

A1 = S. Upadhye A2 = A. Worster

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Funding and conflicts of interest

Funding Reported; not funded.
Conflict of interest 2 authors (CL, MM) have received industry grants and speaking fees.

Potential threats to viability

Chance Possible type II errors.
Selection bias Limited electronic search with reference lists from included articles. No gray literature searched. No language restrictions. No reporting on publication bias assessments.
Measurement bias Missing details on study selection; missing results of quality assessments.
Analysis bias Use of random effects analysis due to expected heterogeneity. Some variability in heterogeneity based on Abx compared, duration of Rx, etc.
Confounding Most short-course studies used fluoroquinolones, and long-course studies used beta-lactams.

Administrative details

Key words COPD, acute exacerbations, antibacterial agents, drug resistance
Reference(s) Messous et al. Ther Adv Respir Dis 2022, Vol. 16: 1–10 DOI: 10.1177/17534666221099729

Research Question

What is the risk of major adverse cardiac events (MACE) in ED chest pain patients with prior advanced investigations?

BEEM Bottom Line

Why is this study important? Patients with no known coronary artery disease, may present to the Emergency Department repeatedly for chest pain. If they have had negative advanced investigations for chest pain in the last year, do they need admission or repeat advanced testing when are seen again in the ED? This review summarizes the "warranty period" for such investigations to rule out short term major adverse cardiac events (MACE), assuming a negative ED workup and prior outpatient investigations.

What, if any, threats to validity are most likely to have an impact on the results and how? There is only one RCT on this subject, and this meta-analysis relies on additional observational/cohort data to make conclusions.

How do the key results compare with the current evidence? These results reinforce the SAEM GRACE-1 and ACC-AHA Guidelines for Low-Risk ED Chest Pain (2021), that recommend a "warranty period" of up to 1 year for recent negative advanced CAD testing in otherwise low risk of 30-day MACE in ED chest pain patients.

How should this study impact the care of ED patients? Patients with "negative" ED ECG/troponin testing and negative prior advanced investigations in the preceding 1 year can be safely discharged with low risk of 30-day MACE.

Study Summary

Article	Mehta P, McDonald S, Hirani R, Good D, Diercks D. Major adverse cardiac events after emergency department evaluation of chest pain patients with advanced testing: Systematic review and meta-analysis. Acad Emerg Med. 2022 Jun;29(6):748-764. doi: 10.1111/acem.14407.
Design	Systematic review/meta-analysis. PROSPERO Reg#: 266107
Population	*Included:* Studies recruiting ED chest pain patients with low/intermediate risk chest pain (TIMI <5 or HEART <6), negative ED ECG and troponins, and prior CAD testing within past 12mo (cCTA = coronary CT angiogram, XST = exercise stress test, stress ECHOcardiography/MPS = myocardial perfusion scan) *Excluded:* Unable to access full text of selected studies.
Index Test	ED chest pain testing
Reference Standard	Recent cCTA, XST, stress ECHO/MPS
Diagnoses of Interest	MACE Event rates= Death, MI, hospitalization due to heart failure, percutaneous cardiac catheterization with intervention, or coronary artery bypass grafting. Events at 1mo, 6mo and 12mol.
Key Results	33 articles included (7 RCTs, 17 prospective cohorts, 9 retrospective cohorts). cCTA (7153 pts), XST (521), stress ECHO (1892), nuclear MPS (1237).
Mean age: 54 (+/-11) Female: 47%	*MACE 1mo* (21 studies): MPS – no results pooled (no events) (Figure 1) cCTA = 0.09% (95%CI 0.03-0.26, I^2=9%) XST = 0.23% (0.01-5.8%, I^2=51%) *MACE 6mo* (17 studies): XST and ECHO studies not pooled due to considerable heterogeneity. (Figure 2) cCTA = 0.05% (0-3.41%, I^2=56%) MPS = 0.17% (0.04-0.68%, I^2=0%) *MACE 12mo* (8 studies): cCTA = 0.16% (0.04-0.65%, I^2=0%) ECHO = 1.68% (1.09-2.59%, I^2=0%) (Figure 3) *Subgroups: cCTA no stenosis vs. non-obstructive (<50% stenosis)* MACE 1mo (17 studies): 0.09% (0.03-0.27%, p=1.00, I^2=9%); no CAD 0.17% vs non-Obx CAD 0.06% MACE 12mo (5 studies): 0.50% (0.21-1.2%).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Electronic databases searched (4) with librarian. No mention of gray literature, contacting authors**	X	X
3. The search for studies was unbiased and reproducible. **No mention of duplicated searches**	?	?
4. The selection of studies was unbiased and reproducible. **Dual independent**	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **Not reported**	?	?
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible. **Use of Cochrane RoB2 (RCTs) and RoBIN-I (non-RCTs) tools for included studies**	✓	✓
7. The quality of the primary studies is high. **Most studies low RoB (Table 1), but only 1 RCT**	✓	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	N/A	?
9. The subgroups were stated a priori and appropriate. **Subgroup analyses based on advanced modality; cCTA further sub-analyzed based on "no CAD" vs "non-obstructive CAD" detected**	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = M. Welsford

Clinical Appraisal faculty

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Professor & Division Director, Emergency Medicine, McMaster University

Funding and conflicts of interest

Funding None reported.
Conflict of interest Reported; no conflicts declared.

Potential threats to viability

Selection bias *Specify comprehensive searches; publication bias?* No duplicate search nor assessment of publication bias reported.

Measurement bias Some variability in MACE definitions within included studies.

Analysis bias *Fixed/random effects? Heterogeneity mgt?* Heterogeneity assessed by Cochran Q and I^2 statistics (random effects analysis). I^2 = 47%. Only 1 RCT included and the rest are observational.

Confounding *Enter independent factors affecting the outcome; clinicians to comment.* Patients lost to follow-up in individual studies were not included in this review (even if no MACE was documented in chart).

Administrative details

Key words Coronary CTA, ECG, emergency department, low-risk chest pain, MACE, major adverse cardiac events, meta-analysis, myocardial perfusion scintigraphy, stress ECHO, stress EKG, stress testing, systematic review, TIMI

Reference(s)

1. Musey Jr PI, Bellolio F, **Upadhye S**, *et al*. Guidelines for reasonable for appropriate care in the emergency department (GRACE): Recurrent low-risk chest pain in the emergency department. Acad Emerg Med 2021; 00:1-27. DOI: 10.1111/acem.14296
2. Gulati M, Levy PD, Mukherjee D, et al. 2021 AHA/ACC/ASE/CHEST/SAEM/SCCT/ SCMR Guideline for the Evaluation and Diagnosis of Chest Pain: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2021 Nov 30;144(22):e368-e454.

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Eddy Lang MD CCFP(EM) FCFP FCAHS **No conflicts of interest/Identify conflicts (ICMJE)**
Professor and Department Head, University of Calgary

Funding and conflicts of interest

Funding	Reported; American College of Emergency Physicians (ACEP)
Conflict of interest	Reported; no conflicts of interest declared.

Potential threats to viability

Development	*Consider appropriate stakeholders, systematic evidentiary base & recommendations consistent with the literature? Transparent and reproducible?* No patient/caregiver values and perspectives elicited nor reported. Evidence base analyzed and summarized as per usual ACEP Policy processes (Schriger 1993); not necessarily intuitive for ED physicians?
Presentation	*Well organized with easy to find recommendations?* Yes; it would be optimal to have all Recs summarized early in the document, as per ED physician preferences (Aboulsoud et al, 2011)
Comprehensive	*Was the information to inform decision-making complete?* Yes; good discussions of Rec benefits, harms and potential resource issues.
Clinical Validity	*Are the recommendations clinically sound and appropriate for the intended patients?* Yes.

Administrative details

Key words Acute heart failure, diuretics, emergency department, point-of-care ultrasound (POCUS), risk stratification tools, vasodilators.

Reference(s)

1) Lee DS, Straus SE, Farkouh ME, et al; COACH Trial Investigators. Trial of an Intervention to Improve Acute Heart Failure Outcomes. N Engl J Med. 2022 Nov 5. doi: 10.1056/NEJMoa2211680 PMID: 36342109
2) Aboulsoud S, Huckson S, Wyer P, Lang E. Survey of preferred guideline attributes: what helps to make guidelines more useful to emergency health practitioners. Int J Emerg Med 2012; 5:42-29. DOI: 10.1186/1865-1380-5-42 PMID: 23140222
3) Michaud AM, Parker SIA, Ganshorn H *et al*. Prediction of Early Adverse Events in Emergency Department Patients With Acute Heart Failure: A Systematic Review. Can J Cardiol 2018; Vol 34(2): 168-179. DOI:https://doi.org/10.1016/j.cjca.2017.09.004

Research Question

What is the benefit of using IV acetazolamide in acute decompensated heart failure with volume overload?

BEEM Bottom Line

Why is this study important? Emergency Department management of acute decompensated heart failure (ADHF) may involve use of nitroglycerin, BIPAP, and diuretics. Aggressive diuretic Rx of fluid overload as an inpatient is known to alleviate symptoms, and may reduce need for NIPPV/intubation and thus ICU admission. Adding acetazolamide (carbonic anhydrase inhibitor) to usual standard diuretics can augment fluid diuresis.

What, if any, threats to validity are most likely to have an impact on the results and how? No significant design flaws; use of clinical congestion scores could be at risk of subjective interpretation, and may lack validity and applicability in ED settings. The study is focused on inpatient management and may not be applicable to early ED treatment.

How do the key results compare with the current evidence? Early diuresis is recommended in most international ADHF guidelines, and use of IV acetazolamide can add benefit to standard diuretic practices.

How should this study impact the care of ED patients? Adding a loading dose of IV acetazolamide 500mg to usual diuretic orders can promote early diuresis/natriuresis, improve clinical congestion and shorten hospital length of stay.

Study Summary

Article	Mullens W, Dauw J, Martens P, *et al*; ADVOR Study Group. Acetazolamide in Acute Decompensated Heart Failure with Volume Overload. NEJM 2022 Sep 29;387(13):1185-1195. doi: 10.1056/NEJMoa2203094.
Design	Multi-centre randomized controlled trial (Belgium, 27 sites); ClinicalTrials.gov #: NCT03505788
Population	***Included:*** Adults admitted with ADHF and 1+ signs of volume overload (edema, ascites, pleural effusion, elevated pro/BNP markers, and already using loop diuretics for 1mo preadmission. ***Excluded:*** Patients on maintenance acetazolamide Rx, or other proximal tubular diuretics, SGLT2 inhibitors, sBP <90mmHg, or eGFR <20ml/min per 1.73m^2 BSA. Also excluded those patients using IV acetazolamide or furosemide 80+mg prior to randomization, dialysis, pregnant/breastfeeding, concurrent ACS with ST ischemic changes, Hx of cardiac congenital heart disease surgery, transplantation, use of LVAD or exposure to nephrotoxic agents.
Intervention	IV acetazolamide (ACET) 500mg daily with std IV loop diuretics (2x usual oral dose).
Comparison	Placebo (PLAC) with std IV loop diuretics.
Outcomes	***Primary:*** Successful decongestion (defined as the absence of signs of volume overload, within 3 days after randomization and without an indication for escalation of decongestive therapy). ***Secondary:*** Composite of death from any cause or rehospitalization for heart failure during 3 months of follow-up. Safety was also assessed. Subgroups: Stratification based on LVEF <40% or >40%.
Key Results	**519 patients randomized; 259 acetazolamide, 260 placebo.** Mean age 78yo, 62% males. ***Primary:*** ACET 108/256 (42.2%) and PLAC 79/259 (30.5%) successfully decongested; RR 1.45 (95%CI 1.17-1.82, p<0.001) Subgroups: Primary affect sustained across all planned subgroups. For patients discharged alive, benefit of ACET was sustained (RR 1.27, 1.13-1.43). No impact due to onset of SARS-COVID19 pandemic during trial on sensitivity analysis.

