Critical decisions in emergency medicine

THE 2022 LLSA LITERATURE REVIEW

The LLSA Literature Review

Synopses of articles from ABEM's 2022 Lifelong Learning and Self-Assessment Reading List

FROM THE EDITORS

Since April 2003, *Critical Decisions in Emergency Medicine*, ACEP's monthly CME publication, has included the feature "The LLSA Literature Review." The impetus for this section was our desire to provide ACEP members with yet another tool to use when preparing for the continuous certification initiative of the American Board of Emergency Medicine (ABEM), specifically the Lifelong Learning and Self-Assessment (LLSA) tests. Each year, as part of this program, ABEM publishes a list of articles focused on selected portions of the emergency medicine core content. These articles become the LLSA reading list for that year, and the questions for the tests are drawn from these articles.

Since November 2019, *Critical Decisions* has provided a summary of one of the articles from ABEM's reading lists each month, with bullets highlighting the elements relevant to the practice of emergency medicine. This online supplemental issue includes a full collection of those summaries, which are intended to highlight the important concepts of each article. We are pleased to offer this benefit FREE to ACEP members, and hope you find it useful. ACEP members can also download full versions of the articles by logging in at **acep.org/llsa**.

If you would like to see what else *Critical Decisions* has to offer (clinical lessons, ECG and imaging reviews, clinical cases in orthopedics and trauma, clinical pediatrics, drug reviews, and more), we invite you to explore a sample issue online at **www.acep.org/cdem**.

Best wishes,

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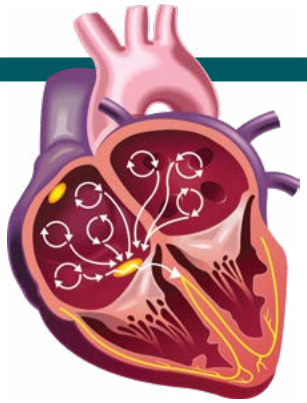
Critical Decisions in Emergency Medicine is the official CME publication of the American College of Emergency Physicians. Additional volumes are available.

ISSN2325-0186 (Print) ISSN2325-8365 (Online)

The LLSA Literature Review

Cardioversion Strategies for Acute Uncomplicated Atrial Fibrillation



By Megan J. Rivera, MD; and Nicholas G. Maldonado, MD, FACEP
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Reviewed by Andrew J. Eyre, MD, MS-HPEd

Scheuermeyer FX, Andolfatto G, Christenson J, Villa-Roel C, Rowe B. A multicenter randomized trial to evaluate a chemical-first or electrical-first cardioversion strategy for patients with uncomplicated acute atrial fibrillation. *Acad Emerg Med.* 2019;26(9):969-981.

KEY POINTS

- AF is a common, yet complex, dysrhythmia with multiple management strategies in the acute setting, depending on its classification and presentation.
- In emergency department patients with first-onset or recurrent episodes of acute uncomplicated paroxysmal AF of less than 48 hours and a CHADS2 score of 0 to 1, chemical-first and electrical-first cardioversion, using the alternative strategy if unsuccessful, are management options with similar discharge rates and conversion to sinus rhythm.
- Electrical-first cardioversion results in a higher proportion of patients discharged within 4 hours, a shorter emergency department LOS, and higher rates of initial cardioversion compared to chemical-first cardioversion.

Atrial fibrillation (AF) is a common dysrhythmia and can be classified based on the duration of symptoms (ie, paroxysmal, persistent, long-standing, or permanent), the presence or absence of moderate-to-severe mitral stenosis or artificial heart valve (ie, valvular versus nonvalvular), the heart rate on presentation (ie, normal or rapid ventricular rate and response), and the level of stability (ie, stable versus unstable). Patients can also be categorized by their thromboembolic risk of cardioversion based on the timing of presentation after symptom onset (ie, less than or greater than 48 hours) in those with first-onset or recurrent episodes of acute paroxysmal AF as well as in all forms of AF based on previously studied risk factors.

In the emergency department, presentations of first-onset or recurrent episodes of acute uncomplicated paroxysmal AF of less than 48 hours may be encountered. Rate- versus rhythm-control strategies for these cases have wide institutional and regional variability. For rhythm-control strategies, literature is emerging on whether a chemical or electrical cardioversion strategy should be used solely or in combination and, if combined, in what order. In this article, the authors sought to determine whether a cardioversion strategy using a chemical-first or electrical-first approach resulted in higher rates of sinus rhythm and faster disposition.

This multicenter randomized trial was conducted at six university-affiliated urban emergency departments in Canada. Patients included adults aged 18 to 75 years with AF of less than 48 hours as a primary diagnosis and a CHADS2 score of 0 to 1. The study excluded patients who presented for other reasons and were incidentally found in AF; those with hemodynamic instability (defined as altered mental status, acute chest pain or heart failure, and systolic blood pressure <90 mm Hg); patients with atrial flutter; those having had a cardiac procedure within the last 2 weeks (ie, coronary artery bypass grafting, percutaneous coronary intervention, electrophysiologic ablation, or pacemaker or defibrillator insertion); and those acutely intoxicated or withdrawing from alcohol or illicit drugs.

With allocation concealment, patients were randomized to receive chemical-first cardioversion, followed by electrical cardioversion if unsuccessful, or electrical-first cardioversion, followed by chemical cardioversion if unsuccessful. Although there was no standard treatment protocol in either group, the authors recommended that physicians manage the chemical-first cardioversion patients with procainamide 17 mg/kg IV (to a maximum of 1,500 mg) over 1 hour and the electrical-first cardioversion group with propofol sedation and a synchronized biphasic waveform sequence of 100 to 150 to 200 J (to a maximum of 3 shocks).

The primary outcome was the difference in the number of patients discharged within 4 hours of arrival (defined as the time the patient registered at triage). Secondary outcomes included additional median time intervals (ie, randomization to conversion and randomization to discharge), emergency department–based adverse events (AEs), and 30-day patient-centered outcomes (physician or hospital visits and quality-of-life [QoL] assessment using the SF-8 Health Survey at 3 and 30 days). Although it was unfeasible to blind physicians to the treatment arms, they were blinded to the study outcome measures.

Of the 135 eligible patients, 86 patients (63.7%) were enrolled. Although there was no loss to follow-up, one patient

in each group withdrew; thus, 41 patients in the chemical-first group and 43 patients in the electrical-first group were analyzed with no significant between-group differences. Most patients were men (62%), aged 50 to mid-60 years, with a history of AF; more than half had a prior cardioversion of any type; and 44% were on aspirin. Few patients were on anticoagulation, nodal blocking agents, or antiarrhythmics.

There was a statistically significant difference in the proportion of patients discharged within 4 hours in the electrical-first group compared to the chemical-first group (67% versus 32%, a difference of 36% [95% CI = 16%-56%, P <0.001]). With respect to secondary outcomes, the electrical-first group had a significantly shorter median emergency department length of stay (LOS) (3.5 hours versus 5.1 hours, a difference of 1.2 hours [95% CI = 0.4-2.0, P <0.001]) and higher rates of cardioversion with the initial method (88.4% verus 53.7% [P <0.001]). All patients were discharged home, with 99% in sinus rhythm. AEs occurred in 25% of cases, all classified as minimal-risk outcomes with no difference between groups. At 30 days, there were no strokes or deaths in either group. Although no statistical analysis was performed, a higher number of patients in the chemical-first group presented to the emergency department at 3 and 30 days for recurrent AF and required admission compared to the electrical-first group. QoL scores were similar for both groups.

