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## Emergency Medicine Journal Club

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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

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

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### Conflict of Interest Statement

The authors have no personal 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:* Journal club, Emergency medicine, 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 18 papers reviewed herein.

## 1. Topic: Trauma

**Question:** Is CT angiography (CTA) adequately sensitive to rule out aerodigestive injuries (ADI) in penetrating neck trauma?

**Study:** Paladino L, et al. Computed tomography angiography for aerodigestive injuries in penetrating neck trauma: A systematic review. *Acad Emerg Med.* 2021 May 21.

**Methods:** This was a systematic review of published studies evaluating the sensitivity and specificity of CTA for detecting ADI.

**Results:** 1242 citations were identified. Ultimately 7 studies met inclusion criteria. There was an ADI prevalence of 13.4%. CTA for ADI had a sensitivity of 92%, and specificity of 88%. Of the 26 identified esophageal injuries, five (19%) were initially missed by CTA.

**Limitations:** There were significant variations in the quality of studies, and only 7 studies met

criteria for inclusion. Risk of bias and lack of blinding to outcomes also may affect the validity of results.

**Bottom Line:** CTA appears to be insufficiently sensitive to reliably exclude esophageal injuries in penetrating neck trauma. Additional diagnostic modalities (swallowing studies, endoscopy, or surgical exploration) should be utilized to safely exclude esophageal injury. These injuries have high morbidity and delayed diagnosis can lead to serious complications. Further evaluation should strongly be considered when the mechanism suggests the possibility of ADI.

## 2. Topic: COVID

**Question:** What is the incidence of myocarditis following vaccination for COVID-19?

**Study:** Simone A, et al. Acute Myocarditis Following COVID-19 mRNA Vaccination in Adults Aged 18 Years or Older. *JAMA Intern Med.* 2021 Oct 4.

**Methods:** This was a population cohort based study performed within the Kaiser Permanente Southern California healthcare system of adults 18 years of age and older who received at least one dose of the Pfizer or Moderna mRNA vaccine between December 14, 2020, and July 20, 2021. Potential cases of post-vaccine myocarditis were identified based on reports from clinicians and by

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record review of patients hospitalized within 10 days of vaccine administration with a discharge diagnosis of myocarditis. The incidence of post-vaccine cases was compared with the incidence of myocarditis in unexposed individuals between December 14, 2020, and July 20, 2021 and with vaccinated individuals during a 10-day period 1 year prior to vaccination.

**Results:** 2,392,924 vaccine exposed individuals were compared with 1,577,741 non-exposed individuals. The groups were relatively similar in regards to sex and ethnicity. There were 15 cases of myocarditis in the vaccinated group, with an incidence of approximately 5.8 cases per million during the 10 day period following vaccination after receiving two vaccine doses. All cases were observed in men with a median age of 25 years. Estimated 10-day incidence in non-exposed individuals was 2.2 cases per million, with 52% of cases occurring in men, with a median age of 52 years. An analysis using vaccinated individuals as their own controls yielded similar results. No individuals required ICU admission and symptoms resolved in all cases with conservative measures.

**Limitations:** This is observational data, therefore a causal link between vaccination and myocarditis can not be established using this data. There may be reporting bias, and a more extensive cardiac workup may have been performed in patients presenting with chest pain after vaccination than in the control group.

**Bottom Line:** The incidence of post-vaccination myocarditis is very low, but significantly higher than in non-exposed individuals. It was observed to be much more common (universally in this cohort) in young males. There were no cases requiring intensive care treatment and all observed cases resolved with supportive care and without apparent long-term sequelae.

### 3. Topic: Electrolytes

**Question:** What is the ideal emergency department (ED) management of hyperkalemia?

**Study:** Rafique Z, et al. Hyperkalemia management in the emergency department: An expert panel consensus. *JACEP Open*. 2021; 2:e12572.

**Methods:** This is a review of the best available evidence and consensus expert opinion on the management of hyperkalemia in patients presenting to the ED. This panel was sponsored by the American College of Emergency Physicians (ACEP) with the goal of creating a consensus guide for the management of acute hyperkalemia.

**Results:** The authors propose a stepwise algorithm for the management of hyperkalemia, which they define as  $K^+ > 5.5$  mEq/L and symptoms of acute illness).