	Secondary: 1) All-cause death/rehospitalization: ACET 29.7% vs PLAC 27.8% (HR 1.07, 0.78-1.48); NSS 2) Duration of index hospitalization: ACET 8.8days (8.0-9.5) vs PLAC 9.9days (9.1-10.8); NSS 3) All-cause death 3mo: ACET 12% vs PLAC 15.2%; HR 1.28 (0.78-2.05); NSS 4) Rehospitalization 3mo: ACET 17.4% vs PLAC 18.4%; HR 1.07 (0.71-1.59); NSS 5) Adverse events: NSS during hospital phase, nor during 3mo follow-up period.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively. **Not reported.**	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed. **Supp materials Section S3**	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	✓	✓
6. All groups were treated equally except for the intervention. **Table 1**	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = M. Welsford

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Michelle Welsford, MD FRCPC Professor & Director, Division of Emergency Medicine, McMaster University	**No conflicts of interest (ICMJE)**

Funding and conflicts of interest

Funding	Reported; funded by Belgian Health Care Knowledge Center
Conflict of interest	Reported; multiple authors declared various industry relationships. No clear outline of conflicts management.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Sample size needed = 519 patients; successfully recruited.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Yes
Measurement bias	Treating physician calculated the congestion score, on a scale from 0 to 10 on the

	basis of the sum of scores for the degree of edema (0 to 4), pleural effusion (0 to 3), and ascites (0 to 3), with higher scores indicating a worse condition on all scales. Clinically intuitive, subjective, validity of scale? Calculating amount of ascites not applicable to ED
Analysis bias	*ITT, Per Protocol, As Treated.* ITT; adverse events analysis based on per protocol group assignments.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Samples lacked ethnic diversity (99% white in both arms), which could limit generalizability across other racial groups.

Administrative details

Key words	Acetazolamide, acute decompensated heart failure, emergency department, volume overload
Reference(s)	

Research Question

What is the impact of implementing a risk-stratified decision support system for ED acute heart failure patients?

BEEM Bottom Line

Why is this study important? Acute heart failure (AHF) is a common condition with high morbidity/mortality, and high admissions/resource consumption. This trial studied an ED-based standardized approach with risk-stratification and transition to early follow-up for patients discharged.

What, if any, threats to validity are most likely to have an impact on the results and how? The primary outcome measure shows a benefit of up to 12% for death/hospitalization at 30days (NNT 40), but the upper boundary of the 95%CI shows that this benefit may be as small as 1% (NNT 100). Also, interventions were applied to patients who were admitted and evaluated within 3days for risk, so this may limit generalizability to those being evaluated during ED visit.

How do the key results compare with the current evidence? There is a growing body of evidence of implementing decision support systems with validated risk-stratification tools to support safe discharge of ED AHF patients. More trials are needed.

How should this study impact the care of ED patients? "Low-risk" (using validated tools) AHF patients may be safely discharged from the ED, provided that they can rapidly access a heart failure clinic within a few day's time.

Study Summary

Article	Lee DS, Straus SE, Farkouh ME, Austin PC, Taljaard M, Chong A, Fahim C, Poon S, Cram P, Smith S, McKelvie RS, Porepa L, Hartleib M, Mitoff P, Iwanochko RM, MacDougall A, Shadowitz S, Abrams H, Elbarasi E, Fang J, Udell JA, Schull MJ, Mak S, Ross HJ; COACH Trial Investigators. Trial of an Intervention to Improve Acute Heart Failure Outcomes. N Engl J Med. 2022 Nov 5. doi: 10.1056/NEJMoa2211680
Design	Stepped-wedge cluster randomized controlled trial (Ontario, 10 hospitals); COACH ClinicalTrials.gov number, NCT02674438
Population	***Included:*** Adults >18yo presenting to ED with symptoms of AHF ***Excluded:*** Patients without AHF (Framingham criteria, negative BNP tests), end-stage/ palliative care, invalid health card/inability to link to databases, unable to attend outpt f/u clinic, no permanent home address/non-Ontario residents, LAMA.
Intervention	Clinical decision support using Emergency Heart Failure Mortality Risk Grade (EHMRG30-ST) for 30day mortality, with discharge of "low risk" patients and f/u with rapid AHF clinic
Comparison	Admission of "high risk" patients, and clinical judgement for "intermediates"
Outcomes	***Primary:*** "Early" = composite of all-cause death or hospitalization within 30d of index ED visit "Extended" = composite outcome up to 20mths after index ED visit ***Secondary:*** Hospitalization for any cardiac cause or heart failure, all-cause death. Serious adverse events = death/hospitalization for CV or any other cause in low/intermediate risk patients after early discharge & before 1st outpt f/u visit.
Key Results	**5452 patients recruited.** Mean age 78yo, 45% females. *High-risk patients*: 423/1564 (27%) had early discharge (from ED/within 3d admission) in CTRL phase, and 207/1984 (19.1%) during INT phases. Median time to 1st outpt visit was 3 days for both phases, and median time to internist/cardiologist was 11d INT and 13d CTRL.

	Intermediate risk: Early discharge for 364/824 (44.2%) during CTRL phase, and 397/783 (50.7%) during INT phase. Median time to 1st outpt visit was 4days with INT (internist/ cardiologist 7d) and 5days in CTRL (Int/cardiology 9d). *Low risk*: Early discharge for 309/531 (58.2%) during CTRL, and 328/575 (57%) during INT phases. Low-risk with early discharge had 1st f/u visit within by 4days in both groups. Median time to internist/cardiologist 6d during INT phase, 12d during CTRL phase. ***Primary:*** Death/hospitalization within 30d occurred in 12% INT and 14.5% CTRL patients (adj HR 0.88, 95%CI 0.78-0.99, p=0.04). **Absolute Diff: 2.5% (NNT 40)** CV hospitalization 30d: Lower during INT phase; adj HR 0.85 (0.74-0.98). Heart failure hospitalization 30d: Lower during INT; adj HR 0.81 (0.69-0.95). All-cause death 30d: INT 5.9% vs CTRL 6.6%; adj HR 0.94 (0.72-1.19) ED visit/all deaths/CV hosp 30d: INT 27.7% vs CTRL 28.6%; adjHR 0.978 (0.85-1.11) ***Secondary:*** Median f/u time was CTRL 280 days vs INT 144d. Any death/CV hospitalization: 54.4% INT vs 56.2% CTRL; adjHR 0.95 (0.92-0.99). Serious AEs: No significant differences during either phase within 30d

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively. **Not reported (manuscript, Supp appendix)**	?	?
2. The patients were adequately randomized (allocation sequence adequately generated). **Covariate-constrained randomization by site to ensure balance for ED volumes, teaching vs community ED**	✓	✓
3. The allocation sequence was adequately concealed. **Impractical; hospital sites blinded to assignment until start of intervention period (start of training 4mo prior to implementation).**	X	X
4. The patients in all groups were similar with respect to prognostic factors. **Table 1, S12**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Impractical as above.**	X	X
6. All groups were treated equally except for the intervention.	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	?	?

A1 = S. Upadhye A2 = M. Welsford

Clinical Appraisal faculty

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Funding and conflicts of interest

Funding	Reported; Supported by the Ontario SPOR (Strategy for Patient-Oriented Research) Support Unit, the Ted Rogers Centre for Heart Research, the Peter Munk Cardiac Centre, a Foundation

	Grant (FDN 148446) from the Canadian Institutes of Health Research, and ICES, which is funded by an annual grant from the Ontario MOHLTC.
Conflict of interest	Reported; 3 authors reported some govt and industry supports, unrelated to current work.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Sample size of 8700 needed, 5452 enrolled.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Yes; unable to establish race/ethnicity in >50% of both groups.
Measurement bias	N/A.
Analysis bias	*ITT, Per Protocol, As Treated.* ITT to group assigned.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Hospital sites randomly assigned to control then intervention phases (no return to control); each transition period 4mo duration. Varied f/u care in heart failure clinics by nurses, internists and/or cardiologists could have had an impact on later outcomes.

Administrative details

Key words	Acute heart failure, emergency department
Reference(s)	Lee DS, Lee JS, Schull MJ, *et al.* Prospective Validation of the Emergency Heart Failure Mortality Risk Grade for Acute Heart Failure: The ACUTE Study. Circulation 2019; 9(26): 1146-1156. https://doi.org/10.1161/CIRCULATIONAHA.118.035509.

NEUROLOGY

Research Question

Are peripheral nerve blocks effective for primary headaches?

BEEM Bottom Line

Why is this study important? Primary headaches are the most common neurological ED presentation, and can be time- and resource-consuming depending on therapeutic agents selected. Peripheral nerve blocks (and trigger point injections) may offer a rapid, safer and resource-saving alternative to traditional headache therapies in the ED.

What, if any, threats to validity are most likely to have an impact on the results and how? There is limited data to confirm early benefits (<15min). Blinding is difficult in these types of studies, as medication delivery and local responses may be very different for analgesics delivered. **Significant heterogeneity in control agents used with few using metoclopramide IV. Very little longer-range data.**

How do the key results compare with the current evidence? There is a growing body of evidence in support of interventional anesthetics for acute pain control in the ED, primarily for musculoskeletal pain syndromes. This work expands the indications for PNB in the ED setting. Current analgesics for ED headache are slower in onset, less favourable administration routes, and unpleasant side effects. PNBs are less invasive and more rapid-acting, and may overcome HA-related nausea & vomiting problems that limit the utility of oral analgesics.

How should this study impact the care of ED patients? Peripheral nerve blocks and trigger point injections may be useful alternatives for rapid and effective treatment of primary headaches in the ED.

Study Summary

Article	Patel D, Yadav K, Taljaard M, Shorr R, Perry JJ. Effectiveness of Peripheral Nerve Blocks for the Treatment of Primary Headache Disorders: A Systematic Review and Meta-Analysis. Annals Emerg Med 2021; 1-11. DOI: 10.1016/j.annemergmed.2021.08.007
Design	Systematic Review of human RCTs (PROSPERO ID: CRD42020212187)
Population	*Included:* Patients with primary headaches (any age). Primary headache = acute/chronic migraines, tension or cluster headaches. *Excluded:* Nonrandomized trials, review articles, and studies that assessed patients with secondary headache disorders.
Intervention	Peripheral Nerve Block (PNB) = Greater occipital nerve (GON), sphenopalatine ganglion block (SGB) and trigger point injections (TPI)
Comparison	Placebo (10 trials) or other treatments (NS 1 trial, DA agonists 2 trials)
Outcomes	*Primary:* Effectiveness of PNBs for treating ED primary headaches on reducing pain intensity within 120min (reported on VAS, NRS or similar pain scale). *Secondary:* Pain intensity between 2-72hrs, adverse events, headache relapse resulting in ED revisit or clinic within 72hrs.
Key Results	11 studies, 860 patients (67% women). Eight studies conducted in ED setting. Lidocaine 10-80mg used in 5 studies, bupivacaine 3-80mg in 3 studies. SGB delivered by intranasal drops (5 studies) or Tx360 device (2 studies) *All time intervals favoured PNB vs control:* 1 min (2 studies): SMD -1.33 (-2.56 to -0.09); I^2= 41% 2 min (2 studies): SMD -0.51 (-1.86 to 0.85); I^2=78% 5 min (5 studies): SMD -1.07 (-1.79 to -0.35); I^2=46% 15min* (7 studies): SMD -1.17 (-1.82 to 0.51); I^2=49%, p=0.0005 30min* (5 studies): SMD -0.99 (-1.66 to -0.32); I^2=36%, p=0.04 **Most clinically important time points (survey 10 academic EM physicians)*

No change in outcomes after sensitivity analyses after excluding highly biased & out-patient clinic studies.