For patients with acute uncomplicated AF of less than 48 hours and a CHADS2 score of 0 to 1, the results suggest that chemical-first and electrical-first cardioversion, using the alternative strategy if unsuccessful, are equally effective with respect to discharge rates in normal sinus rhythm, and both are well tolerated with minimal-risk AEs. Although no strokes occurred at 30 days in either group, this study was relatively small to detect this outcome in lower-risk populations. However, the results also suggest that electrical-first cardioversion results in a higher proportion of patients discharged within 4 hours, shorter emergency department LOS, and higher rates of initial cardioversion compared to chemical-first cardioversion. These results can be used to consider regional, institutional, and individual practice patterns and risk tolerance; for emergency department throughput decisions; in patient accessibility to close outpatient cardiology follow-up; and in shared decision-making in those who present with acute uncomplicated paroxysmal AF. If a rhythm-control strategy is considered appropriate in selected patients with AF, electrical-first cardioversion appears to be the optimal method with respect to throughput for these patients.

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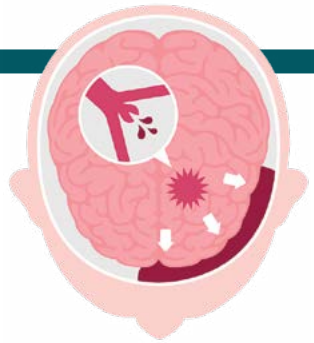
The LLSA Literature Review

Ruling Out Subarachnoid Hemorrhage



By Adam Bossert, MD; and Michael E. Abboud, MD, MSEd
University of Pennsylvania, Philadelphia, Pennsylvania

American College of Emergency Physicians Clinical Policies Subcommittee (Writing Committee) on Acute Headache. Clinical policy: critical issues in the evaluation and management of adult patients presenting to the emergency department with acute headache. *Ann Emerg Med.* 2019 Oct;74(4):e41-e74.

KEY POINTS

- The Ottawa SAH Rule can be used to rule out SAH.
- Preferentially use nonopioids over opioids to treat acute headache.
- A noncontrast CTH can rule out SAH if performed within 6 hours of headache onset.
- If suspicion remains high for SAH despite a negative noncontrast CTH, then it is recommended to pursue either an LP or head CTA to rule out SAH after discussing the risks and benefits of each modality with the patient.

As the fifth most common chief complaint in the emergency department, acute headache can be benign or life-threatening. A systematic approach must be developed to identify those at risk for dangerous conditions such as subarachnoid hemorrhage (SAH). This ACEP clinical policy report published in 2019 focuses on nontraumatic acute headache presentations in the adult population, updating a 2008 policy guideline. The report focuses on four critical questions, answering each using a systematic literature review in addition to expert opinion and an open forum.

Are there risk-stratification strategies that reliably identify the need for emergent neuroimaging in acute headache presentations?

The Ottawa SAH Rule was the only clinical decision-making tool identified to help risk stratify patients; it was found to have a sensitivity of 100% if all criteria were negative. This tool may be used to rule out SAH if a patient lacks all the following: neck pain or stiffness, age 40 years or older, witnessed loss of consciousness, onset during exertion, thunderclap headache, and limited neck flexion on examination. Using fewer criteria, such as solely relying on the absence of neck pain or stiffness, cannot safely rule out SAH.

Are nonopioids preferred over opioids?

In short, yes. From the limited studies that directly compare opioid to nonopioid headache management, opioids are not superior in symptom management. Other evidence-based therapeutic options that do not have the risk of addiction (which is inherently problematic with opioid analgesia) include prochlorperazine, valproate, ketorolac, metoclopramide, naproxen, sumatriptan, and haloperidol. Regardless of the agent used, physicians must remember that a response to treatment is not suggestive of a benign cause of the headache.

Can a noncontrast head CT (CTH) performed within 6 hours of headache onset preclude the need for further diagnostic workup for SAH?

Yes; if a noncontrast CTH is performed within 6 hours of headache onset, it is reported to be 100% sensitive and specific for identification of SAH. This was studied in third-generation CT scanners, and patients were excluded if they had neurologic deficits, history of SAH, papilledema, ventricular shunt, or brain neoplasm.

Is CT angiography (CTA) as effective as a lumbar puncture (LP) to diagnose SAH if the noncontrast CTH is negative but the patient is still considered high risk for SAH?

The recommendation is to use shared decision-making to decide whether to perform an LP or CTA to safely rule out SAH after a negative noncontrast CTH. Both CTA and LP have reported sensitivities of 100% to rule out SAH. The downsides of LP are that it is time-consuming, painful, has a high rate of post-LP headache, and often has uninterpretable results. A CTA avoids many of these downsides; however, CTA increases radiation exposure and the risk of finding an incidental aneurysm (false positive), while missing alternative diagnoses such as meningitis.

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The LLSA Literature Review

Breastfeeding Patients

By Courtney Sakas, MD; and Laura Welsh, MD
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Black AD. Managing the breastfeeding patient in the emergency department. *Ann Emerg Med*. 2020 Jan;75(1):105-110.

KEY POINTS

- Indiscriminate "pump and dump" advice can be harmful and cause early weaning.
- There are free and low-cost resources that can be easily accessed on shift to help guide medication use in breastfeeding patients.
- Breastfeeding patients differ from pregnant patients; they have more safe options for pain control and imaging studies.
- Few illnesses are absolute contraindications to breastfeeding, and it is generally safe for patients to continue to breastfeed while ill.

The lack of education surrounding breastfeeding patients in the emergency department can lead to well-intentioned but confusing advice. Often, to protect themselves and the infant, breastfeeding patients are advised to "pump and dump" if they are exposed to certain medications, contrast agents, or infectious illnesses. However, this advice can be misguided and harmful. A brief interruption in breastfeeding can lead to disruptions in milk production and result in early weaning. Even if a breastfeeding patient is not exposed to potentially harmful substances, a prolonged emergency department wait time without the ability to pump at regular intervals can interrupt milk supply and increase the risk of complications such as mastitis.

Medications that are contraindicated in pregnancy are not necessarily contraindicated during breastfeeding. For instance, NSAIDs and opioids with shorter half-lives (eg, fentanyl and morphine) are safe options for analgesia. If an oral opioid is needed, hydrocodone is the oral agent preferred by the Academy of Breastfeeding Medicine, with a recommended dose of 30 mg or less daily. Hydromorphone has a long half-life, and oxycodone concentrates in the breast milk — both should therefore be avoided. If procedural sedation is performed, midazolam, fentanyl, propofol, and etomidate are safe, but there are insufficient data on ketamine to support its use in breastfeeding patients. When determining the safety of other classes of medications, physicians should consider the concentration of the substance in the breast milk relative to the patient's blood; if the drug can be absorbed orally by the infant; and if the drug can interfere with breast milk supply or affect the taste of breast milk, thereby reducing the infant's desire to feed.