**Step 1.** Determine if the  $K^+$  value is correct and is not due to pseudo or spurious hyperkalemia.

**Step 2.** Evaluate for cardiac involvement with electrocardiography and give calcium if ECG changes are present.

**Step 3.** Treat appropriately based on the  $K^+$  level and clinical condition.

**Step 4.** Reassess  $K^+$  level in 2–4 h.

**Step 5.** Determine disposition. Select patients may be suitable for discharge, but most will need to be admitted for monitoring and some will need ICU level of care.

**Limitations:** There is a lack of strong published literature to support many of these recommendations and even experts vary widely in their views on hyperkalemia management.

**Bottom Line:** This document is an attempt by ACEP to standardize management of hyperkalemia in the emergency department. It serves as a reasonable framework for evaluation and treatment of these patients and is as evidence-based as we are likely to get on this topic. Some recommendations may not be practical at your institution, and it is obviously important to discuss with nephrology and use shared decision making in many cases, especially when dialysis is recommended.

### 4. Topic: Cardiac Arrest

**Question:** Does the use of methylprednisolone or vasopressin for in-hospital cardiac arrest affect rates of ROSC or favorable neurologic outcomes?

**Study:** Granfeldt A, et al. Effect of Vasopressin and Methylprednisolone vs Placebo on Return of Spontaneous Circulation in Patients With In-Hospital Cardiac Arrest: A Randomized Clinical Trial. *JAMA*. 2021 Sep 29:e2116628. doi: 10.1001/jama.2021.16628. Epub ahead of print.

**Methods:** Multicenter placebo controlled randomized trial of in-hospital cardiac arrest patients who either received usual care or usual care + methylprednisolone/vasopressin. Primary outcome was time to return of spontaneous circulation. Secondary outcomes included survival and favorable neurologic outcomes at 30 and 90 days.

**Results:** Among 512 patients who were randomized, 501 met all inclusion and no exclusion criteria and were included in the analysis. 100 of 237 patients (42%) in the vasopressin and methylprednisolone group and 86 of 264 patients (33%) in the placebo group achieved return of spontaneous circulation (risk ratio, 1.30 [95% CI, 1.03–1.63]; risk difference, 9.6% [95% CI, 1.1%–18.0%];  $P = 0.03$ ). At 30 days, 23 patients (9.7%) in the intervention group and 31 patients (12%) in the placebo group were alive (risk ratio, 0.83 [95% CI, 0.50–1.37]; risk difference:  $-2.0\%$  [95% CI,  $-7.5\%$ – $-3.5\%$ ];  $P = 0.48$ ). A favorable neurologic outcome was observed in 18 patients (7.6%) in the intervention group and 20 patients (7.6%) in the placebo group at 30 days (risk ratio, 1.00 [95% CI, 0.55–1.83]; risk difference,  $0.0\%$  [95% CI,  $-4.7\%$ – $-4.9\%$ ];  $P > 0.99$ ). In patients with return of spontaneous circulation, there were increased rates of hyperglycemia and hyponatremia in the treatment arm.

**Limitations:** Significant fraction of eligible patients did not participate in study limiting generalizability and time to steroid/vasopressin dose varied significantly in patients. Trial was not powered to detect differences in favorable neurologic outcomes so a larger study is needed to determine if it is beneficial long term.

**Bottom Line:** This study suggests vasopressin and methylprednisolone shortens arrest time and increases frequency of ROSC but we need more data to determine whether it helps favorable neurologic outcomes.

## 5. Topic: Toxicology

**Question:** Is haloperidol superior to ondansetron in the management of cannabis hyperemesis?

**Study:** Ruberto AJ, et al. Intravenous Haloperidol Versus Ondansetron for Cannabis Hyperemesis Syndrome (HaVOC): A Randomized, Controlled Trial. *Ann Emerg Med.* 2021.

**Methods:** Randomized, triple-blind crossover trial of up to 3 treatment periods per subject from 2 academic emergency departments from 2017 to 2019. 30 patients were enrolled who received at least 1 treatment. They were randomized to either 0.05 mg/kg haldol, 0.1 mg/kg haldol, or 8 mg ondansetron IV. Primary outcome was a reduction in abdominal pain and nausea in a 10 cm visual analog scale at 2 h post treatment.

**Results:** Haldol at either dose was superior to ondansetron for decreasing nausea and pain on a visual analog scale (difference of 2.3 cm [95% confidence interval 0.6–4.0 cm]) and shorter time to ED

discharge (3.1 h vs 5.6 h a difference of 2.5 [95% confidence interval 0.1–5.0 h]).