Most adverse events (6 studies) were minor (burning/numbness sensation, dizziness, injection site pain).

Need for rescue meds – see Appendix

ED Revisits (2 studies): See Appendix

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible.	✓	✓
7. The quality of the primary studies is high.	?	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%).	?	X

A1 = S. Upadhye A2 = E. Lang

Funding and conflicts of interest

Funding	None (reported)
Conflict of interest	None (reported)

Potential threats to viability

Chance	A small number of studies (and included patients) may have resulted in a Type II error (failure to detect a real treatment difference), as suggested by the 95%CI crossing the MCID threshold.
Selection bias	Thorough validated independent searches/retrievals. No comment on publication bias analysis.
Measurement bias	*Missing details on study selection; missing results of quality assessments.* Majority of studies were of low (4)/to moderate certainty and at low (4) risk of bias (using Cochrane Risk of Bias tool). GRADE certainty of evidence = Moderate. Blinding is a challenge based on different delivery modalities, or local responses to injected solutions.
Analysis bias	*Fixed vs. random effects, combined results of studies of different design.* Varying levels of heterogeneity in outcomes analyzed by random effects models. Most individual pain scale pooled estimates were <1.5 point change on 10pt scale (MCID), the CI's did surpass this threshold of possible clinically significant improvements.
Confounding	Heterogeneity in time points measured in included studies, dosing of lidocaine vs. bupivacaine, and pooling of GON and SGB blocks. Minimal reporting of TPI outcomes. Difficult to blind patients in individual studies.

Administrative details

Key words	Emergency department, primary headache, peripheral nerve block
Appraisers	S. Upadhye, A2 E. Lang A2
Reference(s)	https://www.youtube.com/watch?v=6Dj5zYbvLxo

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Research Question

Is IV tenecteplase non-inferior to alteplase for acute stroke reperfusion?

BEEM Bottom Line

Why is this study important? Tenecteplase (TNK) can be delivered via single bolus administration and has a longer plasma half-life than alteplase (ALT), making it a potentially attractive alternative to alteplase infusions for acute ischemic stroke (AIS).

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. Lack of consecutive recruiting/other factors during COVID19 pandemic are a research reality, but required sample size (with built-in LTFU buffers) was still met.

How do the key results compare with the current evidence? Prior phase 2 trials show a benefit of TNK over alteplase for AIS at varied doses. This is the first phase 3 trial to demonstrate benefit with larger sample sizes.

How should this study impact the care of ED patients? Eligible AIS patients presenting within the reperfusion window (<4.5 hours) would do just as well with IV bolus TNK compared to infusion ALT. ED AIS reperfusion protocols could be adapted for such.

Study Summary

Article	Menon BK, Buck BH, Singh N, *et al*; AcT Trial Investigators. Lancet. 2022 Jul 16;400(10347):161-169. doi: 10.1016/S0140-6736(22)01054-6. Epub 2022 Jun 29. PMID: 35779553
Design	Pragmatic multi-centre open-label non-inferiority RCT (22 primary stroke centres in Canada); ClinicalTrials.gov, NCT03889249
Population (as per Cdn Best Stroke Practices Recs)	*Included:* Adults >18yo with AIS with disabling neurologic deficits with symptom onset 4-5hrs. *Excluded:* Absolute = Active bleeding, high risk of bleeding, pregnant women. Many other relative exclusions in Supplemental Appendix.
Intervention	TNK at 0.25mg/kg single bolus dose, max dose 25mg
Comparison	Alteplase 0.9mg/kg IV, delivered as loading bolus (10% of dose) + infusion (remaining 90% of dose), max dose 90mg
Outcomes	*Primary:* Modified Rankin Scale (mRS; 7pt Likert scale) score of 0-1 at 90 and 120 days post-treatment. *Secondary:* 90-120 day mRS scores (0-2, any), return to baseline function 90d, 90-120d EQ-VAS and EQ-5D-5L scores, door-to-needle time, recanalization status at first endovascular angiography test, baseline CT to arterial puncture time for patients undergoing endovascular Rx, cognitive assessment tool scores (telephone interview), hospital length of stay (LOS), and discharge destination. *Adverse events:* Symptomatic ICH <24hrs, orolingual angioedema <24hrs, or any extracranial bleeding requiring blood transfusion <24hrs. 90day all-cause mortality. Pre-specified subgroups analyzed (for both ITT and Per Protocol analyses): Age < and >80yo, gender, baseline NIHSS stroke severity, large vessel occlusion on baseline CT angiography, type of enrolling centre, and source registry (OPTIMISE vs QuICR).

Key Results Median age: 74yo (IQR 63-83) Female 47.9% vs male 52.1% Median symptom onset to Rx: 2hrs (IQR 1.5-3hrs) Loss to follow-up at 90-days: 0.6% (N=10)	806 TNK pts in ITT group (800 treated, 6 lost to follow-up, 790 analyzed per protocol) 771 alteplase pts in ITT group (762 treated, 4 LTFU, 760 analyzed PP) *Primary:* TNK 36.95% vs. ALT 34.8%; Unadj Risk Diff 2.1% (95%CI -2.6% to 6.9%); lower bound 95%CI >-5%, so TNK is non-inferior to ALT. TNK not superior to ALT in secondary analysis (p=0.19). Efficacy results similar in ITT vs PP analyses. *Secondary:* No significant differences in all outcomes (Table 2). No heterogeneity of treatment effects in pre-specified subgroups, nor in sensitivity analyses with imputation for missing data. No significant differences in any safety outcomes (rare in both groups, both ITT and PP analyses).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	X	X
2. The patients were adequately randomized (allocation sequence adequately generated). **Central randomization, allocation balance per site.**	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Treatment was open label, but outcomes assessments blinded.**	?	?
6. All groups were treated equally except for the intervention. **As per Cdn Best Stroke Practices**	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up). **Minimal LTFU**	✓	✓
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = K. Lin

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Katie Lin, MD MPH FRCPC **Associated with AcT Trial Investigator Group (ICMJE)**
Assistant Professor, Emergency Medicine/Clinical Neurosciences, University of Calgary

Funding and conflicts of interest

Funding	CIHR (Alberta SPOR Unit); no role in study design, conduct nor data analysis.
Conflict of interest	Various authors declared financial interests (stock ownership, consulting fees, industry grants, advisory boards, speaking honoraria) and some public grant supports.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* NI margin of -5%, sample size recruiting target met.
Selection bias	*Is the sampling method representative of the target population; are the groups balanced?* Unable to guarantee consecutive recruiting during COVID19 pandemic (and other potential institutional restrictions). Groups otherwise balanced at initiation.
Measurement bias	Unable to practically blind patients and treating clinicians, but were able to blind outcomes assessors.
Analysis bias	*ITT, Per Protocol, As Treated.* Both ITT and PP analyses used for all outcomes assessed.
Confounding	*Independent factors affecting the outcome; clinicians to comment.* Impractical to blind patients and treating clinicians, although outcomes assessors were blinded.

Administrative details

Key words	Acute ischemic stroke, alteplase, tenecteplase, thrombolysis
Reference(s)	Menon BK, Buck BH, Singh N, et al. Intravenous tenectaplase compared with alteplase for acute ischaemic stroke in Canada (AcT): a pragmatic, multicentre, open-label, registry-linked, randomised controlled, non-inferiority trial. Lancet. 2022;400(10347):161-169.

Research Question

What is the utility of CT head in patients with acute atraumatic altered mental status?

BEEM Bottom Line

Why is this study important? CT scans of the head are commonly performed in ED for patients with acute atraumatic mental status (AAMS).

What, if any, threats to validity are most likely to have an impact on the results and how? High heterogeneity may limit the generalizability of these results. Results were robust nonetheless to serial trial removal meta-analysis.

How do the key results compare with the current evidence? There is a growing body of evidence of over-utilization of CT scans in ED settings, but no increased rates of positive findings.

How should this study impact the care of ED patients? ED physicians need evidence-based tools to help risk-stratify AAMS patients for higher-yield CT head scanning. Following appropriate guidance (eg. Choosing Wisely) may help reduce low-value scans.

Study Summary

Article	Acharya R, Kafle S, Shrestha DB, Sedhai YR, Ghimire M, Khanal K, Malla QB, Nepal U, Shrestha R, Giri B. Use of Computed Tomography of the Head in Patients with Acute Atraumatic Altered Mental Status: A Systematic Review and Meta-analysis. JAMA Netw Open. 2022 Nov 1;5(11):e2242805. doi: 10.1001/jamanetworkopen.2022.42805.
Design	Systematic review with Meta-analysis; PROSPERO (CRD42022324211)
Population	*Included:* Studies (RCTs observational cohorts, case-control studies) with adults >18yo with atraumatic AMS, confusion, loss of consciousness or disorientation without focal neurologic deficits. *Excluded:* Pediatric patients <18yo. Conference abstracts, reviews, letters, case reports, case series, systematic reviews and meta-analyses.
Index Test	CT Head.
Reference Standard	N/A
Diagnoses of Interest	*Primary:* Proportion of CTH use in AMS patients. *Secondary:* Proportion of positive CT heads (acute ischemic stroke, intracranial hemorrhage/mass, cerebral edema, and new identifiable lesions on CT head [CTH]), CTH outcomes, use of CTH in ED/ICU/inpatient wards, changes in management as per CTH use, costs of CTH studies in AMS patients. Subgroups: US vs European studies.
Key Results	S6 studies included for systematic review, 25 for meta-analysis; 79201 pts analysed. 11 studies completed in ED settings. *Primary:* CTH use 94% (95%CI 76-100%). Settings: ED 96% (64-100%), ICU 100%, inpt wards 99%, mixed settings 76%. *Secondary:* Positive overall CTH rate 11% (7-15%). ED positives 17% (12-24%), ICU 12%, mixed 7%, inpt ward 3%). No difference in CHT rates in Europe vs USA. No studies reported on patient management changes as a result of CTH results. One study examined CTH costs: Costs ranged from $USD211-U2200. Results robust with sequential trial removal sensitivity analysis.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Gray literature excluded.**	X	X
3. The search for studies was unbiased and reproducible. **No duplicate searches reported.**	?	?
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **Not reported.**	?	?
6. The quality assessment of the primary studies used was unbiased, and reproducible. **Use of JBI checklists. Unclear if quality assessments done in duplicate.**	?	?
7. The quality of the primary studies is high. **11 studies high quality, 15 moderate.**	✓	✓
8. The populations, cut-off thresholds, and reference standards were similar for combined studies. **No diagnostic test thresholds defined.**	?	?
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate **random effects**).	✓	✓

A1 = S. Upadhye A2 = K. Lin

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Funding and conflicts of interest

Funding None reported.
Conflict of interest Reported; no conflicts of interest declared.

Potential threats to viability

Chance N/A.
Selection bias *?* Non-comprehensive searches. Authors acknowledge serious publication bias detected on funnel plot analyses (Supp eFigure 1 & 2).
Measurement bias Although study screening/selection was performed with two independent reviewers and a third author adjudicator for discrepancies, it is unclear/unreported whether data extraction itself was performed independently by two different reviewers.
Analysis bias Significant heterogeneity I^2>50% in most ED outcomes (>95%). High heterogeneity ascribed to diverse mix of included studies/patient cohorts.
Confounding *N/A*

Administrative details

Key words Altered mental status, computerized tomography
Reference(s) N/A

Research Question

What is the effectiveness of corticosteroids in the treatment of vestibular neuritis?