Contrast and radiation exposure recommendations also change in breastfeeding patients compared to pregnant patients. X-rays confer no risk to the breastfed infant, and CTs with contrast are also safe. There are no reports of direct harm to a breastfed infant from iodinated contrast in the breast milk. MRI with gadolinium is safe, according to the American College of Radiology, because the infant dose is negligible compared to the patient dose. Nuclear medicine study safety depends on the specific isotope used and the half-life of that agent. For instance, a hepatobiliary iminodiacetic acid (HIDA) scan requires no interruption in breastfeeding, but a V/Q scan requires a 13-hour interruption in breastfeeding due to its radioactive half-life. For all nuclear studies, there is no need to "pump and dump" because the breast milk can be saved until the radioactivity has dissipated.

Infectious disease is another area that can be confusing in regard to breastfeeding recommendations. In general, ordinary infections frequently encountered in the emergency department are not a reason to discontinue breastfeeding. The few absolute contraindications to breastfeeding are Ebola virus, HIV, Marburg virus, Lassa fever, smallpox, African trypanosomiasis, rabies, human T-lymphotropic virus type 1, and brucellosis. If a breastfeeding patient has an airborne illness like varicella or tuberculosis, direct breastfeeding should be avoided, but pumping is safe. Zoster infection is only a contraindication if breastfeeding patients have lesions across their breasts. Mastitis is not a contraindication unless there is an associated abscess, in which case it is recommended to discard breast milk for the first 24 hours of antibiotics.

Emergency physicians do not often receive formal education on human lactation, and these knowledge gaps can harm the nursing infant or breastfeeding relationship. If a physician has questions regarding the safety of medications, many online resources exist, including LactMed (an online database) and InfantRisk (a website and an app). Additionally, because most newborns nurse about every 2 to 3 hours, providing a patient with a breast pump while in the emergency department can help preserve supply and prevent painful complications like clogged ducts or mastitis.

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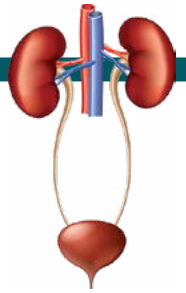
The LLSA Literature Review

Imaging in Suspected Renal Colic



By Morgan Sehdev, MD; and Andrew Eyre, MD, MS-HPEd
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Moore CL, Carpenter CR, Heilbrun ME, et al. Imaging in suspected renal colic: systematic review of the literature and multispecialty consensus. *Ann Emerg Med.* 2019;74(3):391-399.

KEY POINTS

- Increased use of CT scans to diagnose renal stones has not affected patient-centered outcomes.
- Ultrasonography is underused in the workup of renal colic.
- Ultrasonography is the preferred diagnostic imaging modality for patients with flank pain suspicious for renal colic if they are pregnant, pediatric, or younger (≤35 years) with a history of prior stones or typical history with adequate pain control in the emergency department.
- Low-dose radiation CT is preferred to work up renal colic in older patients (≥75 years), patients with atypical presentations or inadequate pain control, or middle-aged patients without prior stones.

Over the past two decades, it has become increasingly common for patients who receive the diagnosis of renal colic in the emergency department to undergo CT scanning as part of their workup. However, rates of admissions, interventions, and other patient-centered metrics remain unchanged despite this increase in CT use. Ultrasonography, an effective imaging modality in the evaluation of renal colic, remains underused in comparison to CT scanning.

An extensive literature review on imaging in the diagnosis of renal colic informed a multidisciplinary expert panel seeking consensus on when CT use would and would not be appropriate in the emergency department.

As part of the review, the authors found radiology-performed ultrasonography to have a sensitivity of 3% to 98% in the diagnosis of renal colic, depending on the need for direct (stone) or indirect (hydronephrosis) ultrasonographic findings. Ultimately, they determined that radiology-performed ultrasonography was unlikely to miss stones requiring intervention. Point-of-care ultrasound, using the presence of hydronephrosis as indirect diagnostic criteria, possessed a sensitivity of 70.2% and specificity of 75.4%. Given that CT was the reference modality, the review highlighted CT's ability to identify other acute, clinically relevant alternate diagnoses, which were determined to be present less than 5% of the time. Finally, the review yielded evidence that no significant difference exists between the initial imaging modality used in renal colic and the time to urologic intervention, and should CT ultimately be the preferred method, reduced-radiation-dose CT is recommended because it still possesses a sensitivity of 90% to 95% and specificity of 97% to 99% for detecting renal calculi that require intervention.

The authors constructed 29 brief clinical vignettes representing common scenarios in which renal colic may be higher or highest in the differential diagnosis. Representatives from the American College of Emergency Physicians, the American College of Radiology, and the American Urological Association used a three-round modified Delphi consensus process with anonymous voting to determine the "optimal diagnostic imaging strategy" for each of the 29 vignettes. Possible options for this "optimal strategy" included (1) no (further) imaging, (2) point-of-care ultrasonography, (3) radiology-performed ultrasonography, (4) reduced-radiation-dose CT, (5) standard CT (noncontrast), and (6) CT with IV contrast.

The group reached at least moderate-level consensus for all vignettes (moderate = 5 out of 9 representatives agree). Perfect (9 out of 9) or excellent (8 out of 9) consensus was obtained for 80% of the vignettes. CT remained the recommended imaging modality in 7 of the 29 scenarios: younger patients (≤35 years) when pain is not adequately controlled with sufficient analgesia in a typical presentation with or without a prior history of stones, middle-aged patients (55 years) without a history of stones or with an atypical presentation, and all older patients (≥75 years) regardless of history. When CT was preferred, CT with a reduced-radiation approach was specifically recommended. For pregnant patients, pediatric patients, patients with prior stones or prior urologic intervention, or younger patients with adequate pain control, ultrasonography, either radiology performed or point of care, was the agreed upon optimal diagnostic modality.

This systematic review and consensus process is the first multispecialty and evidence-based initiative to delineate a preferred approach to patients presenting with flank pain and a history concerning for renal colic. The consensus achieved by this work may subsequently improve diagnostic decision-making for patients with renal colic without negatively impacting rates of necessary admission and intervention. It may also limit patient exposure to excessive radiation and longer emergency department stays waiting for CT scans.

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The LLSA Literature Review

Cerebral Intraparenchymal Hemorrhage

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Reviewed by Andrew J. Eyre, MD, MS-HPEd

Gross BA, Jankowitz BT, Friedlander RM. Cerebral intraparenchymal hemorrhage: a review. *JAMA*. 2019;321(13):1295-1303.

KEY POINTS

- IPH composes up to 20% of all strokes and has a 40% chance of survival within 1 year.
- A patient presenting with acute-onset headache, seizure, or focal neurologic deficit should be evaluated for IPH.
- Rapid CT or MRI is required for diagnosis, and a baseline IPH severity score should be obtained.
- Neurosurgery should be consulted early to evaluate the need for surgical intervention.
- Aggressively lower systolic blood pressure greater than 220 mm Hg with continuous infusion.
- Lower initial systolic blood pressure between 150 and 220 mm Hg to less than 140 mm Hg.
- In patients with a high international normalized ratio due to vitamin K antagonists, prothrombin complex concentrates are preferred over fresh frozen plasma.
- Patients should be managed in a dedicated stroke or neurosurgery unit with experienced nursing.