**Limitations:** Small study of 30 patients which did not achieve its enrollment goal and utilized a convenience sample.

**Bottom Line:** Although the study is underpowered, the treatment effect was large and it may be reasonable to utilize haloperidol as a first line agent in patients with cannabis hyperemesis. Results are consistent with other published literature supporting the use of haloperidol for cannabis hyperemesis syndrome and cyclical vomiting.

## 6. Topic: Infectious Disease

**Question:** Can a monoclonal antibody reduce the chance of developing COVID 19 infection in at risk individuals?

**Study:** O'Brien MP, et al. Covid-19 Phase 3 Prevention Trial Team. Subcutaneous REGEN-COV Antibody Combination to Prevent Covid-19. *N Engl J Med.* 2021 Sep 23; 385 (13):1184–1195.

**Methods:** Prospective randomized double blind controlled trial of 1550 patients who had in-home contact with COVID positive persons, randomized into placebo or subcutaneous REGEN-COV (casirivimab and imdevimab). Primary outcome was development of symptomatic COVID infection at day 28.

**Results:** Symptomatic SARS-CoV-2 infection developed in 11 of 753 participants in the REGEN-COV group (1.5%) and in 59 of 752 participants in the placebo group (7.8%) (relative risk reduction [1 minus the relative risk], 81.4%;  $P < 0.001$ ). In weeks 2–4, a total of 2 of 753 participants in the REGEN-COV group (0.3%) and 27 of 752 participants in the placebo group (3.6%) had symptomatic SARS-CoV-2 infection (relative risk reduction, 92.6%). REGEN-COV also prevented symptomatic and asymptomatic infections overall (relative risk reduction, 66.4%). Among symptomatic infected participants, the median time to resolution of symptoms was 2 weeks shorter with REGEN-COV than with placebo (1.2 weeks and 3.2 weeks, respectively), and the duration of a high viral load ( $>10^4$  copies per milliliter) was shorter (0.4 weeks and 1.3 weeks, respectively).

**Limitations:** Industry funded trial, possibly introducing bias. Additionally, excluded those with previous evidence of COVID 19 infection limiting generalizability to those with previous COVID infections. Authors chose only to report on relative risk reduction (common in industry sponsored trials), but the absolute risk reduction for symptomatic

COVID infection was relatively low (6.3%) with a number needed to treat of almost 17.

**Bottom Line:** In this well done study, subcutaneous monoclonal antibodies appear to reduce the chance of acquiring COVID 19 infection and its severity. It is questionable whether the costs of treatment justify widespread use for this purpose, but it may have a place for prophylaxis in high-risk individuals.

#### 7. Topic: Covid-19

**Question:** How effective is the REGEN-COV monoclonal antibody combination for preventing hospitalization in outpatients with Covid-19?

**Study:** Weinreich DM, et al. REGN-COV2, a Neutralizing Antibody Cocktail, in Outpatients with Covid-19. *N Engl J Med.* 2021 Jan 21; 384 (3):238–251. doi: 10.1056/NEJMoa2035002. Epub 2020 Dec 17.

**Methods:** This is the phase 3 portion of a trial studying the effectiveness of combination infusion therapy with casirivimab and imdevimab when given to outpatients with Covid-19 who have risk factors for severe disease. Patients were assigned to varying doses of antibodies and were followed for 29 days. Endpoints were hospitalization or death. Viral load was also measured and safety was assessed.

**Results:** Hospitalization or death from any cause occurred in a total of 25 of 2091 (1.1%) patients in the group receiving REGEN-COV antibodies and 86 of 2089 patients receiving placebo (4.1%) for a relative risk reduction of 71.0% and absolute risk reduction of about 3%. Number needed to treat was 34 to prevent hospitalization or death. Only 5 deaths occurred, two in the placebo group and one in the REGEN-COV group. There were few adverse events generally, with more adverse events recorded in the placebo than intervention group. There did not appear to be a significant difference in efficacy between the various doses.

**Limitations:** The study was industry sponsored, which must prompt additional scrutiny. Relatively few deaths occurred, limiting the ability to draw conclusions as to mortality benefit. Trial enrollment ended in January of 2021, before the Delta variant was predominant. It remains to be seen if this drug cocktail will continue to be effective against new variants.

