Critical decisions in emergency medicine

THE 2023 LLSA LITERATURE REVIEW

The LLSA Literature Review

Synopses of articles from ABEM's 2023 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.

This online supplemental issue of *Critical Decisions in Emergency Medicine* includes the 11 summaries of the 2023 LLSA reading list, 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/moccenter/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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Contents

Critical decisions in emergency medicine

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Conservative Versus Interventional Treatment for Spontaneous Pneumothorax

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Objective

On completion of this article, you should be able to:

- Compare and contrast conservative and interventional management of spontaneous pneumothorax.

Brown SGA, Ball EL, Perrin K, et al; PSP Investigators. Conservative versus interventional treatment for spontaneous pneumothorax. *N Engl J Med*. 2020 Jan 30;382(5):405-415.

KEY POINTS

- Conservative management with observation and watchful waiting may be reasonable for a subset of patients ages 14 to 50 years with a first-time unilateral spontaneous pneumothorax and who meet certain symptom and physiologic criteria.
- A conservative approach to spontaneous pneumothorax likely spares many patients from unnecessary invasive procedures.
- Conservative management for pneumothorax lowers the risk of serious adverse events and pneumothorax recurrence.

Management approaches for moderate to large primary spontaneous pneumothoraces vary widely. The most common approach includes insertion of a chest tube. However, more conservative approaches propose that a chest tube be placed only if conservative treatment fails or if patients meet certain symptomatic or physiologic criteria. Brown et al designed a nonblinded, multicenter, noninferiority trial to determine whether conservative management is an acceptable alternative to immediate intervention.

The trial included 316 participants, aged 14 to 50 years, who presented with a first-time unilateral, moderate to large primary spontaneous pneumothorax. They were randomized to either conservative or interventional management groups, and the rates of lung re-expansion within 8 weeks were compared between the two groups.

In the interventional group, a small-bore chest tube was inserted, and repeat chest x-rays were completed 1 and 5 hours post procedure; if patients in this group had a fully re-expanded lung without recurrence of the pneumothorax, the chest tube was removed, and they were discharged. Otherwise, they were admitted to the hospital.

Patients in the conservative arm were observed for a minimum of 4 hours before repeating a chest x-ray. Patients who did not need supplemental oxygen and were able to walk were discharged. Intervention was reserved for those patients with clinically significant symptoms despite adequate analgesia, chest pain or dyspnea that prevented mobilization, physiologic instability (systolic blood pressure <90 mm Hg, shock index value ≥1, or SpO_2 <90% on room air), an enlarging pneumothorax on repeat x-ray, or an unwillingness to continue with conservative treatment.

All study participants were reassessed at 2 weeks, 4 weeks, 8 weeks, 6 months, and 12 months. A noninferiority margin of –9 percentage points was used: Researchers accepted a successful re-expansion rate of 90% in the conservative management group compared to an anticipated 99% in the interventional group.

The interventional group consisted of 154 participants, and the conservative group consisted of 162 participants. Of the conservative participants, 137 (84.6%) did not undergo intervention, while 25 (15.4%) did. Lung re-expansion data were successfully collected on 131 of the interventional participants and 125 of the conservative participants. Successful lung re-expansion by 8 weeks occurred in 120/131 (98.5%) of the interventional group and 118/125 (94.4%) of the conservative group, which was considered noninferior. However, if all missing data were assumed to represent failed lung re-expansion, the results no longer met the noninferiority threshold.

Secondary outcomes demonstrated that the median time to radiographic resolution was 16 days in the interventional group versus 30 days in the conservative group; however, both groups had similar times to symptom resolution. Conservative management was associated with greater patient satisfaction; lower rates of serious adverse events, progression to surgery, and 12-month pneumothorax recurrence; and length of hospital stay.

Overall, conservative management spared 85% of patients from invasive intervention and had noninferior rates of successful lung re-expansion by 8 weeks. This trial showed modest but statistically fragile evidence that conservative management is noninferior to interventional management. Results support the idea that in patients with first-time spontaneous pneumothoraces who are hemodynamically stable and meet specific symptom criteria, emergency physicians should discuss with them both immediate intervention and more conservative watchful waiting management options.

End-of-Life Care

By Mobolaji Fowose, MD, MPH; and Michael E. Abboud, MD, MSEd
Department of Emergency Medicine, University of Pennsylvania in Philadelphia
Reviewed by Andrew J. Eyre, MD, MS-HPEd

Objective

On completion of this article, you should be able to:

- Explain how to appropriately deliver EOL care in the emergency department.

Long DA, Koyfman A, Long B. Oncologic emergencies: palliative care in the emergency department setting. *J Emerg Med*. 2021 Feb;60(2):175-191.