Stroke is an essential diagnosis of emergency medicine in which early recognition and management are paramount. Intraparenchymal hemorrhage (IPH) accounts for 6.5% to 19.6% of all stroke cases and has a 1-year survival rate of 40%. This article provides an overview of IPH, including its epidemiology, pathophysiology, diagnosis, and treatment.

Epidemiology and Pathophysiology

IPH can be classified into two categories: primary and secondary. Primary IPH accounts for nearly 90% of all cases and refers to the rupture of damaged small vessels, mostly secondary to hypertension or cerebral amyloid angiopathy (CAA). Hypertension induces degenerative changes in small arterial perforating vessels, whereas CAA results from the accumulation of ß-amyloid in cortical vessels, causing weakening. Both mechanisms risk vessel rupture and associated IPH. The location of affected vasculature helps explain the tendency for IPH to occur in characteristic locations, with hypertensive IPH commonly occurring in the basal ganglia, thalamus, brainstem, and cerebellum and IPH due to CAA occurring in lobar locations. Hypertension is the most significant risk factor for primary IPH; other notable risk factors include smoking and heavy alcohol use (ie, more than 30 drinks per month or binge drinking). Secondary IPH has multiple causes, including hemorrhagic conversion of ischemic stroke, coagulopathy, vascular malformation rupture, cerebral venous thrombosis, moyamoya, tumors, mycotic aneurysm rupture, or vasculitis. Knowledge and identification of the cause of secondary IPH is important because it impacts surgical options for therapy.

Clinical Presentation and Diagnosis

IPH from any cause should be suspected in patients who present with acute-onset headache, nausea or vomiting, seizures, or focal neurologic deficits, and it may resemble an ischemic stroke's presentation. In those who present with stroke-like symptoms, signs such as severe hypertension or depressed mental status should increase suspicion for IPH. Common deficits seen in patients with primary IPH include arm or leg paralysis, dysphagia, or aphasia. Within one of the reviewed studies, 60% of patients presented with a Glasgow Coma Scale (GCS) score of 12 or below. Nearly half of all patients with IPH deteriorate during transport to the hospital or in the emergency department, highlighting the urgency of diagnosis. Thus, a rapid neurologic examination with GCS assessment should be part of the initial evaluation when IPH is suspected. In taking a history, it is important to elicit the time of symptom onset, a history of hypertension, and anticoagulation use. Rapid CT or MRI is the imaging of choice for diagnosis. CT angiography and venography can identify specific causes of secondary IPH; a "spot sign" on CT angiography suggests the presence of active contrast extravasation and is predictive of hematoma expansion. Once IPH is diagnosed, the American Heart Association/American Stroke Association (AHA/ASA) guidelines recommend calculating a baseline severity score as part of the initial assessment, using the Intracerebral Hemorrhage Score, which is easy to use and reliably predicts mortality. Neurosurgical consultation should also be rapidly obtained.

Treatment

A summary approach to the initial management of IPH, using information present in the article and clinical practice recommendations from the AHA/ASA, is provided (*Table 1*). Mainstays of treatment include emergency stabilization with airway management when indicated, blood pressure control, reversal of anticoagulation, treatment of seizures, and neurosurgical consultation for surgical management.

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STEP 1		
Early Recognition	Symptoms of IPH	Patient presentation of acute-onset headache, nausea or vomiting, seizure, or stroke symptoms
	Signs of IPH	Presence of severe hypertension, focal neurologic deficit, or depressed mental status
STEP 2		
Emergency Stabilization	Assess ABCs	Manage airway, if indicated, to reduce the risk of secondary injury from aspiration or hypoxia
	Bedside assessment	Obtain history with emphasis on time of onset and anticoagulant use; neurologic or stroke examination
STEP 3		
Rapid Diagnostic Workup and Neurosurgical Consultation	Laboratory and ancillary testing	Obtain early finger-stick glucose, routine laboratory tests (eg, CBC, PT, PTT, INR) as well as troponin and ECG for screening
	Neuroimaging	Obtain rapid CT head or MRI and consider more advanced imaging (ie, CT angiography)
	Interpret IPH severity	Assess intracerebral brain hemorrhage location, volume, and "spot sign," and calculate Intracerebral Hemorrhage Score
	Early consultation	Obtain neurosurgical consultation to assess the need for surgical management
STEP 4		
Medical Management	Blood pressure control	Reduce SBP to <140 mm Hg, using rapid-acting (ie, labetalol) or titratable medications (ie, nicardipine or clevidipine)
	Hemostasis and coagulopathy reversal	Administer repletion for coagulation factor deficiency or thrombocytopenia
	Seizure control	Manage seizures with antiepileptics (AEDs); however, prophylactic AEDs are not recommended
STEP 5		
Surgical Management Options	Ventricular drainage	Ventricular drainage for hydrocephalus
	Surgical drainage	Surgical drainage for hydrocephalus, worsening cerebellar IPH, or clinical deterioration
	Craniectomy	Craniectomy for coma, large hematomas with shift, or refractory high intracranial pressure
STEP 6		
Disposition	Admit to ICU	Admit or transfer for initial management in ICU or dedicated stroke unit with neurologic expertise

STEP 1 PEARLS

Risk Factors for Primary IPH

- Hypertension (significant)
- Smoking
- Heavy alcohol intake
- High HDL cholesterol
- Low total cholesterol
- Low non-HDL cholesterol

STEP 3 PEARLS

Neuroimaging in IPH

- CT angiography/venography can identify secondary causes of IPH.
- A "spot sign" suggests the presence of contrast extravasation and is predictive of hematoma expansion.
- The Intracerebral Hemorrhage Score predicts mortality and includes GCS score, age, IPH location, IPH volume, and presence of intraventricular hemorrhage. A baseline severity score should be obtained.

STEP 4 PEARLS

Coagulopathy	Reversal Agent
Severe thrombocytopenia	Platelets
Heparins	Protamine sulfate
Vitamin K antagonists (warfarin)	Vitamin K Prothrombin complex concentrate (PCC)*
Direct thrombin inhibitors (dabigatran)	Idarucizumab
Factor Xa inhibitors (apixaban, rivaroxaban)	Andexanet alfa

*PCCs are preferred over fresh frozen plasma.

Not recommended: Empiric recombinant factor VIIa, tranexamic acid, or platelet transfusion for antiplatelet agents (eg, clopidogrel)

STEP 5 PEARLS

Secondary IPH	Surgical Options
Hemorrhagic brain tumor or metastasis	Surgical resection
Arteriovenous malformations or fistulas	Excision, embolization, or radiosurgery
Cavernous malformations	Excision
Distal or mycotic aneurysms	Embolization or surgery
Cerebral venous thrombosis	Anticoagulation or thrombectomy
Moyamoya	Revascularization
Vasculitis	Immunomodulatory agents

TABLE 1. Summary approach to the emergency management of IPH

The LLSA Literature Review

2019 AHA Update for Pediatric Advanced Life Support

By Christopher Fahlsing, MD, LT, MC, USN; and Daphne Morrison Ponce, MD, CDR, MC, USN
United States Navy

Reviewed by Andrew J. Eyre, MD, MS-HPEd

Duff JP, Topjian AA, Berg MD, et al. 2019 American Heart Association focused update on pediatric advanced life support: an update to the American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Pediatrics*. 2020;145(1):140(24):e20191361.

