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Emergency Medicine Journal Club

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Abstract

In this column, we provide a brief review of important papers recently published that relate to the field of Emergency Medicine. The goal is to provide the busy clinician a bullet-like summary of the study, focusing on the research question, methods, results, limitations and bottom line interpretation.

Keywords

emergency medicine, journal club, evidence-based medicine, review

Conflict of Interest Statement

We, the authors, have no conflicts of interest to disclose.

REVIEW

Emergency Medicine Journal Club

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Abstract

In this column, we provide a brief review of important papers recently published that relate to the field of Emergency Medicine. The goal is to provide the busy clinician a bullet-like summary of the study, focusing on the research question, methods, results, limitations and bottom line interpretation.

Keywords: Emergency medicine, Journal club, Evidence-based medicine, Review

In this quarter's column, we provide a brief review of important papers published in the last year that relate to the field of Emergency Medicine. Our goal is to provide busy clinicians a concise summary of the study, focusing on the research question, methods, results, limitations and bottom line interpretation. There are 12 papers reviewed herein.

Topic: Resuscitation; Cardiac Arrest

Question: What are the most common causes of cardiac arrest in hospitalized patients?

Study

Allencherril J, Lee PYK, Khan K, Loya A, Pally A. Etiologies of In-hospital cardiac arrest: A systematic review and meta-analysis. *Resuscitation*. 2022; 175:88–95. https://doi.org/10.1016/j.resuscitation.2022.03.005

Methods: Comprehensive database meta-analysis through May 2021 of studies reporting on in-hospital cardiac arrest etiologies. Patients in the emergency department, critical care units, or operating rooms were excluded. Arrests were organized into 7 cardiac and 7 noncardiac subtypes. Initial cardiac rhythm was analyzed when available.

Results: 9 studies were included, representing 27,102 cardiac arrests. Hypoxia (26.5%), acute coronary syndrome (18.2%), hypovolemia (14.8%), infection (14.4%), and heart failure (12.6%) were the most common causes. 14.2% of cases had no known cause. The most common initial cardiac rhythm was pulseless electrical activity (69.8%), followed by ventricular tachycardia or fibrillation (21.8%). Electrolyte/metabolic (3.0%), tamponade (3.0%), pulmonary embolism (2.7%), and pneumothorax (0.1%) were less common causes of cardiac arrest.

Limitations: Retrospective, overlap exists between some categories (such as dysrhythmia and electrolyte/metabolic derangement), study is international and the United States population may be different, meta-analysis included papers for which etiology was not part of the primary analysis which could lessen data reliability.

Bottom Line: According to this study, the most common causes of in-hospital cardiac arrest are hypoxia, acute coronary syndrome, hypovolemia, sepsis, and heart failure, in that order. Pulseless electrical activity was nearly 3 times as common as a shockable rhythm.

Topic: Cardiology

Question: Among patients who receive troponin testing in the emergency department, how have rates of discharge, cardiac testing, and mortality changed since implementation of high-sensitivity cardiac troponin T (hs-cTnT) assays?

Study

Younis A, Farooq S, Bisognano JD, et al. Outcomes Associated with Introduction of the 5th Generation High-Sensitivity Cardiac Troponin in Patients Presenting with Cardiovascular Disorders. *J Emerg Med*.

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2022; 62(5):657−667. https://doi.org/10.1016/j.jemermed.2022.01.011

Methods: Retrospective single-system (University of Rochester) chart review of all emergency patients in whom at least 1 troponin test was performed from January−September 2018. Patients with noncardiac complaints were excluded. Troponins were obtained at 0-hour and 3-hour intervals, with a positive result based on a combination of absolute value and amount of change. High-sensitivity troponin testing began in April, so approximately half of the months reviewed used standard, 4th generation troponin (cTnT) assays, and half the newer, hs-cTnT assays. Patients were analyzed in groups separated by whether they were evaluated to rule out acute coronary syndrome (RO-ACS) versus other cardiovascular problems (O-CV).

Results: 5377 patients were included. cTnT and hs-cTnT groups were similar save for a slight predominance of Black and diabetic patients in the hs-cTnT, O-CV subgroup. Among RO-ACS patients, rates of discharge from the emergency department increased after hs-cTnT implementation (48% from 37%) as did length of stay (5.9h from 5.4h). Among O-CV patients, rates of repeat troponin testing increased (87% from 40%), increasing length of stay (5.7h from 4.9h) and diagnosis rate of myocardial infarction (60% from 15%). After emergency evaluation, rates of stress testing and other cardiac testing increased. Mortality was unchanged at 9 months.