KEY POINTS

- EOL care is an important and common part of health care in the emergency department.
- Advance directives and goals of care should be confirmed for each patient. When plans are not already documented, physicians should empathetically discuss developing EOL plans with patients and their health care proxies.
- Dyspnea is the EOL symptom that distresses patients the most but can be managed with opioids.
- Pain at EOL can be managed with opioids, but nonopioid alternatives should also be considered.
- The WHO estimates that by 2050 the worldwide number of people older than 60 years will increase by 10%. Unfortunately, many of these individuals will develop terminal illnesses that require emergency care, so emergency physicians must be competent in EOL matters. EOL care aims to provide quality care by maximizing comfort and alleviating distress while respecting patients' wishes to avoid aggressive, life-sustaining treatment.

Advance Directives

Many patients with terminal illnesses document their medical care goals in an advance directive. Common orders that go along with an advance directive include a do-not-resuscitate (DNR) or a do-not-intubate (DNI) order. A more specific type of advance directive is the physician orders for life-sustaining treatment (POLST) form that specifies medical orders for interventions like noninvasive ventilation and intravenous fluids. Emergency physicians use these documents to provide quality end-of-life (EOL) care according to patients' wishes.

One of emergency physicians' biggest challenges in caring for EOL patients is accessing their advance directives in a timely manner before managing their condition. Even in patients with clearly written and obtainable directives, it is often still difficult to decide how aggressive treatment should be when patients become critically ill. Thoughtful communication between emergency physicians, patients, and their health care proxies is crucial to building a therapeutic alliance that ensures medical decisions are made according to patients' wishes. Emergency physicians should educate patients and their proxies about the available medical therapies and expectations of EOL care and then should collaborate on a care plan and clearly document it in the medical record.

Symptom Management

Patients with terminal illnesses display signs and symptoms that life is near its end. Symptoms that suggest a short survival time include anorexia, asthenia (lack of energy), dry mouth, and confusion. In patients with advanced malignancy, symptoms of dyspnea, anorexia, tachycardia, or low systolic blood pressure are associated with being near the end. Distressing symptoms along with symptoms that are less severe, but still uncomfortable, must be treated. Nausea is treated with antiemetics. The "death rattle" — noisy breathing caused by the pooling of secretions in the airway — can be treated with glycopyrrolate.

Although dyspnea can be managed in multiple ways, studies suggest that intubation and mechanical ventilation increase suffering. Noninvasive therapies for dyspnea should be considered in patients with a DNI status; however, the masks in noninvasive, bilevel ventilation are often uncomfortable and can also increase suffering. Additionally, oxygen therapy has not been shown to relieve EOL dyspnea. The best-studied therapy for EOL dyspnea is opioid therapy. Opioids reduce the chemoreceptor response to hypercapnia and decrease anxiety and the sensation of breathlessness. Physicians may fear that the utilization of narcotics may hasten death, but the literature does not support this belief when low-dose opioids are used — the dose needed to relieve EOL dyspnea is lower than that for pain control. Starting with intravenous morphine at 1 to 2 mg or with intravenous hydromorphone at 0.2 to 0.4 mg, with redosing as needed, can be sufficient.

Benzodiazepine use for EOL dyspnea is more controversial. Although benzodiazepines can relieve the anxiety associated with dyspnea, they can also increase sedation. Some studies encourage low-dose benzodiazepines in combination with other agents in some patient populations.

Pain is another common, distressing symptom in terminally ill patients; it can be nociceptive, neuropathic, or bone related. Nociceptive pain is caused by the stretching of organs, usually from malignancy; neuropathic and bone-related pain are from pathologic fractures or metastatic disease. Opioids are the first-line therapy for severe pain. When selecting the type and quantity of opioids, physicians must consider the duration of effect, potential side effects, and patient tolerance.

Nonopioid alternatives should be considered for mild to severe pain. Nociceptive and bone-related pain can be treated with NSAIDs, acetaminophen, or low-dose intravenous ketamine (0.1-0.3 mg/kg). Gabapentin, anticonvulsants, or antidepressants can be effective for neuropathic pain.

The LLSA Literature Review

Management of Acute Ischemic Strokes

By Jamie Aron, MD; and Andrew J. Eyre, MD, MS-HPEd
Harvard Affiliated Emergency Medicine Residency and Brigham and Women's Hospital/Harvard Medical School, Boston, Massachussetts

Objective

On completion of this article, you should be able to:

- Discuss the timing of acute ischemic stroke treatment options.

Powers WJ. Acute ischemic stroke. *N Engl J Med*. 2020 Jul 16;383(3):252-260.

KEY POINTS

- Intravenous alteplase should be considered in patients who present within 4.5 hours of symptom onset regardless of the hospital setting.
- Mechanical thrombectomy can be considered up to 24 hours from the time of onset.
- No evidence currently suggests that either alteplase or tenecteplase is superior to the other.