**Bottom Line:** The REGEN-COV drug cocktail containing casirivimab and imdevimab appears to be at least moderately effective in preventing hospitalizations in patients with risk factors for severe Covid illness. Given the paucity of effective treatments for

outpatients with Covid, referral for the antibody infusion is probably warranted.

#### 8. Topic: Pediatrics/Trauma

**Question:** What is the prevalence of serious injury in pediatric patients presenting with blunt trauma from a bicycle handlebar impact?

**Study:** Vandewalle RJ, Barker SJ, Raymond JL, Brown BP, Rouse TM. Pediatric Handlebar Injuries: More Than Meets the Abdomen. *Pediatr Emerg Care.* 2021 Sep 1; 37 (9):e517-e523.

**Methods:** Retrospective chart review of pediatric bicycle accidents from a trauma registry over an 8 year period at a single tertiary pediatric center (Indiana Health). Injuries were classified as “handlebar” or “non-handlebar” and injuries were classified by body zone (abdomen, thorax, etc.) and type (hollow-viscus, solid organ, soft-tissue, etc.). Injury severity and need for operative intervention or a procedure was recorded.

**Results:** 385 patients met inclusion criteria. Mean age was approximately 9 years. Handlebar injuries were involved in 27.9% of bicycle related trauma cases. 34.6% of these patients had a solid organ injury and 9.3% had a hollow-viscus injury. 21.6% of handlebar injury cases required surgery and/or a procedure such as embolization. Most patients presented with both physical findings and a history consistent with a handlebar injury but some significant injuries were identified on history alone. Two patients with no evidence of bowel injury on initial CT scan required laparotomy for bowel perforation after developing peritonitis less than 12 h after injury. CT scans in some cases of serious hollow-viscus injury were negative or showed only pericolic/pelvic free fluid.

**Limitations:** Retrospective data obtained by chart review, so some cases may have been missed and documentation may have been incomplete. Data is from a large referral hospital, so the patient population likely reflects a sicker group than that seen in the typical emergency department.

**Bottom Line:** Be sure to perform a careful physical examination and history when evaluating pediatric trauma involving bicycle handlebars and bicycle accidents in general. Have a low threshold to obtain imaging and lab studies and transfer these patients to a pediatric trauma center for surgical evaluation and/or observation.

#### 9. Topic: Neurology

**Question:** Does IV TPA improve outcomes when given before endovascular procedures for large vessel occlusions in stroke?

**Study:** LeCouffe N, et al. A Randomized Trial of Intravenous Alteplase before Endovascular Treatment for Stroke. *N Engl J Med.* 2021 Nov 11; 385 (20):1833–1844. doi: 10.1056/NEJMoa2107727.

**Methods:** Open label, multicenter controlled trial of patients in Europe with stroke who were candidates for both TPA and endovascular repair (EVT). They were randomized to TPA + endovascular or endovascular alone. Primary outcome was functional outcomes on modified Rankin scale at 90 days. Secondary outcomes include mortality and symptomatic intracerebral hemorrhage.

**Results:** Median score on the modified Rankin scale at 90 days was 3 (interquartile range, 2 to 5) with EVT and 2 (interquartile range, 2 to 5) with alteplase plus EVT. The adjusted common odds ratio was 0.84 (95% confidence interval [CI], 0.62 to 1.15;  $P = 0.28$ ), which showed neither superiority nor noninferiority of EVT alone. Mortality was 20.5% with EVT alone and 15.8% with alteplase plus EVT (adjusted odds ratio, 1.39; 95% CI, 0.84 to 2.30). Symptomatic intracerebral hemorrhage occurred in 5.9% and 5.3% of the patients in the respective groups (adjusted odds ratio, 1.30; 95% CI, 0.60 to 2.81).

**Limitations:** The study only used those patients presenting to an EVT center so not generalizable to non primary stroke centers. There was no blinding and there were also some differences in the groups (occlusion location, presence of atrial fibrillation) that may have skewed results.

**Bottom Line:** In this well done trial, TPA does not appear to add much to the care of large vessel occlusion patients who are also receiving endovascular therapy in patients presenting to a primary EVT center.

#### 10. Topic: Infectious Disease

**Question:** What is the resistance rate to 3rd generation cephalosporins in patients with febrile UTIs presenting to the emergency department?