Limitations: Retrospective, single system (although multiple hospitals), analysis occurred during transition to hs-cTnT assay and some issues may reflect uncertainty about how to interpret the test or problems in implementation, this studied a 3h delta rather than 1h delta, some tests were ordered by nursing at triage and may not reflect decision-making by physicians and other practitioners, myocardial infarction diagnosis did not differentiate between type I (occlusive) and type II (supply-demand mismatch).

Bottom Line: Implementation of hs-cTNT led to higher rates of emergency department discharge among RO-ACS patients, while increasing overall length of stay, troponin testing, invasive cardiac testing, and diagnosis of myocardial infarction in all studied patients without change in mortality.

Topic: Trauma

Question: Can patients with small pneumothorax (PTX) of 35mm or less on CT be safely observed without chest tube placement?

Study

Figueroa JF, Karam BS, Gomez J, et al. The 35-mm rule to guide pneumothorax management: Increases appropriate observation and decreases unnecessary chest tubes. *J Trauma Acute Care Surg*. 2022; 92(6):951−957. https://doi.org/10.1097/TA.0000000000003573

Methods: Single-center retrospective review of adult trauma patients who had a PTX diagnosed on CT before (2015−2016) and after (2018−2019) guideline implementation. Patients with chest tubes inserted before CT, concurrent hemothoraces, mechanical ventilation, or mortality in the first 24 hours were excluded.

Results: 266 patients met inclusion criteria. Ninety-nine (37.2%) and 167 patients (62.7%) were admitted before and after 2017, respectively. Overall, there were no significant demographic differences or differences in severity between the groups. Observation rates increased after guideline implementation. Tube thoracostomies decreased from 28.3% to 18%. There were no statistically significant changes in observation failure rates, hospital or ICU length of stay, complications, or mortality.

Limitations: Single-center, retrospective study, and some significant patient-centered measures such as pain and patient satisfaction were not measured. Patients with hemothorax and those undergoing mechanical ventilation were excluded.

Bottom Line: Observation of small pneumothoraces of $\leq$35mm appears to be safe and decreases unnecessary tube thoracostomy in hemodynamically stable patients without hemothorax.

Topic: Neurology

Question: Is the use of IV tenecteplase at a dose of 0.4mg/kg safe and effective for the treatment of acute ischemic stroke in patients with moderate to severe stroke when compared to IV alteplase at a dose of 0.9mg/kg?

Study

Kvistad CE, Næss H, Helleberg BH, et al. Tenecteplase versus alteplase for the management of acute ischaemic stroke in Norway (NOR-TEST 2, part A): a phase 3, randomised, open-label, blinded endpoint, non-inferiority trial. *Lancet Neurol*. 2022; 21(6):511−519. https://doi.org/10.1016/S1474-4422(2200124-7)

Methods: Phase 3, randomized, open-label superiority trial conducted at 11 hospitals in Norway. Adults with suspected acute ischemic stroke eligible for thrombolysis with an NIHSS of 6 or greater and presenting within 4.5 hours of symptom onset were included. Patients were randomly assigned to IV tenecteplase at a dose of 0.4 mg/kg (max 40 mg) or alteplase 0.9mg/kg (max 90mg). Patients were not aware of group allocation, but treating physicians were. Outcome assessment was masked. Primary

outcome was excellent functional outcome defined as modified Rankin Scale (mRS) of 0−1 at 3 months.

Results: 216 patients met inclusion criteria. Enrollment was stopped after a per-protocol safety review showed an imbalance in the rates of symptomatic intracranial hemorrhage (ICH) between the treatment groups. A favorable functional outcome was reported less frequently in patients receiving tenecteplase (31 [32%] of 96 patients) compared with alteplase (52 [51% of 101 patients). Mortality at 3 months was significantly higher with tenecteplase (15 [16%] of 96 patients) than with alteplase. More cases of symptomatic ICH were reported with tenecteplase (six of 101 patients) than with alteplase (one of 104 patients; unadjusted OR 6.57 [95% CI 0.78−55.62]; p = 0.061.

Limitations: Single-center study, stopped early due to concern for harm.

Bottom Line: This study suggests that the dose of 0.4mg/kg of tenecteplase confers worse outcomes than traditional-dose alteplase when used to treat patients with moderate or severe stroke (NIHSS≥6). An ongoing study (NOR-TEST 2, Part B) will examine the effectiveness of 0.25mg/kg tenecteplase to 0.9mg/kg alteplase in this same patient population. This is the dosing currently used in the RRH system.

Topic: Infectious disease, critical care

Question: Does a restrictive fluid strategy in sepsis confer a mortality advantage over traditional fluid therapy in sepsis?