Acute ischemic strokes can be life-altering, if not fatal. Signs and symptoms of a stroke must be promptly recognized to initiate treatment as soon as possible. With ongoing research and improving technology, stroke guidelines and therapeutic options continue to evolve. Treatment for patients with acute ischemic strokes largely depends on symptom duration, symptom severity, medical history, and imaging findings. Physicians should inquire about the time of onset (ie, the last time the patient was known to be well), and patients should undergo a rapid neurologic examination and noncontrast head CT to rule out an intracranial hemorrhage, a mass, or an alternative diagnosis. Although noncontrast head CT is the recommended initial imaging modality, additional advanced imaging such as CT angiography (CTA) or MRI may be needed for further management. The team should also obtain a point-of-care glucose reading and standard blood tests to evaluate for metabolic or toxicologic causes of altered mental status or acute neurologic deficits.

Although emergency physicians should follow institutional protocols and collaborate with stroke experts, the evidence-based guidelines offered by Powers regarding stroke treatment options at different times from symptom onset are useful.

From Time of Onset to 4.5 Hours After Onset

Guidelines recommend administering intravenous thrombolytics for patients who meet imaging, stroke severity, and other inclusion criteria. The thrombolytic agent used in treatment will likely depend on the hospital. Alteplase and tenecteplase are both tissue plasminogen activators (tPA) that are widely available and have their own eligibility criteria. Alteplase is better studied, but tenecteplase has a longer half-life and can be given as a single bolus, making it easier to administer. Currently, these two thrombolytics demonstrate no difference in effectiveness.

If available, a subsequent CTA or MR angiography (MRA) should be performed, and a mechanical thrombectomy should be considered in eligible patients.

From 4.5 to 9 Hours After Onset

A CTA or MRA should be obtained, and a mechanical thrombectomy should be considered in eligible patients. If patients are ineligible for a mechanical thrombectomy or transfer to a thrombectomy center for the procedure is unfeasible, administer intravenous alteplase, if appropriate.

From 9 to 24 Hours After Onset

A CTA or MRA should be performed; in eligible patients, a mechanical thrombectomy or transfer to a thrombectomy center where one can be performed should be considered. After administration of intravenous alteplase or completion of a mechanical thrombectomy, patients should be admitted to the ICU for careful monitoring of blood pressure, temperature, blood glucose levels, and signs of brain herniation, cerebral edema, or a rapid change in neurologic status.

By 24 Hours After Onset

Patients should be evaluated for dual antiplatelet treatment eligibility. A combination of clopidogrel and aspirin for 21 days after an acute ischemic stroke has been shown to lower the risk of a subsequent ischemic or hemorrhagic stroke.

By 48 Hours After Onset

Aspirin should be considered for patients not already on dual antithrombotic therapy

Summary

Although each health care institution varies greatly in its capabilities, intravenous tPA is broadly available, and eligibility criteria exist. If the patient is not in a hospital where a mechanical thrombectomy can be performed, transfer to a mechanical thrombectomy–capable center should be considered within 24 hours of symptom onset. If a patient presents to a hospital with mechanical thrombectomy capabilities and is eligible for intravenous alteplase at 4.5 hours or less since symptom onset, they should continue to be treated with intravenous alteplase even if they may also receive a mechanical thrombectomy.

Buprenorphine for Opioid Withdrawal in the Emergency Department

By Bethanne Bartscherer, MD; and Laura Welsh, MD
Boston Medical Center and Boston University Chobanian & Avedisian School of Medicine, Massachussetts

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

Objective

On completion of this article, you should be able to:

- Explain when and how to initiate buprenorphine treatment of opioid withdrawal in the emergency department.

Herring AA, Perrone J, Nelson LS. Managing opioid withdrawal in the emergency department with buprenorphine. *Ann Emerg Med.* 2019 May;73(5):481-487.

KEY POINTS

- Although opioid withdrawal itself is generally non–life-threatening, a subsequent opioid overdose from trying to counteract withdrawal symptoms carries a high mortality risk.
- Emergency physicians who care for patients in opioid withdrawal can initiate medication-assisted therapy both as a withdrawal treatment and as a bridge to long-term treatment.
- Buprenorphine should be considered for patients in opioid withdrawal who have abstained from short-acting opioids for over 12 hours, extended-release opioids for over 24 hours, and methadone for over 72 hours.
- Approximately 30 to 60 minutes after an initial 8-mg dose of buprenorphine, an additional 8 to 24 mg can be given if withdrawal symptoms persist or are precipitated. After symptoms lessen, patients can be discharged with 16 mg buprenorphine-naloxone daily for 3 to 7 days until follow-up is established.