**Study:** Mark D, et al. Third-Generation Cephalosporin Resistance and Associated Discordant Antibiotic Treatment in Emergency Department Febrile Urinary Tract Infections. *Ann Emerg Med.* 2021 Sep; 78 (3):357–369. doi: 10.1016/j.annemergmed.2021.01.003. Epub 2021 Mar 27.

**Methods:** Retrospective cohort study of all adults with febrile UTI at 21 hospitals in the Kaiser system in California between Jan 2017–June 2019. Inclusion criteria included fever, admitting diagnosis of UTI, pyelonephritis, or sepsis and urine culture >100,000 CFU of a EKP species (*E.coli*, *K.pneumoniae*, *P.mirabilis*). Primary outcome was discordant antibiotic treatment when compared to

antimicrobial susceptibility testing. Secondary outcomes were hospital length of stay and 90 day mortality.

**Results:** 4107 patients were included. Of these patients, 12.9% had EKP-resistant to 3rd generation cephalosporins. There was a 63% discordant antibiotic therapy with susceptibility testing in case groups (OR 21.0; 95% CI 16.9 to 26.0). Hospital stay was longer in EKP-resistant organism cases with an adjusted mean difference of 29.7 h (95%CI 19.0 to 40.4) and 90 day mortality was higher 12% vs 8% (aOR 1.56; 95% CI 1.07 to 2.28). 89% of resistant isolates were susceptible to piperacillin/tazobactam and 100% of isolates were susceptible to meropenem.

**Limitations:** Retrospective study. It was limited to California, which may have a unique resistance pattern not seen elsewhere and limits generalizability. They did not comment on asymptomatic bacteriuria which could have made up some of the cases and they did not account for catheter associated infections.

**Bottom Line:** A significant fraction of admitted patients with febrile UTI have resistance to 3rd generation cephalosporins, suggesting we should take this into account along with our local resistance patterns when determining the best agent for this patient population. It may be reasonable to choose meropenem or a similar extremely broad spectrum choice in the sickest patients, especially if risk factors for drug resistance are present.

#### 11. Topic: Toxicology/Addiction Medicine

**Question:** Among discharged patients treated for alcohol withdrawal, does phenobarbital lead to fewer return ED visits than benzodiazepines?

**Study:** Lebin JA, et al. Return Encounters in Emergency Department Patients Treated with Phenobarbital Versus Benzodiazepines for Alcohol Withdrawal. *J Med Toxicol.* 2021 Oct 25. doi: 10.1007/s13181-021-00863-2. Epub ahead of print.

**Methods:** Retrospective chart review of a single academic medical center. Primary outcome was any return ED visit within 3 days. Secondary outcomes were any return ED visit within 3–7 days and evidence of survival after discharge. Return ED visits and survival were identified via Care Everywhere (i.e. although the study was single-center, charts from throughout the local region were reviewed for return visits).

**Results:** 470 patients met inclusion criteria (discharged with diagnosis of alcohol withdrawal and received treatment in the ED for same). 133 were treated with phenobarbital, 235 with

benzodiazepines, 102 with a combination of both. Overall, populations were similar. Patients treated with phenobarbital had substantially lower risk of return ED visit within 3 days (10% versus 25% for benzodiazepines,  $p = 0.001$ ), although this difference was not statistically significant between 3 and 7 days (6% versus 10% for benzodiazepines,  $p = 0.36$ ). Patients treated with phenobarbital received substantially more lorazepam equivalents than patients treated with benzodiazepines (26 mg vs. 6 mg,  $p < 0.001$ ). Survival was not significantly different between the two groups (97.7% in phenobarbital group, 94.5% in benzodiazepine group, 94% in combination group,  $p = 0.12$ ).

**Limitations:** Single center, unable to assess whether discharge medications were used or filled, survival statistics are secondary outcome and hypothesis-generating rather than hypothesis-confirming. Patients not re-presenting to a local Care Everywhere participating center may have been lost to follow-up.

**Bottom Line:** Patients not requiring inpatient management treated for alcohol withdrawal with phenobarbital had fewer return ED visits, received substantially more lorazepam equivalents, and had similar mortality to patients treated with benzodiazepines. Phenobarbital treatment appears to be safe and may reduce ED bouncebacks. The increase in equivalent dosing was hypothesized as resulting from clinician and nursing discomfort with diverging from 'standard' doses of benzodiazepines when larger doses are necessary, as is also seen when comparing morphine and hydromorphone dosing. (For a non-academic review of phenobarbital treatment for alcohol withdrawal, see *PulmCrit*).