BEEM Bottom Line

Why is this study important? Vestibular neuritis (VN) is the most common cause of acute vestibular syndromes in the ED, and available symptom treatments are sparse. There is some evidence that use of corticosteroids can reduce vestibular nerve inflammation (usually post viral); this meta-review summarizes prior systematic reviews (SR's) of this topic, in support of an upcoming 3rd Guidelines for Reasonable & Appropriate Care in Emergency Department (GRACE-3) practice guideline from SAEM.

What, if any, threats to validity are most likely to have an impact on the results and how? There were few SR's of sufficient quality included (only 2), with small trials/included patients. Level of certainty for included evidence was usually low/very low. This compromises confidence/trustworthiness in the study conclusions.

How do the key results compare with the current evidence? Small trials/reviews in prior publications suggest a possible benefit for steroids in acute VN.

How should this study impact the care of ED patients? For patients with an accurate diagnosis of VN, ED physicians may consider offering a course of corticosteroids to help ameliorate symptom severity/duration and recovery.

Study Summary

Article	Oliveira J E Silva L, Khoujah D, Naples JG, Edlow JA, Gerberi DJ, Carpenter CR, Bellolio F. Corticosteroids for patients with vestibular neuritis: An evidence synthesis for guidelines for reasonable and appropriate care in the emergency department. Acad Emerg Med. 2022 Aug 17. doi: 10.1111/acem.14583.
Design	Umbrella review of systematic reviews (Meta-review)
Population	*Included:* SR's of RCTs or observational studies of adults with acute vestibular neuritis.* *Excluded:* SR's of low methodological quality (AMSTAR-2 ratings).
Intervention	Corticosteroids (any med, duration or route of administration)
Comparison	Placebo, other usual interventions
Outcomes	*Primary (clinical):* Symptom resolution, Dizziness Handicap Inventory [DHI] score, quality of life, disability, and medication adverse effects *Secondary (objective):* Caloric stimulation testing results
Key Results	5 reviews identified. 2 reviews included, encompassing: 12 primary studies, 660 patients total (323 in ED setting). *Fisman CDSR Review:* 1) Patient-reported vertigo at 24hr: Possible benefit steroids vs placebo; RR 0.39 (95%CI 0.04 to 3.57); very low Certainty of Evidence 2) Complete caloric recovery (n=50pts, 30d): Benefit with steroids; RR 2.81 (1.32 to 6.00); low CoE 3) Electronystagmography (30d): Benefit with steroids? RR 0.36 (0.02 to 7.85); very low CoE *Leong Review: 8 primary studies included* 1) Patient-reported dizziness disability (based on DHI scores): No Difference between steroids vs vestibular rehab exercises; MD +3.99 (–0.21 to 8.2), 2 studies, 80 patients; Very low CoE. 2) Improved caloric recovery (30d): MD −8.33 (–16.33 to −0.32), two studies, 80 patients; Very low CoE. 3) Adverse events: 5.9% in steroids group, most commonly hyperglycemia; very low CoE.

* *Acute VN was defined as the first episode of sudden sustained vertigo measured in days, associated with typical unidirectional horizontal nystagmus, in the absence of auditory or neurologic symptoms or findings suggestive of alternative diagnosis.*

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Librarian assisted search of published SR's; no primary studies, gray literature noted**	?	?
3. The search for studies was unbiased and reproducible. **No duplicate searches reported.**	?	?
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **Not reported**	X	X
6. The assessment of the quality of the primary studies was unbiased and reproducible. **Duplicate**	✓	✓
7. The quality of the primary studies is high. **GRADE assessments; 2 high quality reviews included.**	?	?
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%). **No Forest plots nor heterogeneity testing reported.**	?	?

A1 = S. Upadhye A2 = K. Lin

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Funding and conflicts of interest

Funding Reported; SAEM GRACE (Guidelines for Reasonable & Appropriate Care in Emergency Department) guidelines project (GRACE-3).

Conflict of interest Reported; no conflicts of interest declared.

Potential threats to viability

Chance 2 included SR encompass N=660 patients (across 12 RCT's or observational studies); generally small sample sizes across individual trials though.

Selection bias Meta-review of prior SR's; no publication bias assessments reported.

Measurement bias N/A; included in GRADE Summary of Evidence profiles and Supp materials online.

Analysis bias N/A.

Confounding Variable rates of vestibular rehabilitation used in comparison arms, which has moderate/strong evidence for efficacy and safety for unilateral peripheral vestibular dysfunction.

Administrative details

Key words Caloric test, corticosteroids, dexamethasone, dizziness, head impulse test, methylprednisolone, nausea, Steroid, vertigo, vestibular neuritis, vestibular rehabilitation

Reference(s)

1) Hunter BR, et al. Efficacy of Benzodiazepines or Antihistamines for Patients with Acute Vertigo: A Systematic Review and Meta-analysis. JAMA Neurol 2022; doi:10.1001/jamaneurol.2022.1858
2) Shah VP, et al. Diagnostic accuracyc of neuroimaging in emergency department patients with acute vertigo or dizziness: A systematic review and meta-analysis for the guidelines for reasonable and appropriate care in the emergency department. Acad Emerg Med. 2022 Jul 25. doi: 10.1111/acem.14561.

Research Question

What is the optimal diagnostic strategy for non-traumatic ED sudden onset headache?

BEEM Bottom Line

Why is this study important? Ruling out dangerous pathologies in ED sudden onset headache (eg. SAH) is critically important to avoid significant morbidity/mortality. Having a diagnostic strategy to detect these cases without exposing patients to low-value/harmful interventions is critical to optimize diagnosis, reduce harms and use resources wisely.
What, if any, threats to validity are most likely to have an impact on the results and how? Heterogeneity of various diagnostic definitions, outcomes measured/reported, and low outcome event rates in various subgroups erode certainty in pooled results.
How do the key results compare with the current evidence? Findings align with recent CPG Recs that a CT-only (read by neuroradiologists) for headache <6hrs is a safe strategy to identify potential SAH patients without further testing.
How should this study impact the care of ED patients? Strong evidence supports a CT-only strategy for sudden ED headaches <6hrs, read by neuroradiologists (or experienced rad readers), to rule out SAH.

Study Summary

Article Walton M, Hodgson R, Eastwood A, Harden M, Storey J, Hassan T, Randall MS, Hassan A, Williams J, Wade R. Management of patients presenting to the emergency department with sudden onset severe headache: systematic review of diagnostic studies. Emerg Med J 2022, emermed-2021-211900.

Design Systematic review. PROSPERO reg: CRD42020173265

Population *Included:* Studies with any care pathway for ruling out clinically suspicious SAH (including Dx tests +/- CDRs) in neurologically intact adults with sudden severe headache (max intensity within 1hr).
Excluded: Patients with a head injury, case studies.

Index Test Diagnostic strategies (imaging, CDRs, etc.)

Reference Standard Varied

Diagnoses of Interest Diagnostic strategy accuracy, quality of life, adverse events.

Key Results 37 studies included.

1) Clinical Decision Rules (including Ottawa SAH rule): 13 studies total, 8 OSAHR = 8114pts
   Mean SAH prevalence: 5%
   OSAHR Pooled Sens: 99.5% (95%CI 90.8-100), Spec: 23.7% (15.5-34.4); LR+ 1.3, LR- 0.02
2) CT Scan <6hrs, neurorad read (alone): 4 studies, 2377 pts.
   Mean SAH prevalence 10.8% (9.2-12.7%)
   Pooled Sens: 98.7% (96.5-100), Spec 100% (99.7-100); LR+ infinity, LR- 0.01
3) CT any time: 3 studies, 3889pts.
   Prevalence SAH 2.7-7.7%
   Pooled Sens CT >6hrs: 85.7% (78.3-90.9), Spec 90.0% (76.3-97.2); LR+ 8.57, LR- 0.16
4) CT read by ER physicians (1 study, high RoB): N=269
   Prevalence SAH 8%
   Results: Sens 84% (63.9-95.5), Spec 95% (90.9-97.2); LR+ 16.8. LR- 0.17
5) Spectrophotometric LP CSF after neg CT (3 studies, 1235pts).
   SAH Prev 0.65%.
   Pooled Sens: 100% (100-100), Spec: 95.2 (86-98.5); LR+ 20.83, LR- 0.00
6) Visual LP CSF inspection after neg CT (3 studies, 1043 pts).
   SAH Prev 2%.
   Pooled Sens: 84.9% (60-95.5), Spec 97.6 (95.3-98.8); LR+ 35.37, LR- 0.15
7) LP RBC thresholds (2 studies, not pooled): Sens 81.6-100%, Spec 91.2-97.3 for RBC <2000 $x10^6$/L and neg xanthochromia.
8) CTA after normal CT/LP: 2 small studies, no SAH cases found.
9) Clinical features of SAH: 3 studies, not pooled. Clinical suspicion SAH 49%. No individual feature was strongly predictive of SAH (age>65yo, temp>38C, SBP>160mmHg, neck stiffness, vomiting, transient loss of consciousness).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Electronic databases++, conference abstracts, no other gray literature. All languages.**	?	?
3. The search for studies was unbiased and reproducible. **No mention of duplicated searches, detailed search strategy and terms summarized in Supplement 1**	?	✓
4. The selection of studies was unbiased and reproducible. **Dual independent screening of titles/ abstracts.**	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers). **Extracted by 1 researcher, checked by another (not dual independent with 3rd party adjudications).**	X	X
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible. **Most QUADAS2-rated studies had low Risk of Bias, other non-QUADAS studies "Unclear" RoB**	?	?
7. The quality of the primary studies is high. **As above 6.**	?	?
8. The populations, cut-off thresholds, and reference standards were similar for combined studies. **High degree of heterogeneity for outcomes measured.**	X	X
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = K. Lin

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Funding and conflicts of interest

Funding None reported

Conflict of interest Reported; no significant conflicts noted

Potential threats to viability

Chance Certain pooled outcomes had small numbers of patients/outcome events, leading to potential type I or II errors. Prospective trials do a better job of evaluating eligibility criteria (compared to retrospective designs).

Selection bias *Specify comprehensive searches; publication bias?*

Measurement bias QUADAS2 tool used for most included studies for quality assessment (n=28); for studies without a reference standard, researchers used a previously created/validated tool (n=9); Supp file 3.

Analysis bias *Fixed/random effects? Heterogeneity mgt?* Random effects analysis for pooled meta-analysis. High degree of heterogeneity in reporting outcomes for included studies; X^2 values not reported.

Confounding *Enter independent factors affecting the outcome; clinicians to comment.* Patient collaborator with lived sudden headache experience involved with all aspects of the project, and 3 other patients added into study advisory group.

Administrative details

Key words Emergency department, sudden onset headache

Reference(s)

National Institute for Health and Care Excellence. Subarachnoid haemorrhage caused by a ruptured aneurysm: diagnosis and management. Draft for consultation, 2021. Available: https://www.nice.org.uk/guidance/GID-NG10097/documents/draft-guideline

TRAUMA

Research Question

How accurate is portable ultrasound for detecting blunt traumatic rib fractures?

BEEM Bottom Line

Why is this study important? Blunt traumatic rib fractures are relatively common, and need to be diagnosed accurately. Bedside ultrasound (US) can be useful to detect fractures if traditional Xray or CT scanning is inaccessible/delayed.