KEY POINTS

- For airway management, it is reasonable to continue BVM ventilation versus attempting an advanced airway in patients with OHCA.
- When ECMO protocols and teams are readily available, ECPR should be considered for patients with cardiac diagnoses and IHCA.
- It is reasonable to use TTM of 32°C (89.6°F) to 34°C (93.2°F) followed by 36°C (96.8°F) to 37.5°C (99.5°F) or to use TTM of 36°C (96.8°F) to 37.5°C (99.5°F) for pediatric patients who remain comatose after resuscitation.

The 2019 focused update to the American Heart Association (AHA) pediatric advanced life support (PALS) guidelines for cardiopulmonary resuscitation (CPR) and emergency cardiovascular care (ECC) is based on three systematic reviews and the resulting "2019 International Consensus on Cardiopulmonary Resuscitation and Emergency Cardiovascular Care Science with Treatment Recommendations" (CoSTR) from the International Liaison Committee on Resuscitation (ILCOR) Pediatric Life Support Task Force. AHA guidelines for CPR and ECC are developed in concert with ILCOR's systematic review process.

The update provides recommendations for advanced airway management in pediatric cardiac arrest, extracorporeal cardiopulmonary resuscitation (ECPR) in pediatric cardiac arrest, and pediatric targeted temperature management (TTM) during postcardiac arrest care.

Airway Intervention in Pediatric Cardiac Arrest

Most pediatric cardiac arrests are triggered by respiratory deterioration. Thus, airway management and ventilation are the core components of PALS. Bag-valve-mask (BVM) ventilation, endotracheal intubation, and supraglottic airway (SGA) placement are the primary airway interventions, each with its own risks and benefits. The 2019 ILCOR Pediatric Life Support Task Force and the AHA pediatric writing group reviewed 14 studies of advanced airway interventions in pediatric patients with cardiac arrest. The review included evidence for the use of an advanced airway (ie, endotracheal intubation or SGA) versus BVM ventilation only. When comparing the interventions, there were no significant differences between groups in favorable neurologic outcomes or survival to hospital discharge. There is insufficient evidence to make a recommendation for BVM ventilation compared to an advanced airway for in-hospital cardiac arrests (IHCA). Additionally, no recommendation can be made for endotracheal intubation compared to SGA.

The updated 2019 recommendation is: BVM ventilation is reasonable compared to advanced airway interventions in the management of children during cardiac arrest in the out-of-hospital setting. This recommendation is classified under the American College of Cardiology and the AHA Clinical Practice Guideline Recommendation Classification System (Class) as class IIa (ie, reasonable), with a level of evidence rating of C-LD (ie, limited data). The use of advanced airways in pediatric cardiac arrest was last reviewed in 2010, and there were no significant changes to the recommendations with this most recent review. During out-of-hospital cardiac arrest (OHCA), transport time, personnel skill level and experience, and equipment availability should be considered. If BVM ventilation is ineffective despite appropriate optimization, more advanced airway interventions should be considered.

ECPR for IHCA

The use of extracorporeal membrane oxygenation (ECMO) as a form of mechanical circulatory rescue for failed conventional CPR (ie, ECPR) has gained popularity. ECPR is defined as the rapid deployment of ECMO during active CPR or for patients with intermittent return of spontaneous circulation (ROSC). ECPR is a resource-intense, complex multidisciplinary therapy that should be used for specialized patient populations within dedicated and highly practiced environments. The ILCOR Pediatric Life Support Task Force and the AHA pediatric writing group reviewed three studies on the use of ECPR in pediatric cardiac arrest. Two retrospective studies of pediatric IHCA, after cardiac surgery, found that the use of ECPR was associated with favorable neurologic outcomes and an increased rate of survival to hospital discharge. The third retrospective study of congenital heart disease patients with IHCA during cardiac catheterization found that the use of ECPR was associated with worse survival to hospital discharge compared to conventional CPR.

The updated 2019 recommendation is: ECPR may be considered for pediatric patients with cardiac diagnoses who have

IHCA in settings with existing ECMO protocols, expertise, and equipment (class IIb with a level of evidence of C-LD). In comparison to the 2015 AHA PALS guidelines, there were no significant changes to the recommendations within the 2019 update. Given the ethical and logistical considerations, there have been no prospective comparative analyses between CPR and ECPR. There is insufficient evidence to recommend for or against the use of ECPR for pediatric patients experiencing OHCA or for pediatric patients with noncardiac disease experiencing IHCA refractory to conventional CPR.

Postcardiac Arrest TTM

TTM refers to continuous maintenance of patient temperature within a narrowly prescribed range. Therapeutic hypothermia treats reperfusion syndrome after cardiac arrest by decreasing metabolic demand, reducing free radical production, and decreasing apoptosis. The 2019 ILCOR pediatric CoSTR summarized the evidence supporting the use of TTM (32°C [89.6°F]-34°C [93.2°F]) after pediatric IHCA or OHCA. This pediatric review was triggered by the publication of the THAPCA-IH trial (Therapeutic Hypothermia After Pediatric Cardiac Arrest In-Hospital), a prospective randomized control trial of TTM 32°C (89.6°F) to 34°C (93.2°F) versus TTM 36°C (96.8°F) to 37.5°C (99.5°F) for IHCA. The trial was halted for futility because the primary outcome (favorable neurobehavioral outcome at 1 year) did not differ significantly between groups (36% and 39%, respectively).

The updated 2019 recommendations are: Continuous measurement of core temperature during TTM is recommended (class I with a level of evidence of B-NR [signifying data derived from one or more nonrandomized trials or a meta-analysis]). For infants and children who remain comatose after ROSC, it is reasonable to use either TTM 32°C (89.6°F) to 34°C (93.2°F) followed by TTM 36°C (96.8°F) to 37.5°C (99.5°F) or to use TTM 36°C (96.8°F) to 37.5°C (99.5°F) (class IIa with a level of evidence of B-NR). Since the publication of the 2015 PALS guidelines, the second THAPCA trial and several observational studies of TTM on comatose children after cardiac arrest were published. The ILCOR Pediatric Life Support Task Force and the AHA writing group placed a higher value on pediatric data because the adult studies include patients with arrest causes, disease states, and outcomes that differ from infants and children. Regardless of strategy, physicians should strive to prevent fever greater than 37.5°C (99.5°F).

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Disclosure

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The views expressed in this review article are those of the authors and do not necessarily reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States government.

The LLSA Literature Review

Procedural Sedation

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Reviewed by Andrew J. Eyre, MD, MS-HPEd

Miller KA, Andolfatto G, Miner JR, Burton JH, Krauss BS. Clinical practice guideline for emergency department procedural sedation with propofol: 2018 update. *Ann Emerg Med.* 2019 May;73(5):470-480.