## 12. Topic: Ethics

**Question:** How does the presence of law enforcement impact emergency care?

**Study:** Janeway HH, et al. An Ethical, Legal, and Structural Framework for Law Enforcement in the Emergency Department. *Ann Emerg Med.* 2021 Oct 27;S0196-0644 (21)00796-4. doi: 10.1016/j.annemergmed.2021.08.009. Epub ahead of print. Editorial in review of Harada MY, et al. Policed Patients: How the Presence of Law Enforcement in the Emergency Department Impacts Medical Care. *Ann Emerg Med.* 2021 Jul 28;S0196-0644 (21)00380-2. doi: 10.1016/j.annemergmed.2021.04.039. Epub ahead of print.

**Methods:** Qualitative semi-structured interviews of emergency physicians using snowball sampling (a recruitment technique in which research participants

are asked to assist researchers in identifying other potential subjects) recruited from 3 large, public hospitals serving largely lower socioeconomic status patients. Themes were abstracted and categorized using a grounded theory approach.

**Results:** 20 full-time emergency physicians were interviewed across a range of ages, ethnicities, genders, and experience levels. The majority considered law enforcement to have a mixed, largely negative but sometimes positive impact on clinical care. Positive experiences with law enforcement included increased sense of safety and receiving helpful pre-hospital information. Negative experiences included direct impediments to critical and other emergency care, breaches of confidentiality and patient privacy, loss of patient trust, barriers to patients presenting due to fear of police, physicians feeling intimidated by police, lack of understanding of legal and hospital policy rules and rights for patients and staff, conflation of medical staff with law enforcement, and physicians being threatened with arrest when not complying with police demands.

**Limitations:** Qualitative survey, hypothesis-generating rather than hypothesis-confirming, no quantitative analysis, snowball sampling increases risk of bias (specifically selection bias), no evaluation of patient or law enforcement perspectives, single state (California).

**Bottom Line:** The presence of law enforcement officers can conflict with clinical and patient-centered objectives. Emergency physicians may tolerate or support police over patient interests, leading to breaches in confidentiality, poor rapport, and even obstruction of critical procedures such as intubation and acute resuscitation. Complicity with police demands has the potential to undermine established principles of medical ethics. Simultaneously, police can be helpful in providing information and responding to violence in the ED. A new framework to help clinicians navigate the conflicts between law enforcement objectives and the principles of patient-centered care is needed.

## 13. Topic: Infectious Disease, Resuscitation

**Question:** Does the Surviving Sepsis Campaign (SSC) hour-1 bundle decrease mortality in septic adults at 28 days compared to the hour-3 bundle?

**Study:** Prachanukool T, et al. The 28-Day Mortality Outcome of the Complete Hour-1 Sepsis Bundle in the Emergency Department. *Shock.* 2021; 56 (6):969–974. doi:10.1097/SHK.0000000000001815.

**Methods:** As we are all well aware, the SSC sepsis bundle consists of 1) lactate measurement, 2) blood cultures prior to antibiotics, 3) broad-spectrum antibiotics, 4) 30 mL/kg crystalloid for hypotension or



lactate >4, and 5) vasopressors for MAP <65 after fluid bolus. In 2018, SSC began recommending that this occur after 1 h rather than the previous 3 h. In this prospective, single academic tertiary care center cohort study in Thailand from March–July 2019, 593 adult patients were enrolled and divided into cohorts based on whether these targets were met under 1 h per SSC guidelines or under 3 h. Patients with a DNR, who were transferred, were treated prior to arrival, or had cardiac arrest were excluded. **Results:** Even though the hour-3 patients were sicker, there was no difference in 28 day mortality between the cohorts. Additionally, there was no difference in need for vasopressors or incidence of delayed septic shock, even in subgroup analyses. Patients in the hour-1 cohort were slightly more likely to be admitted to the ICU.

**Limitations:** Single center, cohorts may not truly be comparable, nonrandomized (like all cohort studies), Thai population rather than our American population, few (1.9%) had septic shock.

**Bottom Line:** Giving the SSC sepsis bundle under 1 h did not change patient-centered outcomes compared to under 3 h in this population of septic patients, most of whom did not have septic shock.

#### 14. Topic: Addiction Medicine

**Question:** How often are buprenorphine or naloxone prescribed after opioid overdose in American hospitals, and how does this compare to prescriptions of epinephrine after anaphylaxis?