Emergency physicians play an integral role in addressing the public health crisis of opioid use disorder. Opioid withdrawal without medical therapy carries a high risk of mortality because it increases the chance of a subsequent fatal opioid overdose. Emergency physicians frequently care for patients in opioid withdrawal and can reduce its associated morbidity and mortality by initiating medication-assisted therapy.

To experience withdrawal, patients must be opioid dependent. Using short-acting opioids several times daily for as few as 2 weeks is enough to establish dependence. The intensity of dependence — and, thus, the severity of withdrawal — increases with higher doses that are consumed over longer periods of time. Withdrawing from opioids themselves (ie, without planning to take subsequent doses to self-treat withdrawal symptoms) is generally not life-threatening. Symptoms include restlessness, vomiting, diarrhea, piloerection, diaphoresis, yawning, mydriasis, and mild autonomic hyperactivity. Psychological symptoms such as pain, anxiety, irritability, and drug cravings can persist for weeks. Precipitated withdrawal that is caused by an opioid antagonist, partial agonist, or agonist-antagonist occurs abruptly and can be associated with vomiting, agitation, delirium, and autonomic instability. Most concerningly, precipitated withdrawal can cause massive catecholamine release that leads to pulmonary edema.

Opioid withdrawal is diagnosed clinically. The Clinical Opiate Withdrawal Scale (COWS) is a tool commonly used to assess withdrawal severity and can guide buprenorphine initiation. The Subjective Opiate Withdrawal Scale (SOWS) can guide unobserved buprenorphine inductions at home. Differences in personal practices and institutional cultures have led to wide differences in treatment approaches for opioid withdrawal. One approach involves mitigating withdrawal symptoms with nonopioid medications like α_2-adrenergic agonists and antiemetics. The evidence-based approach favors using an opioid agonist both as a treatment for withdrawal and as a bridge to long-term treatment. Although both buprenorphine and methadone are safe and effective opioid agonists that are used to treat withdrawal, buprenorphine is preferred in the emergency department.

Methadone is a full opioid agonist, and 10 to 20 mg orally can reduce opioid withdrawal symptoms without causing sedation or respiratory depression. Buprenorphine is a partial opioid agonist that does not cause euphoria, sedation, or respiratory depression. A definitive dosing approach in the emergency department is still lacking — the slow titration guidelines for the outpatient setting are impractical in the emergency department. Most patients require at least 8 mg SL buprenorphine to control withdrawal symptoms, and insufficient

dosing can cause withdrawal symptoms to return. Higher doses (a maximum daily dose is 32 mg) should be used cautiously in older adults and in those who use sedatives.

Buprenorphine precipitates withdrawal by displacing a full opioid agonist with a partial agonist. This displacement is also commonly seen with methadone, a full opioid agonist with low binding affinity, and will not occur when buprenorphine users receive full agonist opioids for analgesia. Larger initial doses of buprenorphine may be less likely to precipitate withdrawal symptoms because higher doses provide better partial agonist stimulation.

For patients in opioid withdrawal, buprenorphine initiation is appropriate when more than 12 hours have passed since using short-acting opioids, more than 24 hours since using extended-release formulations, and more than 72 hours since using methadone. For patients with COWS scores greater than 8, start with 4 to 8 mg SL buprenorphine based on withdrawal severity. If patients are still in withdrawal after 30 to 60 minutes, the initial dose is considered to have precipitated withdrawal, and additional buprenorphine (8-24 mg) should be administered.

After symptoms are under control, patients can be discharged from the emergency department with instructions to take 16 mg buprenorphine-naloxone daily for 3 to 7 days or until follow-up with a recovery physician is established. Emergency physicians may also want to consider providing patients with a take-home naloxone kit, screening for HIV and hepatitis C, and although pregnancy is not a contraindication to buprenorphine, providing reproductive health counseling.

The Importance of Lactate

By Michael Platzer, DO, LT, MC, USN; and
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Navy Medical Center in Portsmouth, Virginia

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

Objective

On completion of this article, you should be able to:

- State the diseases associated with elevated lactate levels and the importance of lactate in guiding treatment in the emergency department.

Wardi G, Brice J, Correia M, Liu D, Self M, Tainter C. Demystifying lactate in the emergency department. *Ann Emerg Med*. 2020 Feb;75(2):287-298.

KEY POINTS

- Elevated lactate levels can be caused by overproduction, decreased clearance, or a combination of both; they are associated with acute and chronic disease states and with an increased mortality rate.
- Increased tissue perfusion and circulation or treatment of underlying disease improves outcomes of patients with elevated lactate levels in most instances.
- Elevated lactate levels should be trended and used as a continuous measure to guide treatment and fluid resuscitation efforts.

In their review article, Wardi et al discuss the biochemistry and pathophysiology of elevated lactate levels and address both the previously accepted and emerging explanations for hyperlactatemia. The authors also review treatments for hyperlactatemia and the condition's impact on mortality.