KEY POINTS

- Propofol provides short-acting anesthesia that has been well documented in the literature for use in the emergency department for procedural sedation in both adults and children.
- Relative contraindications for propofol include patients with a propofol allergy, older patients, infants younger than 6 months, and patients with an ASA Class III or higher classification.
- Propofol should be administered by a physician qualified to administer deep sedation and, ideally, with at least two individuals present: one dedicated to sedation and continuous patient monitoring and another performing the procedure.
- Propofol can be administered as a bolus or an infusion, with higher doses in children, and can be coadministered with analgesics, including ketamine and fentanyl.

Propofol is an ultra–short-acting agent that provides both anesthesia and amnesia to patients. Its use has been well documented in the emergency department for procedural sedation. Despite its safety, the use of propofol in children is much lower than in adults. This article provides updated evidence-based guidelines for the use of propofol in the emergency department for deep procedural sedation.

Patients undergoing procedural sedation with propofol require continuous monitoring both via direct visualization and equipment, including continuous cardiac monitoring, capnography, and pulse oximetry as well as careful monitoring of patients' respiratory rate and blood pressure (cycled at least every 5 minutes) throughout the procedure and recovery. Supplemental oxygen should also be administered throughout the procedure because this provides longer periods of normal oxygenation if patients become hypopneic or apneic. Young children are especially at risk, given their smaller pulmonary reserve.

Emergency department procedural sedation requires a physician who is trained and qualified to administer deep sedation. The team should be composed of at least two personnel: one dedicated to the procedure and a second dedicated to sedation, patient monitoring, and any potential resuscitative interventions. If only one physician performs both the procedure and sedation, then they must immediately stop the procedure to perform resuscitation, if needed.

Propofol can be given as a bolus or an infusion. Propofol infusions are becoming more popular because they minimize the risk of respiratory depression, hypotension, and suboptimal sedation seen at propofol's peak and trough. Bolus dosing in adults is an initial dose of 0.5 to 1.0 mg/kg, with additional boluses of 0.25 to 0.5 mg/kg every 1 to 3 minutes as needed. Infusion dosing should be titrated between 100 and 150 µg/kg/min (6-9 mg/kg/hr). Consider starting on the lower end of the dosage range for older patients as well as obese patients because propofol dosing is based on lean body mass and not total body weight. Children require higher doses to achieve a desired level of sedation. Use an initial bolus dose of 2 mg/kg in patients 3 years or younger and 1.5 mg/kg in older children and teenagers, with additional boluses of 0.5 to 1 mg/kg every 1 to 3 minutes as needed. For infusions in children, use 100 to 250 µg/kg/min (6-15 mg/kg/hr).

Propofol does not have analgesic properties, so patients undergoing painful procedures may benefit from propofol coadministration with an analgesic agent. Ketamine is often coadministered with propofol (ketofol) in a 1:1 mixture in a single syringe at the same mL/kg volume as single-agent propofol, which provides a faster onset of deep sedation and analgesia. Fentanyl is also commonly administered with propofol for analgesia. Patients should receive fentanyl prior to receiving propofol to decrease the risk of respiratory depression that can occur with coadministration.

The most common adverse effect of propofol is transient hypotension, which is seen in both adults and children. As such, special consideration should be given to administering propofol to critically ill or hypotensive patients. Respiratory depression, including hypoxia or apnea, can be seen in any patient but is more common in adults than in children. The use of airway adjuncts (eg, bag-valve-mask ventilation and intubation) are rarely needed. Rare side effects include injection site pain and nausea and vomiting. Propofol infusion syndrome has not been documented in the literature for emergency department procedural sedation.

One absolute contraindication for the use of propofol is a previous propofol allergy. Relative contraindications include children younger than 6 months or under 5 kg, patients older than 75 years, and patients with an American Society of Anesthesiologists (ASA) Physical Status Classification System Class III and above. Previous soybean or egg allergy (both used in the manufacturing of propofol) is no longer considered a contraindication because data do not support this concern.

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Pulmonary Embolism

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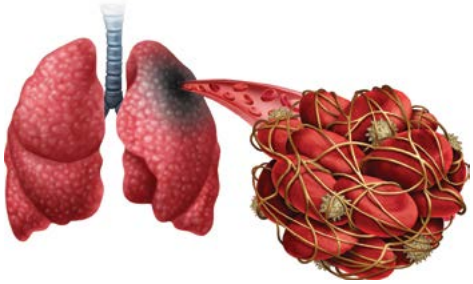
Kearon C, de Wit K, Parpia S, et al. Diagnosis of pulmonary embolism with D-dimer adjusted to clinical probability. *N Eng J Med.* 2019 Nov 28;381(22):2125-2134.

KEY POINTS

- D-dimer testing can be used in combination with the Wells score risk stratification tool to differentiate patients in need of testing to rule out PE.
- This prospective study of 2,017 outpatients in Canada showed that there were no VTEs during a 3-month follow-up period for participants with a low or medium risk of PE per the Wells score, with D-dimer levels less than 1,000 ng/mL for low-risk patients and 500 ng/mL for medium-risk patients, who did not receive CTPA or AC therapy.
- This strategy resulted in a small reduction in the use of chest imaging as compared to the strategy used in the YEARS study and a greater reduction in chest imaging as compared to the age-adjusted cutoff strategy, with an average of 17.6% fewer CTPAs in the low-risk and low–D-dimer category compared to the standard approach.

D-dimer diagnostic tests can be used to determine which patients require further testing, such as CT pulmonary angiography (CTPA), to evaluate for the presence of a pulmonary embolism (PE). Past retrospective studies have shown that a D-dimer level under 1,000 ng/mL is sufficient to rule out a PE in those with a low clinical pretest probability (C-PTP), while a D-dimer level under 500 ng/mL is sufficient to rule out a PE in those with a moderate C-PTP.



This prospective study enrolled 2,017 adult outpatients from Canadian emergency departments or clinics who had a history concerning for PE. Subsequently, physicians used the Wells clinical prediction rule to categorize patients into low-, moderate-, and high-risk C-PTP categories. Those patients with a low or moderate C-PTP underwent D-dimer serum testing. If patients had a low C-PTP with a D-dimer level less than 1,000 ng/mL or if patients had a medium C-PTP with a D-dimer level less than 500 ng/mL, no further testing was performed, and these patients did not receive anticoagulation (AC) therapy. Otherwise, all other patients (ie, those with elevated D-dimers for their risk categories and those with a high C-PTP) underwent CTPA. Patients only received AC therapy if a PE was found on CTPA. All patients in the study were followed for 3 months to evaluate for further venous thromboembolisms (VTEs).

In total, 7.4% of the 2,017 patients enrolled in this Pulmonary Embolism Graduated D-Dimer (PEGeD) diagnostic strategy had a PE on initial testing and, thus, received AC therapy. A total of 1,285 patients had a low C-PTP with a D-dimer level less than 1,000 ng/mL, and 40 patients had a moderate C-PTP with a D-dimer level less than 500 ng/mL. None of these patients had a VTE during the 3-month follow-up period (95% confidence interval [CI], 0.00 to 0.29). By contrast, of the 1,863 patients who did not have a PE on initial workup, only one subsequently had a VTE (0.05%; 95% CI, 0.01 to 0.30).