What, if any, threats to validity are most likely to have an impact on the results and how? Patient selection bias was the highest risk domain for QUADAS testing; could adversely affect the overall pooled diagnostic accuracy in all ED chest trauma patients (attenuated?).

How do the key results compare with the current evidence? There is congruence with prior reviews on the accuracy of US for detecting rib fractures, albeit with slightly different definitions and reference standards.

How should this study impact the care of ED patients? A positive US scan for rib fracture is essentially diagnostic, and no further confirmatory testing is warranted. This is a useful modality in resource-limited ED settings.

Study Summary

Article	Gilbertson J, Pageau P, Ritcey B, Cheng W, Burwash-Brennan T, Perry JJ, Woo MY. Test Characteristics of Chest Ultrasonography for Rib Fractures Following Blunt Chest Trauma: A Systematic Review and Meta-analysis. Annals Emerg Med 2022; 79: 529-539. DOI: 10.1016/j.annemergmed.2022.02.006
Design	Systematic review with meta-analysis; PROSPERO reg#: CRD42021252889
Population	***Included:*** Adult ED patients with blunt chest trauma and suspected rib fractures. ***Excluded:*** Case reports/series, animal or pediatric studies, narrative reviews, studies with costal cartilage fractures.
Index Test	ED ultrasound
Reference Standard	CT chest
Diagnoses of Interest	Rib fracture detection with US (fracture = cortical discontinuity in 5 studies); 2 also reported "chimney phenomenon" (local hematoma, reverberation echoes)
Key Results	**Five of 6 included studies in ED settings;** none from North America. 668 patients included, with 663 data points available for analysis; 83.7% patients = male. Four studies had ED physicians conducting US scans, 2 with radiologists, 1 with pulmonologist + 2 radiologists. All studies used linear probes, 4 also used curvilinear probes, and 1 used phased-array probe. Most patients (71.4%) were awake and able to identify location of maximal tenderness. *Pooled Diagnostic Characteristics:* Sensitivity: 89.3% (81.1-94.3%) LR-: 0.11 (0.06-0.20) Specificity: 98.4% (90.2-99.8%) **LR+: 55.7** (8.5-363.4) Diagnostic Odds Ratio for positive test: 513.6 (66.4-3970.5) No significant differences between ED vs radiologist-performed US (p=0.1119)

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact.	✓	✓	X
3. The search for studies was unbiased and reproducible.	✓	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓	✓
7. The quality of the primary studies is high.	?	?	✓
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	✓	✓	✓
9. The subgroups were stated a priori and appropriate.	X	X	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓	✓

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Funding and conflicts of interest

Funding Reported; no study funding.
Conflict of interest Reported; no conflicts of interest stated.

Potential threats to viability

Chance Convenience sampling in most included studies. Only one study enrolled consecutive patients. Selection bias of patients included may over-estimate the accuracy of US results.

Selection bias English-language studies only; only 4/1660 abstracts excluded on the basis of language translations. Search strategy with librarian/informatics specialist, repeated twice. Broad search from electronic databases, gray literature and conference abstracts.

Measurement bias One author extracted study details, 2 authors independently extracted outcomes variables. High risk of bias for patient selection for index test; low risk of bias for reference standards.

Analysis bias Two reviewers independently assessed study quality using QUADAS-2 tool. Unable to complete subgroup analyses on upper rib injuries (higher risk of mediastinal injury?). Some visual heterogeneity of sensitivity on Forest plots, but no X^2 statistics reported.

Confounding Heterogeneity in US operator training and experience could affect diagnostic test outcomes. Majority of included patients male; reluctance to expose patient's breasts/anterior chest, or possibly different detection characteristics with interposing breast tissue? No international consensus criteria for diagnosing rib fractures with ultrasound.

Administrative details

Key words Blunt chest trauma, rib fracture, ultrasound
Reference(s)

Research Question

What is the diagnostic accuracy of ED POCUS for shoulder dislocation, relocation and associated fractures?

BEEM Bottom Line

Why is this study important? POCUS is growing in indications and diagnostic utility in various emergency conditions, including trauma. Use of US for ED shoulder dislocations can reduce radiation exposures for patients, ED length of stay, and costs. This study reviews the diagnostic performance of ultrasound for shoulder dislocation & relocation.

What, if any, threats to validity are most likely to have an impact on the results and how? There is some evidence of publication bias in favour of POCUS? Significant statistical heterogeneity amongst various outcomes, some of which was accounted for planned subgroup analyses.

How do the key results compare with the current evidence? These studies build on prior primary/review evidence supporting the use of ED POCUS for anterior shoulder dislocation diagnosis. There is one study that is ongoing.

How should this study impact the care of ED patients? ED POCUS for detecting shoulder dislocation/relocation/fracture is a rapidly acquired skill for ED physicians, superbly accurate, quick to use in the ED, and reduces radiation exposures from traditional imaging.

Study Summary

Article	Gottlieb M, Patel D, Marks A, Peksa GD. Ultrasound for the diagnosis of shoulder dislocation and reduction: A systematic review and meta-analysis. Acad Emerg Med 2022; Jan 30. doi: 10.1111/acem.14454.
Design	SRMA of Diagnostic Test; PROSPERO study #CRD42019118887
Population	*Included:* Prospective studies/trials; no language, age or date restrictions. *Excluded:* Case reports, retrospective and cadaver studies.
Index Test	POCUS
Reference Standard	Radiographic imaging (Xray, CT)
Diagnoses of Interest	Primary: diagnostic accuracy of POCUS for shoulder dislocation/reduction, compared to traditional radiographs. Planned subgroup analysis based on transducer type and technique. Secondary: POCUS Dx accuracy for associated fractures.
Key Results	10 studies included (9 in ED), 1836 assessments, 636 confirmed dislocations (34.6%). Majority of POCUS exams by ED physicians; most trained with didactics and 1-2 hr hands-on training. Mean age participants 36.8 yr, 34.9% female. Anterior dislocation 98.6%, posterior 1.1%, inferior 0.3% *Primary:* Sens 100% (95% CI 85.6-100%), Spec 100% (79.4-100). LR+ 11,255 (3.9-3x10^7), LR- <0.1 (<0.1-0.2). Summary ROC 99% (99-100). *Technique/Probes used:* 1) Posterior: Sens 99.8%, Spec 100%, LR+ 3231, LR- <0.1 2) Anterior + Lateral: Sens 92.9%, Sens 100%, LR+ 308.5, LR- <0.1 3) Linear transducer: Sens 99.3%, Spec 100%, LR+ 337.0, LR- <0.1 4) Curvilinear transducer: Sens 99.8%, Spec 100%, LR+ 744.3, LR- <0.1 *Secondary (detection of associated fracture):* Sens 96.8%, Spec 99.7%, LR+ 372.5, LR- <0.1; I^2 68% (high heterogeneity).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Other gray literature (abstracts, etc.)?**	✓	✓
3. The search for studies was unbiased and reproducible.	✓	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The quality assessment of the primary studies used QUADAS, was unbiased, and reproducible.	✓	✓
7. The quality of the primary studies is high. **Low Risk of Bias for most included studies (Table 2)**	✓	✓
8. The populations, cut-off thresholds, and reference standards were similar for combined studies.	✓	✓
9. The subgroups were stated a priori and appropriate.	✓	✓
10. The methods of meta-analyses are valid (e.g., summary ROC or bivariate random effects).	✓	✓

A1 = S. Upadhye A2 = D. Kim

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Funding and conflicts of interest

Funding Reported; no funding obtained for this study.
Conflict of interest Reported; no conflicts disclosed.

Potential threats to viability

Chance Eight studies uncertain risk of bias based on convenience sampling.
Selection bias Evidence of publication bias detected on funnel plot testing illustrated in Figure 4. The search strategy was relatively comprehensive but did not explicitly include a review of the grey literature or conference abstracts. However, topics experts were consulted to help identify any additional relevant studies.
Measurement bias
Analysis bias Heterogeneity high for primary outcome (I^2 85%).
Confounding POCUS is an operator-dependent skill. There was variability in the training of POCUS operators (from a 3-min instructional video to a 6-hr training course).

Administrative details

Key words Musculoskeletal, shoulder dislocation, shoulder reduction, fracture, trauma, ultrasound, POCUS

Reference(s)

Research Question

What is the risk of delayed intracerebral hemorrhage with anticoagulated elderly patients with head injury?

BEEM Bottom Line

Why is this study important? Elderly patients using oral anticoagulants (OACs) with a traumatic brain injury (TBI) and a negative initial CT scan may still be at risk of delayed intracerebral hemorrhage (dICH). The risk of dICH is with various OACs is not well characterized; this study aimed to quantify this risk using administrative data.

What, if any, threats to validity are most likely to have an impact on the results and how? Studies based on administrative data typically have much larger sample sizes than standard cohort studies but also have multiple methodological weaknesses e.g., case finding, misclassification, inability to track evolving Rx changes, concomitant medical conditions that have an impact on study outcomes, etc. that challenge the validity of the study's conclusion(s).

How do the key results compare with the current evidence? This is a planned substudy of a larger published study examining the risk of ICH in elderly TBI patients who are on OACs (Grewal et al, CJAM 2021). These results support initial reports that use of warfarin is associated with initial and delayed ICH, but other OACs are not.

How should this study impact the care of ED patients? Elderly patients with TBI and using warfarin should all get an initial CT head to rule out incident ICH and should be advised that they are at increased risk of delayed ICH for 90days.

Study Summary

Article	Liu S, McLeod SL, Atzema CL, et al. Delayed intracranial hemorrahge after head injury among elderly patients on anticoagulation seen in the emergency department. CJEM. 2022 Dec;24(8):853-861. doi: 10.1007/s43678-022-00392-z.
Design	Administrative cohort study
Population	*Included:* Patients >65yo seen for "head injury" in Ontario ED from Jan 2016 to Dec 2018 (index ED visit only), with negative initial ED CT scan for ICH. *Excluded:* Urgent care visits/ED not open 24hrs, patients who LWBS/LAMA, or died en-route to ED. Patients using heparin in preceding 7days, or on dialysis, or confirmed Dx ICH on initial index ED visit. Patients who died within 90d of index ED visit without Dx ICH also excluded.
Exposure	Use of warfarin or other direct OACs (DOACs = apixaban, dabigatran or rivaroxaban; no edoxaban pts included).
Comparison	No anticoagulation used.
Outcomes	*Primary:* New dICH within 90days of index ED visit. *Secondary:* Patients not having initial ED CT scan, composite of death within 90days or delayed bleed (worst-case scenario = all 90d deaths were due to delayed bleeds).
Key Results	69,321 patients included in analysis. 84% not on OACs, 11.6% on direct OACs, and 4.4% on warfarin. *Delayed ICH rates:* Overall 718pts (1%) No OAC: 586pts (1%) DOAC: 78pts (1%); OR vs no OAC = 0.9 (0.6-1.1); NSS Warfarin: 54 (1.8%); OR vs no OAC = 1.5 (1.1-2.1); SS Higher dICH rates in males (OR 1.9, 1.6-2.2), history of hemorrhagic CVA (OR 1.6, 1.1-2.5), dementia (OR 1.4, 1.2-1.7), age>80yo (OR 1.3, 1.2-1.5) or HTN (OR 1.2, 1.0-1.4). Incidence dICH in unscanned index ED visits = 1.1% with no OAC, 1.7% with warfarin, and 1.0% with DOACs. Odds of dICH in unscanned warfarin patients no longer statistically significant (OR 1.4, 0.9-2.0), and no significant difference noted in unscanned DOAC patients. Composite outcome (death or dICH within 90d) occurred in 5.7% no OAC pts, 8.5% DOAC pts and 11% warfarin group. Use of warfarin was significantly associated with composite outcome (OR 1.2, 1.0-1.4), while DOAC use was not (OR 0.9, 0.8-1.1).