Lactic acid is a naturally occurring organic acid that converts to the lactate ion. In humans, lactate is used at both rest and during exercise for two functions: to maintain blood glucose levels through its role in gluconeogenesis and to support oxidative phosphorylation through its role as an oxidizable agent. The heart and brain increase lactate metabolism during metabolic stress; each uses lactate for its energy demand (up to 60% for the heart and 25% for the brain). Lactate was traditionally believed to be a waste product of skeletal muscle metabolism, mostly from anaerobic metabolism, based on the "oxygen debt model." Contemporary understanding is that lactate is important for both energy use and oxidation-reduction reactions, even in aerobic conditions. Lactate levels can also rise in response to an increased metabolic state caused by proinflammatory cytokine cascades during physiologic stress, such as in cases of sepsis.

Approximately 70% to 75% of lactate is metabolized by the liver, while the remaining 25% to 30% is metabolized by the kidneys. Lactic acidosis refers to elevated serum lactate levels and a pH of less than or equal to 7.35. Type A lactic acidosis occurs from poor tissue perfusion when oxygen supply and demand are mismatched. Type B lactic acidosis occurs due to medications or other disease states that do not result in cellular hypoxia.

Measurements and Monitoring

Lactate measurements are accurate and repeatable when done correctly. Lactate is generated by drawing serum samples in a gray-top tube or by cooling samples to inhibit RBC metabolism. Processing fresh serum samples within 15 minutes of collection does not significantly distort values. Whole blood and finger-stick samples are both accurate methods for point-of-care lactate measurements. Venous tourniquet use has not been shown to significantly affect the accuracy of readings. Although arterial samples most accurately indicate the level of centrally circulating lactate, venous samples are still appropriate for trending — trending of the sample should be done from the same sample type. According to published studies, patients who receive infusions of lactated Ringer solution, which contains sodium lactate, do not show significant lactate elevations in their blood samples as long as samples are not collected in the immediate vicinity of the infusion.

Lactate in Sepsis

In patients with sepsis, the majority of lactate is thought to be generated in the lungs and skeletal muscle. Lactate elevation in sepsis is a result of leukocyte glycolysis: These inflammatory cells undergo accelerated aerobic glycolysis and produce markedly increased lactate. Increasing evidence shows that hyperlactatemia does not directly correlate with tissue hypoperfusion in patients with sepsis and, therefore, may not be a direct symptom of tissue hypoxia. Cryptic shock or occult hypoperfusion are terms that describe the presence of hyperlactatemia with a normal blood pressure. Patients with this finding (with lactate levels >4 mmol/L) have a relatively high mortality rate.

Lactate in Other Disease Processes

Increased lactate levels in trauma patients are also associated with an increased mortality rate. In general, failure to clear lactate is a strong independent predictor of mortality and can indicate infectious complications, organ dysfunction, mortality, or inadequate resuscitation. Elevated lactate levels in these instances are defined as greater than 2 mmol/L and may outperform base excess as a treatment goal for fluid resuscitation. Seizures, convulsions, and extreme exertion increase lactate levels, but

lactate levels do not correlate with patient outcomes in these cases. Thiamine deficiency, which can occur in patients with chronic alcoholism or poor nutritional status, causes hyperlactatemia because pyruvate undergoes anaerobic metabolism. Acetaminophen toxicity can cause lactic acidosis by directly inhibiting the mitochondrial electron transport chain, and lactate elevation in cases of acute liver failure portends a poor prognosis. β-adrenergic agonists (eg, albuterol) accelerate glycolysis and cause transient hyperlactatemia, although hyperlactatemia from these medications does not predict mortality. Cyanide toxicity impairs oxidative phosphorylation and is associated with lactate levels greater than 10 mmol/L. Ethanol intoxication, along with other comorbidities present in patients with this condition, can also increase lactate levels. Metformin overdose can cause a profound hyperlactatemia, but levels do not predict a poor prognosis.

Prognostic Value and Lactate Clearance

For many disease processes, elevated lactate levels and an inability to clear lactate are associated with a worse prognosis. Lactate levels greater than 4 mmol/L are associated with a 28% increased rate of inhospital mortality, independent of shock rate. Even mildly elevated lactate levels can be associated with mortality and a poor prognosis (depending on the cause), and levels should be used as a continuous variable to guide treatment. In the emergency department, an elevated lactate level should prompt investigation into its cause and should guide fluid resuscitation. Lactate levels must be interpreted in the context of the patient's medical history and presentation because they are not an exclusive indicator of disease severity, and physicians should not be falsely assured by low levels.

Disclosures

The views expressed in this 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.