Study

Meyhoff TS, Hjortrup PB, Wetterslev J, et al. Restriction of Intravenous Fluid in ICU Patients with Septic Shock. *N Engl J Med*. 2022; 386(26):2459−2470. https://doi.org/10.1056/NEJMoa2202707

Methods: Randomized control trial of patients who had received at least 1L IVF to either a restrictive strategy or a normal fluid resuscitation strategy. Primary outcome was death from any cause at 90 days.

Results: Of the1554 patients, 770 were assigned to the restrictive-fluid group and 784 to the standard-fluid group. Primary outcome data were available for 1545 patients (99.4%). In the ICU, the restrictive-fluid group received a median of 1798 mL of intravenous fluid (interquartile range, 500 to 4366); the standard-fluid group received a median of 3811 mL (interquartile range, 1861 to 6762). At 90 days, death had occurred in 323 of 764 patients (42.3%) in the restrictive-fluid group, as compared with 329 of 781 patients (42.1%) in the standard-fluid group (adjusted absolute difference, 0.1 percentage points; 95% confidence interval [CI], −4.7 to 4.9; P = 0.96). In the ICU, serious adverse events occurred at least once in 221 of 751 patients (29.4%) in the restrictive-fluid group and in 238 of 772 patients (30.8%) in the standard-fluid group (adjusted absolute difference, −1.7 percentage points; 99% CI, −7.7 to 4.3). At 90 days after randomization, the numbers of days alive without life support and days alive and out of the hospital were similar in the two groups.

Limitations: Patients and providers were not blinded, there were several protocol variations, and there were many deviations in terms of the volume of fluids administered, all of which may confound results.

Bottom Line: A fluid restrictive strategy likely won't confer a significant mortality benefit over standard management in sepsis.

Topic: Infectious Disease

Question: Is there an increased thromboembolic risk following COVID 19 infection?

Study

Thoppil JJ, Courtney DM, McDonald S, et al. SARS-CoV-2 Positivity in Ambulatory Symptomatic Patients Is Not Associated With Increased Venous or Arterial Thrombotic Events in the Subsequent 30 Days. *J Emerg Med*. 2022; 62(6):716−724. https://doi.org/10.1016/j.jemermed.2021.12.020

Methods: Retrospective cohort study of COVID patients from the RECOVER (Registry of Potential COVID-19 in Emergency Care) registry vs case matched controls to determine odds ratio of covid 19 infection on VTE or arterial thrombosis within 30 days of diagnosis.

Results: Comparing 14,056 COVID-19−positive patients with 12,995 COVID-19−negative patients, the overall 30-day prevalence of VTE events was 1.4% vs. 1.3%, respectively (p = 0.44, $\chi 2$). Multivariable analysis identified that testing positive for SARS-CoV-2 status was negatively associated with both VTE (OR 0.76; 95% confidence interval [CI] 0.61−0.94) and AT (OR 0.51; 95% CI 0.32−0.80), whereas intubation, ICU care, and age 50 years or older were positively associated with both VTE and AT.

Limitations: Study was retrospective, does not capture patients that went to different hospital systems after the initial visit, potentially confounding results.

Bottom Line: Pretty good heterogeneous sample suggests the previously stated VTE risk for COVID 19 may be overblown.

Topic: Pediatrics

Question: Does the degree of fever correlate with serial bacterial infections in young infants?

Study

Tan, V.S.R., Ong, G.YK., Lee, K.P. et al. Pyrexia in a young infant − is height of fever associated with serious bacterial infection? *BMC Pediatr* 22, 188 (2022). https://doi.org/10.1186/s12887-022-03264-8

Methods: Retrospective chart review of admitted infants (<90 days) with fever with or without serious bacterial illness (SBI). A multivariable regression was performed to study the association between height of temperature and the presence of SBI, and presented the adjusted odds ratio (aOR) with corresponding 95% confidence intervals (CI).

Results: Among 1057 febrile infants analyzed, 207 (19.6%) had a SBI. Mean temperature of infants with a SBI was significantly higher than those without (mean 38.5 °C, standard deviation, SD 0.6 vs. 38.3 °C, SD 0.5, $p < 0.005$). For temperature ≥39 °C, sensitivity, specificity, PPV and NPV for SBI was 15.5% (95%CI 10.8−21.1%), 90.4% (95%CI 88.2−92.3%), 28.1% (95%CI 21.1−36.3%) and 81.4% (95%CI 80.5−82.4%) respectively. The height of fever was consistently associated with SBI after adjusting for age, gender and SIS (aOR 1.76, 95% CI 1.32−2.33, $p < 0.001$). However, 32 (15.5%) infants with SBIs had an initial triage temperature ≤38 °C.