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were selected consecutively or randomly (i.e., without bias). **All patients meeting administrative inclusion criteria assessed.**	✓	✓
2. The patients were representative of those with the problem.	✓	✓
3. The patients were sufficiently homogeneous with respect to prognostic risk. **Table 1**	✓	✓
4. The outcome criteria were clinically appropriate for the research question.	✓	✓
5. The outcome criteria were explicit.	✓	✓
6. The outcome criteria were applied without bias.	✓	✓
7. The follow-up was complete. **N/A; retrospective subgroup analysis of administrative data.**	✓	✓
8. The effect size of the primary outcome is clinically significant.	✓	✓

A1 = S. Upadhye A2 = A. Worster

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Funding and conflicts of interest

Funding CAEP EM Advancement Fund award.
Conflict of interest Some investigators supported by career research awards; no industry supports reported.

Potential threats to viability

Chance *Type I & II errors?* Large administrative sample acquired; no sample size calculations completed *a priori*.

Selection bias *Is the sampling method representative of the target population; are the groups balanced?* Yes. May have missed some head trauma cases if index chief complaint was other trauma (not just "head injury"); risk of misclassification bias.

Measurement bias OAC status based on govt prescription databases; authors unable to assess compliance, or those OACs prescribed under private insurance plans.

Analysis bias *Are the results data- or hypothesis-driven? Is the model over fitted and not applicable?* Results driven.

Confounding Residual confounding as with all observational studies because of unknown prognostic factors that cannot be controlled for; Independent factors affecting the outcome. (See Limitations discussion). Unable to assess for concomitant aspirin use (usually purchased over-the-counter). Admin data unable to ascertain if OACs were continued, changed or discontinued after index ED visit, which may have impacted on subsequent dICH rates at 30 days.

Administrative details

Key words Head injury, delayed intracranial hemorrhage, anticoagulation, emergency department
Reference(s)
Grewal K, Atzema CL, Austin PC, De Wit K, Sharma S, Mittmann N, et al. Intracranial hemorrhage after head injury among older patients on anticoagulation seen in the emergency department: a population-based cohort study. CMAJ. 2021;193(40): E1561–7.

Research Question

Is use of non-sterile ED wound suturing non-inferior to sterile procedures?

BEEM Bottom Line

Why is this study important? Lacerations treated in the ED are presumably non-sterile and, therefore, could be managed using non-sterile gloves, wound irrigation and dressings resulting in significant cost-savings.

What, if any, threats to validity are most likely to have an impact on the results and how? Failure to meet needed sample size can lead to either type I or II errors, so results here should be interpreted with caution.

How do the key results compare with the current evidence? Prior ED-based trials and related reviews have also shown no difference in simple wound management with non-sterile equipment (Brewer et al, 2016; Perelman et al, 2004).

How should this study impact the care of ED patients? Use of non-sterile (vs sterile) gloves, drapes and dressings for simple traumatic wounds likely does not lead to increased subsequent wound infections.

Study Summary

Article	Zwaans JJ, Raven W, Rosendaal AV, et al. Non-sterile gloves and dressing versus sterile gloves, dressings and draps for suturing of traumatic wounds in the emergency department: a non-inferiority multicentre randomised controlled trial. Emerg Med J. 2022 Sep;39(9):650-654. DOI: 10.1136/emermed-2021-211540
Design	Non-inferiority RCT; trial registration NL 34798.078.11, NTR3541. Multi-centre trial (3 ED sites in Netherlands)
Population	*Included:* Adults ≥18 yo with traumatic wounds requiring sutures. *Excluded:* Complicated wounds (injury to bone/tendon/nerve/cartilage/vessels), bites (human or animal), need for OR, wound>24hrs or signs of obvious infection.
Intervention	Non-sterile gloves, drapes & dressings. All patients received chlorhexidine wound disinfection, lidocaine 1% anesthesia, and sterile sutures (Ethilon, Vicryl 3.0 to 5.0 as needed).
Comparison	Usual wound mgt with sterile gloves, drapes and dressings.
Outcomes	*Primary:* Wound infections = presence of abscess, cellulitis >1cm, purulent discharge, dehiscence or discretionary need for more wound mgt/antibiotics at ED physician follow-up visit (5-14days depending on wound characteristics and local practices).
Key Results	1480pts included (747 sterile, 733 non-sterile). Mean age 39yrs, majority males 74% in both arms. Trial stopped early due to declining inclusions, and integration of GP's into ED practice (changes to triage and wound mgt locations). Analyses included 1340pts available for f/u. *Wound Infections:* Non-sterile 5.7% (95%CI 5.1-8.8%) vs sterile 6.8% (4.0-7.5%). Mean Diff -1.1% (-3.7 to 1.5%). Non-inferiority margin NOT crossed. Wounds more frequently seen in lower extremities (20.2% vs 12.2%) and patients on immunosuppressants (6% vs 1.5%). Two sterile and 1 non-sterile patients required subsequent admission/IV antibiotics.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	✓	✓
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors. **Table 1**	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation. **Impractical at initial visit; ED physician outcomes assessor blinded at subsequent f/u visit**	?	X
6. All groups were treated equally except for the intervention. **Table 3**	✓	✓
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	?	?
8. The patients were analyzed in the groups to which they were randomized (ITT). **Not reported.**	?	?
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant. **Non-inferiority confirmed**	✓	✓

A1 = S. Upadhye A2 = A. Worster

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Funding and conflicts of interest

Funding Reported; no funding for this study.
Conflict of interest Reported; no conflicts declared.

Potential threats to viability

Chance *Sample size, Type I & II errors?* Non-inferiority margin set at 2% based on prior literature. Sample size 2140 pts needed (1070 per arm); required sample sizes NOT met. Decision to stop trial undertaken by researchers who were blinded to Rx allocation/outcomes.

Selection bias *Is the sampling method representative of the target population; are the groups balanced?* Yes

Measurement bias No clear definitions of wound infections, and some expected subjectivity of infection outcomes assessment with different follow-up ED physicians. Majority of patients followed up in ED (93%) vs telephone, reducing risk of misclassification bias.

Analysis bias *ITT, Per Protocol, As Treated.* Lost to follow-up 9%; no differences in patient characteristics with those LTFU.

Confounding Wound management was not standardized but potentially more pragmatic and generalizable. Baseline use of immunosuppressants was higher in the non-sterile vs sterile group (2.3% vs 1.1%). Inclusion of primary care physicians into Netherlands ED practices may have filtered out simpler wounds to these providers, leaving more complex/risky wounds to ED physicians enrolling patients into this RCT.

Administrative details

Key words Non-sterile, sterile, wound management

Reference(s)

Brewer JD, Gonzalez AB, Baum CL, et al. Comparison of sterile vs nonsterile gloves in cutaneous surgery and common outpatient dental procedures: a systematic review and meta-analysis. JAMA Dermatol 2016; 152: 1008–14.

Perelman VS, Francis GJ, Rutledge T, et al. Sterile versus nonsterile gloves for repair of uncomplicated lacerations in the emergency department: a randomized controlled trial. Ann Emerg Med 2004; 43: 362–70.

Research Question

Can functional bracing replace traditional plaster casting for non-operative ankle fracture care?

BEEM Bottom Line

Why is this study important? Plaster casts for ankle fractures hamper physical activity for prolonged time periods, and have significant impact on patient quality of life, sleep, and independence. Removable functional bracing can improve these outcomes without compromising healing.

What, if any, threats to validity are most likely to have an impact on the results and how? Minimal. This large multi-centre trial met its sample size requirements, had balanced comparison groups and accounted for missing patients competently.

How do the key results compare with the current evidence? This large RCT reaffirms prior smaller studies showing no differences between traditional casting vs functional bracing (including 1 large non-inferiority trial).

How should this study impact the care of ED patients? It is reasonable to offer removable functional bracing for closed ankle fractures, with appropriate orthopedic follow-up/cooperation.

Study Summary

Article	Kearney RS, McKeown R, Parsons H, *et al*, on behalf of the AIR trial collaborators. Use of cast immobilisation versus removable brace in adults with an ankle fracture: multicentre randomised controlled trial. BMJ 2021;374:n1506 http://dx.doi.org/10.1136/bmj.n1506
Design	Pragmatic multicentre RCT (superiority design) at 20 UK NHS trauma units; registration ISRCTN15537280
Population	***Included:*** Adults >18yo with a closed ankle fracture; included both operative and non-operative patients. ***Excluded:*** No immobilization needed (treating physician decision), known metastatic fracture, complex intra-articular injury (eg. Pilon), wound complications that contra-indicate bracing, pre-existing neuropathic joint disease, previously enrolled, unable to meet trial follow-up processes, or required close contact casting.
Intervention	Removable functional bracing (minimum 3 weeks); braces not standardized across all study sites. Ankle exercises as soon as pain allowed (10 repetitions TID).
Comparison	Traditional plaster casting (minimum 3 weeks). Ankle exercises after cast removed.
Outcomes	***Primary:*** Olerud Molander ankle (OMA) score at 16 weeks; composite of 9 different ankle functional domains, 0-100pt scale. MCID 10pts previously validated. ***Secondary:*** Manchester-Oxford foot questionnaire, disability rating index, resource use, quality of life (on EQ-5D-5L scale), and complications at 6, 10 and 16 weeks. Complications = DVT/PE, pain, swelling, foot numbness, wound infections, fracture healing.
Key Results	669 patients recruited (334 plaster cast, 335 removable brace). Mean age 46yo, 57% female. 502pts completed the trial (75%). Operative mgt in 54% recruited patients. No statistically significant difference between OMA scores at 16 weeks; mean Diff 1.8pts (-2.0 to 5.6) favours bracing. No differences in OMA scores at other time points, nor any significant differences in any secondary outcomes at any time point. No differences in outcomes for subgroup analyses based on age or non/operative care.

BEEM Critique

Risk of bias assessment

	A1	A2
1. The patients were recruited consecutively.	?	?
2. The patients were adequately randomized (allocation sequence adequately generated).	✓	✓
3. The allocation sequence was adequately concealed.	✓	✓
4. The patients in all groups were similar with respect to prognostic factors.	✓	✓
5. All clinicians, patients, and outcome assessors were unaware of group allocation.	X	X
6. All groups were treated equally except for the intervention.	?	?
7. The follow-up was complete given the study duration (100% if in-hospital follow-up).	X	X
8. The patients were analyzed in the groups to which they were randomized (ITT).	✓	✓
9. All patient-important outcomes were considered.	✓	✓
10. The effect size of the primary outcome is clinically significant.	X	X

A1 = S. Upadhye A2 = J. Owen

Funding and conflicts of interest

Funding	Funding via the UK National Institute for Health Research, for research fellowship lead author. No industry supports.
Conflict of interest	None; various authors do work for different govt health policy agencies.