This work was prepared as part of our official duties as military service members. Title 17 USC § 105 provides that "copyright protection under this title is not available for any work of the United States Government." A United States Government work is defined in 17 USC § 101 as a work prepared by a military service member or employee of the United States Government as part of that person's official duties.

Treating Patients With Recurrent, Low-Risk Chest Pain

By Adam Howell, MD, LT, MC, USN; and
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Navy Medical Center in Portsmouth, Virginia

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

Objective

On completion of this article, you should be able to:

- Explain the recommended guidelines for managing patients with recurrent, low-risk chest pain who present to the emergency department.

Musey PI, Bellolio F, Upadhye S, et al. Guidelines for reasonable and appropriate care in the emergency department (GRACE): recurrent, low-risk chest pain in the emergency department. *Acad Emerg Med*. 2021 Jul;28(7):718-744.

KEY POINTS

- The guidelines from the article represent standards for reasonable and appropriate care, and emergency physicians should always use clinical judgment when applying them.
- Shared decision-making and dissemination of relevant, patient-accessible information should be considered alongside these care guidelines to accommodate for variations in patients' values, preferences, and understanding of medical processes.
- Further prospective investigation into how to manage patients with recurrent, low-risk chest pain is warranted — there is still a paucity of direct evidence to address priority questions.

The Society for Academic Emergency Medicine sponsored the Guidelines for Reasonable and Appropriate Care in the Emergency Department (GRACE) for recurrent, low-risk chest pain. A multidisciplinary panel developed eight questions to assess the certainty of evidence and the strength of the published recommendations on caring for adults with recurrent, low-risk chest pain. The multidisciplinary panel consisted of emergency personnel, a cardiologist, a patient representative, and three methodologists. Their clinical questions emphasized patient-focused outcomes, namely 30-day major adverse cardiac events (MACE). Forty-one studies were included to address the specified questions; however, no direct evidence was available for several of the questions. The expert panelists reached a consensus on all recommendations. The certainty of evidence was assessed using the Grading of Recommendations Assessment Development and Evaluation approach, and each recommendation's strength was labeled as either strong or conditional to indicate the panel's confidence that the management strategy's desirable effects would outweigh its undesirable efffects**.** The final guidelines were analyzed by the Agency for Healthcare Research and Quality's National Guideline Clearinghouse Extent of Adherence to Trustworthy Standards instrument to ensure the best possible adherence to the Institute of Medicine's 2011 standards for trustworthy guidelines. The panel's questions used consensus definitions for targeted key terms.

Recurrent chest pain was defined as chest pain that prompted a previous visit to the emergency department, including two or more visits in a 12-month period, and prompted an evaluation that used a diagnostic protocol but did not demonstrate acute coronary syndrome (ACS) or flow-limiting coronary stenosis. *Low risk* refers to a low risk of ACS or MACE in emergency department patients with recurrent chest pain and was determined by a HEART score (**H**istory, **E**CG, **A**ge, **R**isk factors, and **T**roponin) of less than 4 or an equivalent score from another validated measure that is used in the emergency department. The term *expedited* refers to a follow-up that occurs within 3 to 5 days.

The Eight Priority Questions and Recommendations

In adult patients with recurrent, low-risk chest pain:

1. **Are serial troponin measurements or a single troponin measurement needed to determine ACS outcomes within 30 days?**

Recommendation: Adult patients with recurrent, low-risk chest pain that lasts longer than 3 hours should have a single high-sensitivity troponin measurement that is below a validated threshold to reasonably exclude ACS within 30 days (low level of evidence; for [conditional]).

2. **If they also have normal or nondiagnostic stress testing within the last 12 months, does repeat stress testing affect MACE within 30 days?**

Recommendation: In patients who also had a normal stress test within the previous 12 months, repeat routine stress testing is not recommended to decrease rates of MACE at 30 days (low level of evidence; against [conditional]).

3. **Is admission to the hospital, a stay in the emergency department's observation unit, or outpatient follow-up recommended for ACS outcomes within 30 days?**

Recommendation: Evidence is insufficient to recommend hospitalization (either standard inpatient admission or an observation stay) over discharge as a strategy to mitigate MACE within 30 days (no evidence; either).

4. **For patients who also have negative cardiac catheterization results (defined as <50% stenosis), what is their risk of subsequent ACS and the time to ACS?**

Recommendation: For patients with nonobstructive coronary artery disease (CAD) (<50% stenosis) on prior angiography within 5 years, referral for expedited outpatient testing as warranted rather than admission for inpatient evaluation is recommended (low level of evidence; for [conditional]).

5. **For patients who also have negative cardiac catheterization results (defined as no CAD, or 0% stenosis), what is their risk of subsequent ACS and the time to ACS?**

Recommendation: In adult patients with recurrent, low-risk chest pain and no occlusive CAD (0% stenosis) on prior angiography within 5 years, the recommendation is a referral for expedited outpatient testing as warranted rather than admission for inpatient evaluation (low level of evidence; for [conditional]).