Using the PEGeD diagnostic strategy for outpatient encounters, 34.3% of patients received CTPA. Using the standard approach, where a PE is ruled out using a combination of a low C-PTP and a D-dimer level less than 500 ng/mL, would have resulted in using CTPA in 51.9% of patients (a difference of –17.6 percentage points; 95% CI, –19.2 to –15.9). Additionally, the PEGeD strategy resulted in a small decrease in the use of CT imaging compared to the YEARS strategy (–2.0 percentage points; 95% CI, –2.8 to –1.2), while the PEGeD strategy resulted in a somewhat greater reduction in CTPA as compared to the age-adjusted cutoff strategy (–8.6 percentage points; 95% CI, –10.0 to –7.2).

In summary, with CTPAs having associated risks, including contrast reactions, increased radiation exposure, increased cost, and increased lengths of stay, multiple decision-making tools can be used to evaluate patients who are at low risk of PE. The PEGeD strategy uses a combination of the Wells score and specific D-dimer cutoffs for low- and medium-risk patients and resulted in no VTEs in these patients during a 3-month follow-up period. Additionally, it resulted in less imaging compared to both the age-adjusted cutoff strategy and the YEARS strategy as well as compared to the standard approach of using a low C-PTP and a D-dimer level less than 500 ng/mL.

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Established Status Epilepticus Treatment Trial (ESETT)

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Reviewed by Andrew Eyre, MD, MS-HPEd

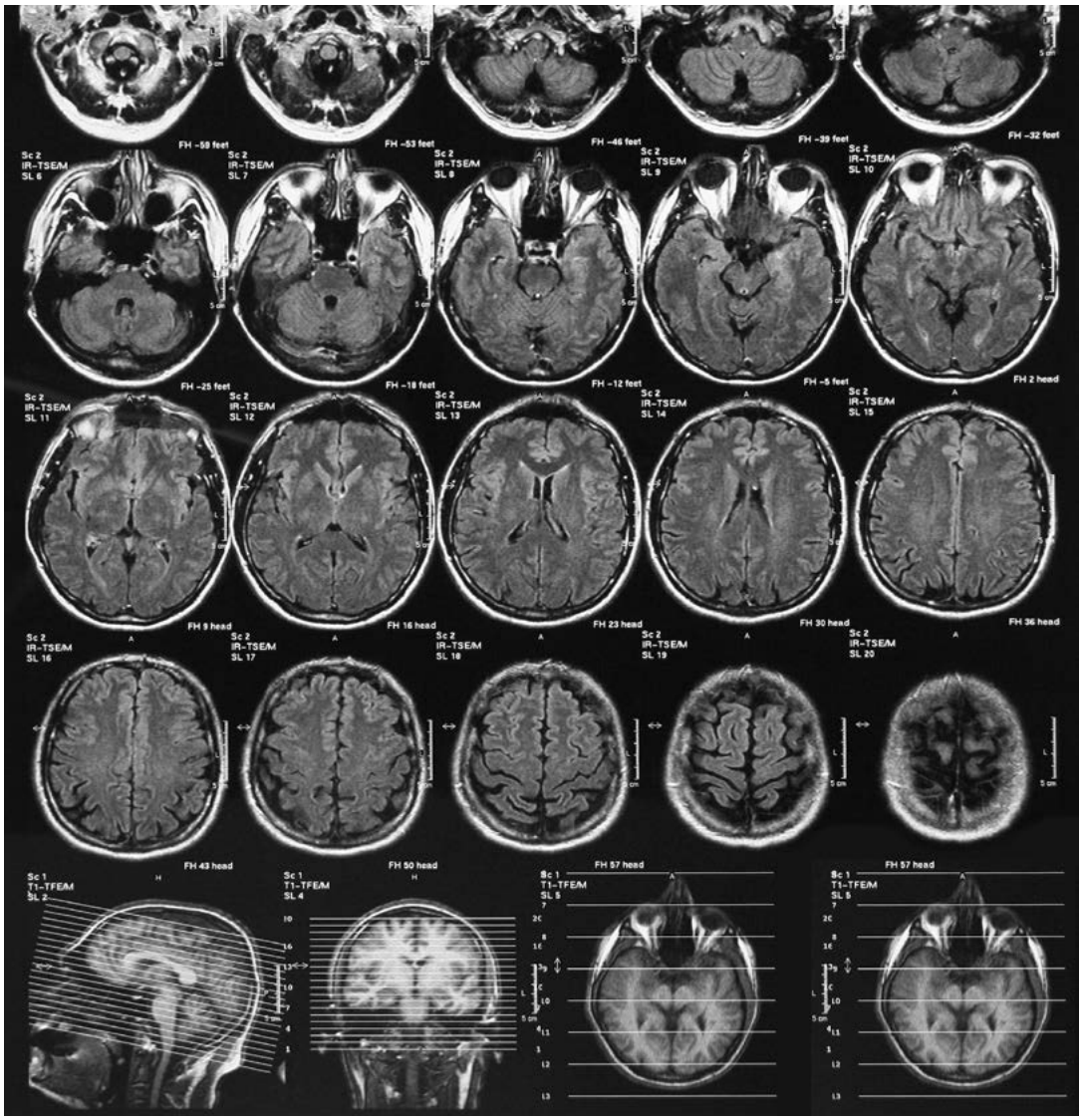
Kapur, J, Elm, J, Chamberlain JM, et al. Randomized trial of three anticonvulsant medications for status epilepticus. *N Engl J Med*. 2019 Nov; 381(22):2103-2113.

KEY POINTS

- Morbidity and mortality associated with status epilepticus are reduced with early seizure cessation.
- Fosphenytoin, levetiracetam, and valproate all resulted in approximately 50% of patients having seizure termination within 60 minutes of drug infusion completion.
- One-third of patients do not respond to appropriately dosed benzodiazepines for termination of convulsive seizures.

The morbidity and mortality associated with status epilepticus are reduced with early seizure cessation. Only fosphenytoin is FDA-approved for benzodiazepine-refractory status epilepticus in adults; no drug is FDA-approved for this indication in the pediatric population. Up to one-third of seizures are benzodiazepine-refractory, and with potential treatment not well-studied, Kapur, et al aimed to compare the efficacy and safety of 3 of the most commonly used anti-epileptics in adults and children in the emergency department.

The authors conducted a multicenter, prospective, randomized, double-blinded, superiority-inferiority clinical trial to compare effectiveness and safety of the three most common second-line agents for benzodiazepine-refractory status epilepticus: fosphenytoin, levetiracetam, and valproate. Patients older than 2 years of age were enrolled in emergency



departments across 57 hospitals in the United States once they had generalized convulsive seizures lasting longer than 5 minutes or recurrent within 30 minutes after appropriate benzodiazepine treatment. Patients were excluded in the setting of trauma, hypoglycemia, hyperglycemia, cardiac arrest, pregnancy, incarceration, having already received a nonbenzodiazepine antiepileptic, or an allergy or contraindication to the trial medications.