Potential threats to viability

Chance	No mention of consecutive vs convenience sampling; difficult to manage in 20 separate units? Sample size calculated for 20% lost to follow-up, and 25% actually missing (not evenly balanced; more missing in cast group).
Selection bias	Both groups demographically well balanced at recruitment. Sampling from 20 different trauma units enhances generalizability.
Measurement bias	Missing data imputed using various models (Rubens rules); no impact on primary outcome.
Analysis bias	Intention to treat analysis specified. Preplanned sensitivity analysis for missing data and protocol adherence differences. Planned subgroup analyses based on non-operative vs operative, and age cutoff 50yrs (presumed higher risk of osteoporotic fractures in age>50).
Confounding	Operative patients randomized after post-operative backslab and routine wound checks, and enrolled 2 weeks post-op if no concerns, whereas non-operative patients enrolled/randomized immediately. Blinding of participants and clinicians not possible. Patients started ankle range exercises ASAP after cast removed, or when pain allowed in removable brace group. Other rehab inputs permitted based on local practices (eg. choice of weight-bearing, duration of immobilization, offer of physiotherapy services).

Administrative details

Key words	ankle fracture, cast immobiliization, functional removable bracing
Appraisers	S. Upadhye, J. Owen
Reference(s)	

CRITICAL CARE

Research Question

What is the optimal defibrillation strategy for refractory ventricular fibrillation (VF)?

BEEM Bottom Line

Why is this study important? Out-of-hospital cardiac arrest (OHCA) is still a frequent cause of adult mortality in North America, and ventricular fibrillation (VF) and tachycardia (VT) are more amenable to electrical therapy than others. However, even early defibrillation is commonly unsuccessful. This trial assesses the effectiveness of double sequential external defibrillation (DSED) i.e., rapid sequential shocks from 2 defibrillators, and vector change (VC) i.e., repositioning defibrillation pads to anterior-posterior position, compared to standard defibrillation strategy.

What, if any, threats to validity are most likely to have an impact on the results and how? The trial was stopped prematurely because of the COVID-19 pandemic which increases the risk of a type I or type II error.

How do the key results compare with the current evidence? This trial builds on prior trials suggesting that rapid stacked electrical therapies for VF/VT can be beneficial for meaningful survival outcomes.

How should this study impact the care of ED patients? If 2 defibrillators are available, the DSED strategy is preferred; otherwise VC should have improved outcomes for adult OHCA patients with refractory VF.

Study Summary

Article	Cheskes S, Verbeek PR, Drennan IR, et al. Defibrillation Strategies for Refractory Ventricular Fibrillation. NEJM 2022; Nov 24;387(21):1947-1956. doi: 10.1056/NEJMoa2207304. DOSE VF ClinicalTrials.gov number, NCT04080986
Design	Cluster randomized controlled trial (with cross-over) in 6 Ontario EMS paramedic services. Each EMS unit crossed over to a different arm every 6mo.
Population	*Included:* Adults ≥ 18 yo with out-of-hospital cardiac arrest (OHCA) and VFib refractory to standard defibrillation (defined as persistent VF/pulseless VT after 3 std defib attempts with appropriate CPR). *Excluded:* Traumatic cardiac arrest, DNR medical directives, drowning, hanging, suspected drug OD
Intervention	Double-sequential external defibrillation (DS-ED), Vector Change defibrillation (VC)
Comparison	Standard defibrillation
Outcomes	*Primary:* Survival to hospital discharge *Secondary:* Termination of VF, return-of-spontaneous-circulation (ROSC), good neurologic outcome (mod Rankin score 2 or less at hospital discharge)
Key Results	405 patients enrolled; Std 36% (n=135), VC 35.6% (144), DSED 30.9% (125). 87.7% received the assigned defib strategy. Mean patient age 63.6yo, 84.4% males. Witnessed OHCA 67.9%, and 58% received bystander CPR (Table 1). Similar time to 1st defibrillation, number of shocks and other resuscitation characteristics in all 3 groups (Table 2). *Primary Outcome: (Table 3)* Std Defib: 18 survivors (13.3%) VC Defib: 31 survivors (21.7%); RR vs Std 1.71 (95%CI 1.01-2.88) DSED: 38 survivors (30.4%); RR vs Std 2.21 (95%CI 1.33-3.67) *Effect estimates are stable across multiple pre-specified sensitivity analyses!! *Fragility Index: If 9 patients in DSED groups or 1 VC patient did not survive to hospital discharge, primary outcome would have been rendered insignificant. *Secondary Outcomes: (RR vs Std, 95%CI) Table 3* Termination of VFib: Std 67.6%, VC 79.9% (RR 1.18, 1.03-1.36), DSED 84% (RR 1.25, 1.09-1.44) ROSC: Std 26.5%, VC 35.4% (RR 1.39, 0.97-1.99), DSED 46.4% (RR 1.72, 1.22-2.42) MRS 2 or less: Std 11.2%, VC 16.2% (RR 1.48, 0.81-2.71), DSED 27.4% (RR 2.21, 1.26-3.88)

BEEM Critique

Risk of bias assessment

	A1	A2
1. The research question is sensible and answerable.	✓	?
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Mostly electronic databases searched, some reference lists**	?	✓
3. The search for studies was unbiased and reproducible. **No duplicate search reported**	?	✓
4. The selection of studies was unbiased and reproducible.	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible. **Duplicate?**	?	?
7. The quality of the primary studies is high. **RCTs low RoB, nonRCTs higher RoB. Included OHCA and IHCA in some studies. Studies included were from 2010-2019. Uncertain characteristics of arrest or cooling time, etc. Short outcome duration (mortality at hospital discharge).**	?	?
8. The methods used to combine the included primary studies were reported and valid.	✓	✓
9. The outcomes are clinically relevant.	✓	?
10. The statistical heterogeneity of the primary outcome is low (< 25%).	✓	✓

A1 = S. Upadhye A2 = J. Owen

Clinical Appraisal faculty

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Funding and conflicts of interest

Funding Not reported
Conflict of interest One author (WB) reported speaker fees from various industries. No other CoI's declared.

Potential threats to viability

Chance *Sample size, Type I & II errors?* Variable sample sizes in included studies, which may affect outcomes of interest in pooled data.

Selection bias *Limited/incomplete search, publication bias, etc.* No assessment of publication bias reported. No mention of grey literature searches.

Measurement bias *Missing details on study selection; missing results of quality assessments.* Contacted authors for missing data.

Analysis bias *Fixed vs. random effects, combined results of studies of different design.* N/A

Confounding *List as reported.* Studies only included temp 34-36C. No analysis of duration of cooling, devices used, time to cooling initiation, rewarming rates.

Administrative details

Key words Cardiac arrest; cooling; network meta-analysis; neurologic outcome; survival; targeted temperature management

Reference(s) N/A

Research Question

What are the latest recommendations for managing difficult airways (DA)?

BEEM Bottom Line

Why is this study important? This clinical practice guideline (CPG) updates recommendations from the American Society of Anesthesiologists Difficult Airway guidance.

What, if any, threats to validity are most likely to have an impact on the results and how? There is no clear linkage between the retrieved evidence and the strength of CPG recommendations.

How do the key results compare with the current evidence? Updated evidence searches and filtering of evidence, and support by international experts surveyed improves confidence in the recommendations.

How should this study impact the care of ED patients? Emergency departments (EDs) should create and implement DA quality improvement programs to operationalize clinical algorithms offered in this document.

Study Summary

Article	Apfelbaum JL, Hagberg CA, Connis RT, Abdelmalak BB, Agarkar M, Dutton RP, Fiadjoe JE, Greif R, Klock PA, Mercier D, Myatra SN, O'Sullivan EP, Rosenblatt WH, Sorbello M, Tung A. 2022 American Society of Anesthesiologists (ASA) Practice Guidelines for Management of the Difficult Airway. Anesthesiology 2022; 136(1): 31-81. DOI: 10.1097/ALN.0000000000004002
Design	Clinical Practice Guideline
Population	*Included:* Adult and pediatric patients in in-patient settings, including the ED (and other critical care settings). *Excluded:* Pre-hospital settings. Not applicable for patients at risk of aspiration, nor physiologic (not anatomic) difficult airways.
Scope of Recommendations	CPGs are intended for adult and pediatric patients with either anticipated or unanticipated difficult airways, obstetric patients, intensive care (ICU) patients, and critically ill patients.

Key Recommendations

LoE = Level of Evidence, Strength of Recs (LoE) NOT explicitly reported in publication

1) Evaluation for Difficult Airway (DA): The most responsible airway personnel should confirm medical, surgical, environmental and anesthetic factors that can influence patient airway outcomes. Get historical information as needed from patient, family, medical records, etc. Complete a physical exam to determine any anatomic predictors of difficult airways. Determine a risk of needing advanced airway equipment (e.g., bronchoscope, surgical airway).
2) DA Preparation: Have all equipment for advanced/emergency airway interventions on hand; consider preparing a "Difficult Airway" cart with appropriate training. Ensure proper positioning and supplement oxygen use prior to initiating DA interventions.
3) Anticipate DA: Identify step-wise strategies for awake intubation, DA patients who can be adequately ventilated, DA patients who can't be ventilated/intubated, and invasive rescue airway procedures. When appropriate, start with awake intubations if: a) difficult ventilation (face mask/supraglottic airway), (b) increased risk of aspiration, (c) DA patient is likely incapable of tolerating a brief apneic episode, or (d) there is expected difficulty with emergency invasive airway rescue. Anticipate need to vary interventions for pediatric or uncooperative patients. Be ready to used combined techniques for DA interventions as clinically warranted. Limit the number of unsuccessful intubation attempts to avoid trauma. Be wary of the passage of time with repeated attempts; monitor oxygen saturation throughout the procedure. Ensure oxygenation between attempts with BVM ventilation.
4) Unanticipated DA: Call for help as needed. Optimize oxygenation (BVM). Determine appropriateness of non-invasive vs invasive interventions. For invasive airway Rx, ensure proper training/experience for airway personnel, and complete the airway intervention as expeditiously as possible.
5) Confirmation of Tracheal Intubation: Use capnography/end-tidal CO_2 monitoring to confirm endotracheal intubation.

BEEM Critique

Risk of bias assessment (amalgamated from AGREE-II/NEATS instruments)

	A1	A2
1. The clinical practice guideline (CPG) discloses and states explicitly its funding source.	?	?
2. Financial conflicts of interest of guideline development group (GDG) members have been disclosed and managed.	?	?
3. The CPG development group includes all of the relevant multidisciplinary stakeholders, including clinicians, methodologists and patients/caregivers.	?	?
4. The CPG objectives, health questions, scope of relevant providers and target recipients of care are clearly defined.	✓	✓
5. Values/preferences of patients, caregivers, advocates and/or the public with experience with the clinical disease management has been sought/integrated into CPG development (reported clearly).	?	?
6. The search strategy for evidence is thoroughly developed and described.	✓	✓
7. The criteria for selecting relevant studies/evidence are clearly described.	✓	✓
8. The quality, strengths and limitations of the body of evidence are clearly described (e.g., GRADE, Cochrane, etc.). Summaries of evidence tables are provided.	✓	✓
9. The health benefits, side effects, and risks were considered in formulating the recommendations.	✓	✓
10. There is an explicit approach linking the evidence to formulate the recommendations.	X	X
11. The strength of recommendations is clearly reported, including confidence in underlying evidence.	X	X
12. Recommendations are clear and unambiguous, and easily identified in the CPG publication.	✓	✓
13. Different options for management for managing the health questions are clearly presented.	✓	✓
14. Experts externally reviewed the guideline prior to its publication.	✓	✓
15. The CPG describes a procedure to update the guideline.	X	X
16. The CPG provides advice, tools and/or clinical pathways for easy adoption/adaptation into practice.	✓	✓
17. The CPG describes barriers and facilitators to implement recommendations.	X	X
18. Performance metrics for monitoring implementation of recommendations for audit/feedback have been defined appropriately.	X	X
19. Resource implications for implementing CPG recommendations have been discussed.	X	X

A1 = S. Upadhye A2 = A. Worster

Clinical Appraisal faculty

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Funding and conflicts of interest

Funding (Reported) Support provided solely by the ASA (pg 51).