Limitations: Many children going home were excluded, and some admitted did not receive a work up for their fever. The overall group selected in this study had a much higher rate of SBI than is typical for this age group. Unusually, while most groups had higher risk of serious bacterial illness the higher the fever went, those in the highest group (>40C), had a relatively lower risk of bacterial illness compared to other higher temperature groups, raising into question causality.

Bottom Line: Degree of fever correlates poorly with serious bacterial illness in infants <90 days.

Topic: Cardiology

Question: Can 30 minute serial troponin measurements rule out MI in the ED?

Study

Bang C, Andersen CF, Lauridsen KG, et al. Rapid Rule-Out of Myocardial Infarction After 30 Minutes as an Alternative to 1 Hour: The RACING-MI Cohort Study. *Ann Emerg Med*. 2022; 79(2):102−112. https://doi.org/10.1016/j.annemergmed.2021.08.024.

Methods: Prospective, single center clinical study enrolling patients admitted to the emergency department. Troponins were measured at 0, 30 min, 1 hr, and 3 hours. Diagnostic accuracy was measured in sensitivity and negative predictive value to MI.

Results: In the validation cohort (n = 503), the 0/30min algorithm ruled out 48% of patients, 11% to rule in, and 41% to the observation zone. This resulted in a sensitivity of 100%, NPV of 100%, specificity of 96.7% and PPV of 72.2%. In comparison the 0/1hr algorithm performed with a sensitivity of 100%, NPV of 100%, specificity of 97.2%, and PPV of 75.5%.

Limitations: Single center Danish study may not be applicable in all areas. There were slight delays to the timing of repeat troponin draws.

Bottom Line: 30 minute serial troponin measurements are effective to rule out MI in the ED and have similar test characteristics to 1 hour serial troponin measurements, and may help speed up the work up of chest pain patients in the ED. An external validation study is needed.

Topic: Pharmacotherapy

Question: Is there a lower rate of VTE recurrence and bleeding with apixaban (Eliquis) compared with rivaroxaban (Xarelto)?

Study

Dawwas GK, Leonard CE, Lewis JD, Cuker A. Risk for Recurrent Venous Thromboembolism and Bleeding With Apixaban Compared With Rivaroxaban: An Analysis of Real-World Data. *Ann Intern Med*. 2022; 175(1):20−28. https://doi.org/10.7326/M21-0717

Methods: Retrospective new-user cohort study utilizing a U.S.-based commercial health care insurance database from January 2015 through June 2020.

Results: 18,618 new users of apixaban and 18,618 new users of rivaroxaban were included. Median follow-up was 102 days. Apixaban was associated with a lower rate for recurrent VTE (hazard ratio, 0.77 [95% CI, 0.69 to 0.87]) and bleeding (hazard ratio, 0.60 [CI, 0.53 to 0.69]). The absolute reduction in the probability of recurrent VTE with apixaban versus rivaroxaban was 0.011 (CI, 0.011 to 0.013) within 6 months of initiation. The absolute reduction in the probability of gastrointestinal and intracranial bleeding with apixaban versus rivaroxaban was 0.015 (CI, 0.013 to 0.015) within 6 months of initiation.

Limitations: Short follow-up period. Absolute risk reduction was low. Only patients hospitalized for thrombosis or bleeding were included in the study. It doesn't appear that the type of event leading to initiation of anticoagulation was recorded. These were privately insured patients and results may not be generalizable to all patients (especially who may have poorer compliance with the twice-daily dosing of apixaban).

Bottom Line: Apixaban appears to be associated with a slightly lower rate of recurrent VTE and bleeding events than rivaroxaban. This may be due

to pharmacokinetics, as apixaban is dosed twice daily and patients may stay within the therapeutic window more consistently. Based on this evidence it may be reasonable to prefer apixaban when prescribing a DOAC for VTE, although patient specific factors taking into account compliance and cost may influence the choice of anticoagulant.

Topic: Cardiology

Question: Is there a meaningful difference in the effectiveness of intravenous metoprolol vs. diltiazem when used for the control of atrial fibrillation with rapid ventricular response (RVR)?

Study

Lan Q, Wu F, Han B, Ma L, Han J, Yao Y. Intravenous diltiazem versus metoprolol for atrial fibrillation with rapid ventricular rate: A meta-analysis. *Am J Emerg Med*. 2022; 51:248−256. https://doi.org/10.1016/j.ajem.2021.08.082

Methods: This was a systematic review of previously published studies comparing the effectiveness of metoprolol and diltiazem.