**Study:** Chua KP, et al. Naloxone and Buprenorphine Prescribing Following US Emergency Department Visits for Suspected Opioid Overdose: August 2019 to April 2021 [published online ahead of print, 2021 Nov 18]. *Ann Emerg Med.* 2021; S0196-0644 (21) 01349-4. doi:10.1016/j.annemergmed.2021.10.005.

**Methods:** Retrospective chart review of emergency department visits via a national database including 5800 hospitals and 70,000 pharmacies (~93% of dispensed prescriptions across the United States) from August 2019–April 2021 by searching for any visit containing a CPT code for opioid overdose or anaphylaxis. 148,966 encounters for opioid overdose and 43,712 for anaphylaxis were included.

**Results:** Naloxone was prescribed after 7.4% of opioid overdose visits and buprenorphine after 8.5%, compared to epinephrine being prescribed after 48.9% of anaphylaxis visits. Emergency department visits for opioid overdose increased by 23.6% after the COVID-19 pandemic began, while overall volume decreased.

**Limitations:** The database used appears to overrepresent commercially-insured patients and

underrepresent Medicaid and uninsured patients, although this likely means these medications are prescribed even less frequently than found here. Multiple visits per day were missed due to database limitations. Fatal overdoses, although likely few, were not able to be excluded due to database limitations. CPT codes are insensitive to identify cases, although they are specific, and so many cases may have been missed. Paper prescriptions were missed. **Bottom Line:** Emergency physicians prescribe naloxone or buprenorphine to fewer than 1 in 10 appropriate patients, a strikingly small number compared to epinephrine after anaphylaxis. Especially as opioid overdoses continue to rise, we should try to induce buprenorphine or prescribe naloxone to patients as often as possible. (To address one common concern, naloxone prescription is not associated with increased opioid usage, as confirmed in a recent publication by Tse et al. in *Int J Drug Pol.*)

#### 15. Topic: Pain Management

**Question:** Is a 15 mg dose of ketorolac (Toradol) given intramuscularly (IM) non-inferior to a 60 mg dose when given for acute musculoskeletal (MSK) pain?

**Study:** Turner NJ, et al. Comparing two doses of intramuscular ketorolac for treatment of acute musculoskeletal pain in a military emergency department. *Am J Emerg Med.* 2021 Dec; 50:142–147.

**Methods:** Single-blinded, randomized controlled, non-inferiority trial of adults presenting to an ED with a chief complaint of acute MSK pain. Patients were randomized to receive a 15 mg or a 60 mg IM ketorolac dose. The primary outcome was the mean difference of change in pain from baseline at one hour between the two groups as reported on a 100-mm (mm) visual analog scale. Only relatively low acuity (ESI 4 or 5) patients were included.

**Results:** 110 patients were randomized. The mean difference in pain score at one hour was 0.2 mm [95% CI-85-8.7). There were no major adverse effects reported, although patients receiving the higher dose reported more burning at the injection site.

**Limitations:** Conducted at a department of defense facility/single center. Patient population may not be completely representative of those seen at some emergency departments. High acuity complaints were excluded. Effects were followed only for one hour so no determination of efficacy or side effects beyond this point can be measured.

**Bottom Line:** For adult patients presenting with acute MSK pain, 15 mg of IM ketorolac was non-inferior to a 60 mg dose when outcomes were measured at one hour. The 60 mg IM dose dogma

seems to be dying hard (still recommended by UpToDate!). Results of this study are consistent with other recent published studies on this topic. We should be limiting the dose of ketorolac for acute MSK pain to 15 mg whether given IV or IM.

#### 16. Topic: COVID/Venous Thromboembolism (VTE)

**Question:** Is there a difference in the risk and prevalence of thrombosis in patients undergoing testing for VTE with confirmed COVID infection when compared to patients without COVID?

**Study:** Wretborn J, et al. Risk of venous thromboembolism in a Swedish healthcare system during the COVID-19 pandemic: A retrospective cross-sectional study. *J Am Coll Emerg Physicians Open*. 2021 Sep 1; 2 (5):e12530.

**Methods:** Retrospective observational study of adult patients in Sweden. Patients were included if they had testing for VTE performed. Groups were separated into COVID positive or negative based on documented PCR results in the 30 days prior to or after testing. The outcome was diagnosis of VTE by ultrasound or CTPA. Logistic regression was used to investigate the risks for VTE by COVID-19 status and the risk of VTE was also compared to risk during the pre-COVID timeframe (2015–2019).