6. **In patients who also have a negative coronary CT angiogram (CTA), what is their risk of subsequent ACS and the time to ACS?**

Recommendation: If patients have a coronary CTA within the past 2 years that showed no coronary stenosis, no further diagnostic testing is warranted other than a single high-sensitivity troponin measurement below a validated threshold to exclude ACS within that 2-year time frame (moderate level of evidence; for [conditional]).

7. **What is the effect of depression and anxiety screening tools on patients' health care use and return visits to the emergency department?**

Recommendation: Depression and anxiety screening tools should be used because they may affect health care use and returns to the emergency department (very low level of evidence; either [conditional]).

8. **What is the impact of anxiety and depression referrals on patients' health care use and emergency department return visits?**

Recommendation: Referrals should be made for anxiety or depression management because these conditions may affect health care use and returns to the emergency department (low level of evidence; either [conditional]).

Disclosures

The views expressed in this 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.

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Outpatient Treatment for Low-Risk Pulmonary Embolism

By Nikita R. Paripati, MD; and Michael E. Abboud, MD, MSEd
University of Pennsylvania in Philadelphia

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

Objective

On completion of this article, you should be able to:

- Explain when outpatient treatment for pulmonary embolism is appropriate.

Maughan BC, Frueh L, McDonagh MS, Casciere B, Kline JA. Outpatient treatment of low-risk pulmonary embolism in the era of direct oral anticoagulants: a systematic review. *Acad Emerg Med.* 2021 Feb;28(2):226-239.

KEY POINTS

- Risk assessment models, including the PESI, sPESI, and Hestia criteria, can be beneficial for identifying low-risk patients with newly diagnosed PE.
- Outpatient treatment for low-risk PE patients is associated with a low risk of mortality and adverse outcomes.
- Published data on the use of DOACs to treat acute PE is limited; however, the few controlled studies that exist show a very low rate of major adverse outcomes with this treatment.
- No statistically significant association exists between anticoagulant treatment class (DOAC, LMWH, vitamin K antagonists) and the rate of major adverse events.

The presentation of pulmonary embolism (PE) varies considerably, ranging from an asymptomatic, incidental finding to a massive clot that causes hemodynamic instability or immediate death. As such, the mortality associated with PE is highly variable and the data unclear. Historically, patients with a new PE diagnosis were admitted to the inpatient setting, mostly because treatment required intravenous or injectable anticoagulant medications (ie, heparin or low-molecular-weight heparin [LMWH]) and titration of vitamin K antagonists (ie, warfarin) to therapeutic levels. However, this treatment practice has changed since direct oral anticoagulants (DOACs) were introduced. Additionally, data suggest that most patients who present with an acute PE are hemodynamically stable and may meet the criteria for outpatient management. The mortality in this subgroup of patients is low, ranging from 0.5% to 2.5%. Several risk assessment models — the pulmonary embolism severity index (PESI), the simplified PESI (sPESI), and the Hestia criteria — are used to help identify short-term mortality in hemodynamically stable patients with acute PE.

Treatment for an acute PE includes anticoagulants such as LMWH, warfarin, and DOACs. In recent years, DOACs have surpassed vitamin K antagonists such as warfarin in effectiveness and are now the leading outpatient therapy for venous thromboembolism (VTE). Robust data do not exist for the outpatient management of PE, so the researchers in the discussed LLSA article sought to systematically analyze the existing studies. The studies analyzed included randomized controlled trials and prospective nonrandomized controlled trials of adults with acute, symptomatic PE who were discharged directly from the emergency department or within 48 hours of hospital admission. These studies were found by searching several databases that contained studies published between 1980 and 2019. Four major adverse outcomes — all-cause mortality, PE-related mortality, recurrent VTE, and major bleeding — and three minor adverse outcomes — clinically relevant nonmajor bleeding (CRNMB), return visit to the emergency department, and hospital readmission — were identified. A subgroup analysis was used to determine the association between anticoagulant class and the rate of the four major adverse events. Twelve studies that were determined to have low to moderate bias were included as high-quality studies in the analysis. Overall, 1,814 patients who were treated in the outpatient setting had less than a 1% risk of the four major adverse outcomes. The rate of CRNMB was 0.2% to 5.1%. The rate of return visits ranged from 14.9% to 16%; the rate of hospital readmissions at 30 days ranged from 1.5% to 3%.

The selection process of PE patients for outpatient management varies. Using an approach that integrates a risk stratification model (eg, PESI, sPESI, or Hestia criteria) can help identify PE patients at a lower mortality risk. Notably, however, these criteria alone are not definitive; the physician's clinical judgment and the patient's presentation should take priority.