Results: Authors identified 17 studies involving 1214 patients in nine randomized controlled and eight cohort studies with 643 patients in the diltiazem group and 571 patients in the metoprolol group. When compared with intravenous metoprolol, intravenous diltiazem was found to have higher efficacy (RR = 1.11; 95% CI = 1.06 to 1.16, $p < 0.00001$), shorter average onset time (RR = −1.13; 95% CI = −1.97 to −0.28, $p = 0.009$), lower ventricular rate (RR = −9.48; 95% CI = −12.13 to −6.82, $p < 0.00001$), less impact on systolic blood pressure (WMD = 3.76; 95% CI: 0.20 to 7.33, $P = 0.04$), and no significant difference in adverse events (RR = 0.80, 95% CI = 0.55 to 1.14, $P = 0.22$.

Limitations: Sample size is small. Some studies were not blinded or were retrospective and there could be bias in patient or drug selection in some studies. Dosing of the drugs also varied significantly between studies.

Bottom Line: In this systematic review, intravenous diltiazem appeared to have higher efficacy for control of atrial fibrillation with RVR and less impact on systolic blood pressure without an increase in adverse events. In patients without contraindications or other compelling reasons to use a beta blocker, diltiazem is likely a superior agent for rate control of atrial fibrillation with RVR.

Topic: Procedural Sedation, Pediatrics

Question: What factors predict laryngospasm during pediatric procedural sedation?

Study

Cosgrove P, Krauss BS, Cravero JP, Fleegler EW. Predictors of laryngospasm during 276,832 episodes of pediatric procedural sedation [published online ahead of print, 2022 Jun 22]. *Ann Emerg Med*. 2022; S0196-0644(22)00323-7. https://doi.org/10.1016/j.annemergmed.2022.05.002

Methods: Retrospective, multicenter, review of the Pediatric Sedation Research Consortium database from 2013 to 2019 of patients under 22 years old.

Results: 276,832 sedations were included with 913 episodes of laryngospasm, an incidence of 0.33%. The majority of episodes were intraprocedural (73.4%). The major risk factors were concomitant upper respiratory infection, airway procedures, patients in ASA class IV, patients under 1 year old, and combinations of medications (for example, ketofol or propofol with dexmedetomidine). The most common negative outcome was hypoxia. Most were managed with repositioning, with only a very small number requiring intubation, paralysis, or other aggressive intervention.

Limitations: Sedations with intramuscular ketamine were excluded; age of 22 is an unusual cutoff for definition of pediatrics, 5821 sedations were excluded due to lacking ASA classification which generally is not a barrier in emergency medicine; a minority of procedures were performed by general emergency physicians (0.2%) with the majority being done by intensivists (56.4%); a minority of procedures were performed in an emergency department (2.7%).

Bottom Line: Laryngospasm is a rare but serious potential complication of procedural sedation, and risks are likely higher in procedural sedations which are for airway procedures, in patients under 1 year old, in patients with a respiratory infection, and with medication combinations.

Topic: Intubation

Question: Does an IV fluid bolus prevent cardiovascular collapse during intubation?

Study

Janz DR, Casey JD, Semler MW, et al. Effect of a fluid bolus on cardiovascular collapse among critically ill adults undergoing tracheal intubation (PrePARE): a randomised controlled trial. *Lancet Respir Med*. 2019; 7(12):1039−1047. https://doi.org/10.1016/S2213-2600(1930246-2)

Methods: Prospective, randomized controlled trial of adult patients undergoing endotracheal intubation in 9 ICUs and 1 emergency department in the United States from 2017 to 2018 prior to being stopped by the review board for futility. Patients

were randomized to receive 500 mL saline versus no fluids during intubation. For practical reasons, blinding was not possible after randomization. Cardiovascular collapse was defined as new systolic blood pressure <65 mmHg, new vasopressor use, cardiac arrest, or death.

Results: 511 patients were included, with 168 assigned to receiving a fluid bolus and 169 assigned to no bolus. Cardiovascular collapse occurred in 20% of patients receiving a fluid bolus and 18% of patients not receiving a fluid bolus.

Limitations: Cardiovascular collapse was defined with a very low blood pressure and used systolic pressure rather than MAP; stopping prior to reaching study endpoint increases bias, although futility was predefined; small study; the volume of IV fluids prior to intubation was not included and may not be equal between groups; predominantly non-emergency patients.

Bottom Line: Routine use of a 500 mL fluid bolus did not appear to change rates of severe hypotension during endotracheal intubation in this study.