**Results:** A total of 8702 tests for VTE were included in the analysis, 1398 of which had been performed in 2020. COVID infection was confirmed in 88 cases, 14 of which were positive for VTE. There was no significant difference in the prevalence of VTEs between the confirmed SARS-CoV-2–positive, SARS-CoV-2–negative, or untested groups (15.9%, 17.6%, and 15.7% in each group, respectively,  $P = 0.85$ ). There was no significant difference in the overall rate prevalence of positive VTE tests in the 2020 cohort when compared to the 2015–2019 cohort. There was a higher prevalence of VTE in COVID positive patients admitted to the ICU.

**Limitations:** This is observational data from a single county in Sweden. Patients were only included if VTE testing was performed and COVID status was not available for a large number of patients. Some patients may have tested positive for VTE outside the healthcare system, and could have been missed.

**Bottom Line:** These results are consistent with other recent studies suggesting that COVID is not a strong independent risk factor for VTE, at least in outpatients. Traditional risk stratification methods for VTE appear to be holding up well when applied to ambulatory patients with COVID.

#### 17. Topic: Cardiac Arrest

**Question:** Does routine use of calcium in out of hospital cardiac arrest affect clinical outcomes?

**Study:** Vallentin MF et al. Effect of Intravenous or Intraosseous Calcium vs Saline on Return of Spontaneous Circulation in Adults With Out-of-Hospital Cardiac Arrest: A Randomized Clinical Trial. *JAMA*. 2021 Dec 14; 326 (22):2268–2276. <https://doi.org/10.1001/jama.2021.20929>.

**Methods:** Double-blind, prospective randomized trial of 397 out of hospital cardiac arrest patients randomized to either intraosseous calcium chloride or normal saline along with routine cardiac arrest protocols. Primary outcome was sustained return of spontaneous circulation (ROSC) and secondary outcomes were survival and favorable neurologic outcome at 30 and 90 days.

**Results:** Trial was stopped early at an interim analysis due to harm in the calcium group. 391 were included in the analysis. 37 patients in the calcium group (19%) had sustained ROSC compared with 53 (27%) in the saline group [risk ratio 0.72 (95% CI 0.49 to 1.03)]. At 30 days, 10 patients (5.2%) in the calcium group and 18 patients (9.1%) in the saline group were alive (risk ratio, 0.57 [95% CI, 0.27 to 1.18], A favorable neurological outcome at 30 days was observed in 7 patients (3.6%) in the calcium group and in 15 patients (7.6%) in the saline group (risk ratio, 0.48 [95% CI, 0.20 to 1.12]).

**Limitations:** The trial did not reach its pre-planned size, it was stopped early, CI are wide and it is possible the results are due to random chance.

**Bottom Line:** It does not appear in this study that addition of calcium chloride is superior to saline, and may actually be harmful, but larger studies are needed to confirm the effects.

#### 18. Topic: Medical Technology

**Question:** Can a patient's pulse be measured with non-contact methods?

**Study:** Caspar M, et al. Contact-Free Monitoring of Pulse Rate For Triage of Patients Presenting to the Emergency Department. *J Emerg Med*. 2021 Aug 30:S0736-4679 (21)00543-6. <https://doi.org/10.1016/j.jemermed.2021.07.005>. Epub ahead of print.

**Methods:** Convenience sample of 446 patients presenting to a single ED. Pulse was estimated with a camera-based prototype application, which measured subtle differences in patient skin that varied with pulse rate and was compared to pulse oximetry for correlation.

**Results:** In the 446 patients, the correlation between CBPA and pulse oximetry in measuring PR was 0.939 (95% confidence interval [CI] 0.927–0.949).

**Limitations:** Single center convenience sample, possibly introducing bias and potentially limiting generalizability. It is unclear if it reliably measures the pulse in arrhythmias as the comparison was pulse oximetry measurements which are notoriously unreliable with arrhythmias. This was performed in Switzerland with a predominantly white population, so may not be generalizable to all skin types.

**Bottom Line:** Contact free pulse measurement seems to be an effective method of pulse measurement, at least in a predominantly white population. More research is needed if it is reliable in all patient skin types. If so, it could be an easy, noninvasive, more sanitary way for us to monitor our patients in the ED.

#### **Conflict of interest**

The authors have no personal conflicts of interest to disclose.