Following appropriate benzodiazepine dosing, study participants received one of the trial drugs from a "use next" medication box that was age stratified. The trial drugs of fosphenytoin (20 mgPE/kg, max 1,500 mgPE), levetiracetam (60 mg/kg, max 4,500 mg), or valproate (40 mg/kg, max 3,000 mg) were administered as infusions via pumps programmed over 10 minutes with a predetermined rate. Rescue therapy was administered, if clinically indicated, 20 minutes after trial treatment was completed.

The primary efficacy outcome was termination of clinical seizures with improved responsiveness 60 minutes after the trial treatment was completed without additional antiepileptic therapy. The primary safety outcome was a composite of life-threatening hypotension and arrhythmia. The secondary efficacy outcomes included time to seizure cessation (when audio recording was available), ICU admission, ICU length of stay, and hospital length of stay. The secondary safety outcomes included death, intubation within 1 hour after starting the trial drug, recurrent seizure 1 hour after starting the trial drug, and anaphylaxis.

Randomization was conducted via response-adaptive comparative effectiveness design. The first planned interim analysis was at 400 enrollments, with the potential for early trial cessation if criteria for success or futility were met. The primary analysis was based on the intention-to-treat population (unique patients for efficacy and all enrollments for safety).

The fosphenytoin (n = 118), levetiracetam (n = 145), and valproate (n = 121) groups had similar baseline characteristics. Eligibility criteria deviation was 27%: Timing of trial drug to benzodiazepine administration (50 patients), inadequate cumulative benzodiazepine dose (26 patients), enrollment of patients without status epilepticus (33 patients). The majority of enrollments (87%) had a final diagnosis of status epilepticus; 10% had a final diagnosis of nonepileptic seizure.

The primary efficacy outcome was achieved in 45% of the fosphenytoin, 47% of the levetiracetam, and 46% of the valproate group. The primary safety outcome was not statistically significant, with life-threatening hypotension or arrhythmia in 3.2% of the fosphenytoin, 1.3% of the levetiracetam, and 1.6% of the valproate group. Only 39 patients met the primary efficacy outcome and had audio recordings, which was used to determine seizure duration. The median time from drug start to seizure cessation was 11.7 minutes for fosphenytoin, 10.5 minutes for levetiracetam, and 7.0 minutes for valproate. Similarly, seizure recurrence and other safety outcomes did not differ significantly.

There was no significant difference in seizure termination among the three treatment groups, with approximately half of patients meeting the primary outcome in each group. There was also no significant difference in safety, although intubation and hypotension were more common with fosphenytoin and death was more frequent with levetiracetam. Prior observational studies showed varying efficacies among these three drugs. The limitations of this study include unblinding (although most occurred after the primary outcome was determined), the relatively large enrollment of nonepileptic seizure diagnoses (10%), the clinical determination of seizure cessation instead of EEG determination, dosing determined from published experience with the most-efficacious dosing unknown, more restrictive maximum-rate infusion of fosphenytoin limiting maximum dose if more than 75 kg, nonserious adverse events not recorded more than 24 hours after enrollment, and large eligibility deviations (primarily due to benzodiazepine timing or dosing).

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Disclosure

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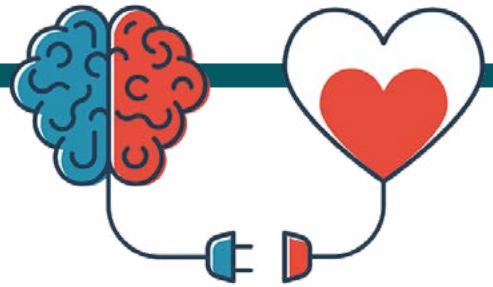
The LLSA Literature Review

Cardiac Syncope



By Elmira Andreeva, MD; and Laura Welsh MD
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Albassam OT, Redelmeier RJ, Shadowitz S, Husain AM, Simel D, Etchells EE. Did this patient have cardiac syncope? The rational clinical examination systematic review. *JAMA*. 2019;321(24):2448-2457.

KEY POINTS

- Cardiac syncope is a common and dangerous cause of syncope that must not be missed in the emergency department.
- Syncope in patients older than 35 years and with a history of CAD or other cardiac conditions significantly increases the likelihood of cardiac syncope.
- A normal ECG and no history of heart disease significantly decrease the likelihood of cardiac syncope.
- Biomarkers such as troponin and NT-proBNP, while helpful, should not be used to definitively diagnose cardiac syncope.

Syncope is defined as a transient loss of consciousness because of decreased cerebral perfusion, followed by a return to baseline. The various causes of syncope range from benign to serious. A dangerous cause is cardiac syncope, which is responsible for 5% to 21% of all cases of syncope presenting to the emergency department.

Cardiac syncope results from decreased cardiac output because of cardiopulmonary issues such as arrhythmias, structural heart disease, or pulmonary emboli. It can often be challenging to distinguish cardiac conditions from other causes of syncope, and the increased morbidity and mortality of cardiac syncope make it a diagnosis that cannot be missed. This article is a systematic review that explores the accuracy of the history, examination, and laboratory findings to identify cardiac syncope. Eleven studies of cardiac syncope were included with a total of 4,137 patients. The studied population represented adult patients presenting to primary care, emergency department, or specialty clinics with syncope.

In terms of historical factors, both a history of coronary artery disease (CAD) and onset of the first syncopal event at 35 years or older were associated with a greater likelihood of cardiac syncope. Additionally, a history of atrial fibrillation or flutter, heart failure, or known severe structural heart disease was associated with an increased likelihood of cardiac syncope. However, these factors all had relatively low sensitivities. Certain precipitating factors such as pain or a medical procedure were less likely to be associated with cardiac syncope.

Prodromal symptoms of dyspnea or chest pain were associated with a higher likelihood of cardiac syncope, while the sensation of palpitations rendered inconclusive results in this review. Absence of a prodrome was not associated with either a high or low likelihood of cardiac syncope. Cyanosis during the syncopal event was associated with a higher likelihood of cardiac syncope, while an inability to recall events leading up to the syncopal event was associated with a lower likelihood. However, both elements had low sensitivity. Traumatic injury from the syncopal event was not associated with either a high or low likelihood of cardiac syncope.

Diagnostically, cardiac syncope was significantly less likely if there was a normal ECG and no history of heart disease. Elevated biomarkers including troponin T or I, as well as NT-proBNP, were associated with a higher likelihood of cardiac syncope; however, high cutoffs for troponin and NT-proBNP were required to achieve a predetermined specificity of 95%.

In summary, while certain factors such as age and presence of known cardiac disease can increase the likelihood of cardiogenic syncope, there is no single variable that can make this diagnosis. Classically taught findings such as palpitations or absence of prodrome lack accuracy in differentiating causes of syncope. In agreement with both the European Society of Cardiology and American College of Cardiology guidelines, the authors advise against the routine use of troponin or NT-proBNP when evaluating syncope.

Limitations of this study include misclassification bias because there is no gold standard to definitively identify cardiac syncope, which may lead to increases in specificity and sensitivity. Moreover, patients with a diagnosis of unexplained syncope were excluded from some of the studies, which could also have altered the sensitivity and specificity of the reported findings.

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