Conflict of interest (Reported) Multiple authors had various disclosures of academic grants, and industry support. Management of those with various conflicts was not clearly disclosed.

Potential threats to viability

Development	The CPG panel had many airway experts & methodologists, but no patient, ED physician/nurse/RT stakeholders.
Presentation	Not well organized, key recommendations are buried at end of CPG, although they are reasonably identifiable in body of manuscript.
Comprehensive	The information to inform decision-making was complete.
Clinical Validity	Useful info graphics and algorithms are provided to support implementation in the workplace.

Administrative details

Key words	Difficult airway, ED.
Reference(s)	Orebaugh SL. Difficult Airway Management in the Emergency Department. J Emerg Med 2002; 22(1): 31-48. Brown NS, Chirico J, Hollidge M, Randall J. Clinical leadership in reducing risk: Managing patient airways. Healthcare Manage Forum 2019;32(2):92-96. doi: 10.1177/0840470418810678. Kornas RL, Owyang CG, Sakles JC, *et al*. Evaluation and Management of the Physiologically Difficult Airway: Consensus Recommendations From Society for Airway Management. Anesth Analg 2021 Feb 1;132(2):395-405. doi: 10.1213/ANE.0000000000005233.

Research Question

What are the most beneficial interventions for cardiogenic shock complicating myocardial infarction?

BEEM Bottom Line

Why is this study important? Cardiogenic shock complicating myocardial infarction (MI-CS) has a higher mortality than other etiologies, and interventions to reduce mortality in this scenario are important. This review synthesizes all available literature for different interventions to reduce MI-CS, including inotropes, vasopressors and mechanical circulatory support (MCS).

What, if any, threats to validity are most likely to have an impact on the results and how? Small number of included RCTs led to greater imprecision of pooled results, and Low GRADE certainty of evidence for most interventions. Also most trials included patients with less severe shock (SCAI A-B), so intervention effects on more severe shock are unknown. Network meta-analysis used as very few direct comparison RCTs available. No data on VA ECMO MCS.

How do the key results compare with the current evidence? Current evidence for inotropes, vasopressors, and MCS in MI-CS is very limited. These results pool all available data from RCTs and provide the most up-to-date review of available evidence..

How should this study impact the care of ED patients? Recognition of MI-CS or patients at risk for MI-CS is critically important in the ED, and initial interventions should focus on evidence-based revascularization strategies. For patients with hypotension, norepinephrine appears to be the first line agent in cardiogenic shock. Further data is required to determine the best inotrope, MCS therapy, and timing of these interventions.

Study Summary

Article	Fernando SM, Mathew R, Sadeghirad B, Brodie D, Belley-Côté EP, Thiele H, van Diepen S, Fan E, Di Santo P, Simard T, Russo JJ, Tran A, Lévy B, Combes A, Hibbert B, Rochwerg B. Inotropes, vasopressors, and mechanical circulatory support for treatment of cardiogenic shock complicating myocardial infarction: a systematic review and network meta-analysis. Can J Anesth 2022; 69: 1537-1553. doi: 10.1007/s12630-022-02337-7.
Design	Systematic Review with Network Meta-analysis. Registered with *Center for Open Science (https://osf.io/ky2gr).*
Population	*Included:* Patients with cardiogenic shock = hypotension (sBP<100mmHg), organ hypoperfusion (cool extremities, altered mentation, elevated lactate, oliguria, other end-organ dysfunction), or severe heart failure requiring inotropes/vasopressors for support. *Excluded:* Post cardiac revascularization patients who may have non-cardiogenic shock.
Intervention	Inotropes, vasopressors, mechanical circulatory support (MCS)
Comparison	Direct & indirect comparisons.
Outcomes	*Primary:* 30day all-cause mortality. *Secondary:* All-cause mortality close to 30days, acute kidney injury/need for dialysis, initiation of MCS, duration of hemodynamic support, hospital length of stay (LOS) and major bleeding.
Key Results	17 RCTs included (n=2339 pts). All parallel designs. *Intotropes: (7 trials, 1145 pts; 5 trials with SCAI A-B shock)* Levosimendan 30d Mort (vs Placebo): OR 0.53 (95%CI 0.33-0.87, Mod LoE) Milrinone (vs Plac): OR 0.52 (0.19-1.39); Low LoE Dobutamine (vs Plac): OR 0.67 (0.30-1.49); Low LoE Enoximine (vs Plac): OR 1.58 (0.39-6.45); Very low LoE **No detectable differences in head-to-head comparisons. Insufficient data to investigate pre-specified secondary outcomes.

Vasopressors: (2 RCTs)
SOAP-II trial (completed, n=280pts): NE vs Dopamine OR 0.58 (0.36-0.94, p=0.03) for 28d mortality favouring NE.
OptimaCC trial (stopped early, n=57pts): NE vs Epi OR 2.55 (0.84-7.72)

Mechanical Circulatory Support: (8 trials)
No effect on mortality with IABP (OR 0.94, 0.69-1.28) nor percutaneous MCS (OR 0.96, 0.47-1.28) against no MCS (Low LoE), uncertain effect of IABP + pMCS vs no MCS (OR 5.56, 0.21-144.20, very low LoE), and no difference between IABP vs pMCS (OR 0.98, 0.51-1.88, Low LoE). All other comparisons had uncertain effects (wide CI's, very low LoE).

Major bleeding (5 trials): No difference between IABP and no MCS (OR 1.00, 0.69-1.45, Low LoE), but IABP may have lower bleeding vs pMCS (OR 0.20, 0.06-0.69; Low LoE). pMCS may have higher bleeding vs no MCS (OR 4.91, 1.38-17.44; Low LoE).

BEEM Critique

Risk of bias assessment

	A1	A2	A3
1. The research question is sensible and answerable.	✓	✓	✓
2. The search for studies included all languages, databases, abstracts, bibliographies, and expert contact. **Search of 6 electronic databases (librarian-assisted), no language restrictions. No comment on gray literature searches.**	?	?	✓
3. The search for studies was unbiased and reproducible. **Unclear duplicate searches.**	?	?	✓
4. The selection of studies was unbiased and reproducible. **Duplicate screening/selections.**	✓	✓	✓
5. The data abstraction was unbiased (e.g., conducted independently by 2 researchers).	✓	✓	✓
6. The assessment of the quality of the primary studies was unbiased and reproducible. **Cochrane RoB tool, duplicate assessments. GRADE based certainty of evidence.**	✓	✓	✓
7. The quality of the primary studies is high. **Mostly low RoB for all included studies (high RoB for blinding in most studies). ESM eTable 2.**	?	X	X
8. The methods used to combine the included primary studies were reported and valid.	✓	✓	✓
9. The outcomes are clinically relevant.	✓	?	✓
10. The statistical heterogeneity of the primary outcome is low (< 25%). **Low I^2 values for included Forest plots.**	✓	✓	✓

A1 = S. Upadhye A2 = J. Owen A3 = K. Al Lawati

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Funding and conflicts of interest

Funding	None.
Conflict of interest	Multiple authors have received industry funding, advisory board work and personal fees; most outside of submitted work.

Potential threats to viability

Chance	*Sample size, Type I & II errors?* Relatively few trials included for most outcomes.
Selection bias	*Limited/incomplete search, publication bias, etc.* Limited search, no gray literature. No specific discussion of publication bias (embedded in GRADE certainty of evidence assessment?).
Measurement bias	*Missing details on study selection; missing results of quality assessments.* Small number of trials reduced heterogeneity, but increased imprecision.
Analysis bias	*Fixed vs. random effects, combined results of studies of different design.* Random effects analyses preplanned.
Confounding	*List as reported.* Most patients had lower severity of MI-CS (SCAI A-B, not higher), so effects of interventions on more severe shock states unknown.

Administrative details

Key words	Cardiogenic shock, cardiology, critical care medicine, inotropes, mechanical circulatory support, vasopressors
Reference(s)	

Research Question

What is the benefit of using fentanyl with ketamine and rocuronium during ED rapid sequence intubation (RSI)?

BEEM Bottom Line

Why is this study important? RSI is a common ED procedure and significant hemodynamic changes associated with it can contribute to adverse outcomes. This clinical trial examined hemodynamic changes with and without fentanyl for RSI with ketamine and rocuronium (KetRoc).

What, if any, threats to validity are most likely to have an impact on the results and how? The relatively small and very heterogeneous group of patients needing ED RSI precluded subgroup analyses based on diagnosis that may have shown important differences in outcomes. The primary outcome, systolic blood pressure (SBP) change outside of a pre-specified limit, is a surrogate for patient-important outcomes. Possible SBP measurement errors using non-invasive devices may introduce some variability, but likely better reflect real-world ED practice.

How do the key results compare with the current evidence? Prior trials/reviews show mixed results, based on different study design issues, patient inclusion/exclusions and other trial variables.

How should this study impact the care of ED patients? Selective use of fentanyl with KetRoc ED RSI is likely safe and useful, assuming that there is a no need to avoid episodes of hypotension.

Study Summary

Article	Ferguson I, Buttfield A, Burns B, Reid C, Shepherd S, Milligan J, Harris IA, Aneman A, for the Australasian College of Emergency Medicine Clinical Trials Network. Fentanyl versus placebo with ketamine and rocuronium for patients undergoing rapid sequence intubation in the emergency department: The FAKT study-A randomized clinical trial. Acad Emerg Med 2022; 29(6): 719-728. DOI: 10.1111/acem.14446
Design	Multi-centre RCT, 5 Australian hospital EDs. Trial Registration: ANZ Clinical Trials Registry, ACTRN12616001570471 (anzctr.org.au). Mixed academic/community centers, adults & peds.
Population	*Included:* Adults (>18yo) needing ED RSI. *Excluded:* Allergy to study meds, need for "paralysis-only" or "no-drug" intubation, need for alternative induction regimen, ED "overwhelmed" or no staff available trained in study protocols.
Intervention	Fentanyl 100ug in 20ml NS; matched 1:1 with ketamine (0.5-2.0mg/kg IV) dosing volume. Drug order = Study drug *then* ketamine *then* rocuronium. Laryngoscopy initiated 60sec post Roc. Post RSI sedation continued after 10min with fentanyl and propofol.
Comparison	20ml NS, also matched to ketamine dose volume. Same drug sequence, sedation as above.
Outcomes	*Primary:* Change in SBP outside of 100-150mmHg within 10min after induction sequence (measured every 2min). If pre-induction sBP >151mmHg, then primary outcome met if sBP rose >10% or outside limits during 10min interval. For initial sBP <99mmHg, then primary outcome met if sBP fell >10% or outside 10min interval limits. *Secondary:* Hypoxia (SpO_2 <93%), tachycardia (HR >120), or cardiac arrest within 10min induction interval. Airway outcomes = laryngoscopic views, first-pass intubation success, use of supraglottic airway devices (SAD), or need for surgical airway. 30day mortality, vent-free days.
Key Results	277 patients analyzed for primary outcome (95.5% recruited). *Primary:* Fent 66% vs Placebo 65%; Difference 1% (95%CI -10% to 12%, p=0.86). No statistically significant differences with missing 13pts added to either group. *Secondary:* Higher tachycardia in placebo (61%) vs fentanyl (48%); Diff 13% (2-25%). No significant differences in hypoxia (Diff 6%, 95%CI -2% to 15%), airway outcomes, 30day mortality (Fent 19%, Plac 24%; Diff 5% [-4% to 15%]), or vent-free days. Higher rates of hypertension with placebo, and hypotension with fentanyl.