Generally, patients with PE are at a lower risk of mortality if they have normal vital signs and no respiratory distress; oxygen requirement; or comorbidities, including malignancy, thrombocytopenia, heart disease, chronic lung disease, and kidney or liver failure. Once patients are identified as low risk, they can be evaluated for high-risk features by undergoing an echocardiogram and laboratory tests for troponin and BNP levels. If right ventricular dilation or hypokinesis or bowing of the interventricular septum is identified, hospital discharge should be promptly reconsidered. Physicians should also evaluate for concomitant lower-extremity deep vein thrombosis because a higher clot burden can cause clinical worsening and increase the risk of recurrence.

Patients should also be educated on their PE diagnosis and the risks and benefits of anticoagulation therapy. Stable patients with dementia, altered mental status, medical illiteracy or poor

medical literacy, poor social support, or a history of medication nonadherence should be more readily admitted. Physicians should also consider admitting patients who will have difficulty with follow-up, like those with no fixed residence or limited access to transportation.

Before an anticoagulant is selected for treatment, patients should be confirmed to have no contraindications to treatment. Contraindications include conditions that increase the risk of bleeding, like thrombocytopenia, active bleeding, recent major surgery, trauma, stroke, and malignancy (especially intracranial, spinal, or oropharyngeal). A patient's fall risk, especially for older adults, should be considered as well in determining bleeding risk. There is no definitive consensus on selecting an anticoagulant for outpatient therapy. The researchers who published this study found no statistically significant association between anticoagulant class and the rate of adverse events. Overall, outpatient management of PE has a low risk of major adverse events at 90 days post discharge and has many advantages when patients are appropriately selected, including an improved quality of life and reduced hospital costs.

Emerging and Re-emerging STIs

By Bryanna Carpenter, MD, MPH; and Laura Welsh, MD
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Reviewed by Andrew J. Eyre, MD, MS-HPEd

Objective

On completion of this article, you should be able to:

- List prevalent STIs and their recommended treatments.

Williamson DA, Chen MY. Emerging and reemerging sexually transmitted infections. *N Engl J Med*. 2020 May 21;382(21):2023-2032.

KEY POINTS

- Rates are rising for the STIs *N. meningitidis* and *M. genitalium*.
- A different strain of *C. trachomatis* has given rise to LGV and proctitis, which can be severe.
- Syphilis rates have significantly increased in MSM in the last decade, especially among those who receive pre-exposure prophylaxis against HIV. Infection rates have also increased generally, leading to an increase in congenital syphilis infections.
- Rising rates of drug-resistant *N. gonorrhoeae* infections are of increasing concern.

Since the 1990s when sexually transmitted infections (STIs) reached their lowest levels, STI rates have been increasing, especially in men who have sex with men (MSM). This increase has been especially prevalent in high-income countries. Outbreaks of nonclassic STIs have also become more common, including infections with *Shigella*, hepatitis A virus (HAV), and *Neisseria meningitidis*. Antibiotic resistance accompanies these increased outbreaks.

Sexually transmitted *Shigella* infections can range from self-limiting gastroenteritis to severe bloody dysentery. They are associated with HIV, are most prevalent in MSM, and are often seen in populations that engage in direct oral-anal contact, have condomless sex, attend sex parties, use dating apps, and use drugs to enhance sex (also known as *chemsex*). *Shigella* is often resistant to multiple antibiotics, with some areas reporting up to 93% resistance to azithromycin. Susceptibility testing is needed to determine the best course of treatment.

HAV is known to be transmitted by contaminated water. High-income countries have fewer incidents of HAV via contaminated water, which has led to large populations of nonimmune adults and, in turn, several outbreaks, particularly in MSM. Phenotyping these outbreaks confirmed that most outbreaks worldwide are tied to one of three strains of HAV, demonstrating the role international travel has had in its spread. Recent efforts to control these outbreaks have focused on education and vaccination, especially in those coinfected with HIV.

Sexually transmitted *N. meningitidis*, typically thought to colonize the nasopharynx, has been identified more recently in mucosal sites such as the cervix, urethra, and rectum. It has recently been linked to two conditions: urethritis in men who have sex with women and invasive meningococcal disease in MSM. These outbreaks have so far been seen in small clusters and have been successfully treated by a one-time dose of intramuscular ceftriaxone and a one-time oral dose of azithromycin.

Rising rates of *N. gonorrhoeae* infections are also accompanied by a rise in antibiotic resistance. In the United States alone, 550,000 drug-resistant infections are estimated to occur annually. Resistance to ceftriaxone and azithromycin is of increasing concern. Recent clinical trials have examined the efficacy of newer antibiotics such as solithromycin, zoliflodacin, and gepotidacin.

Recently, a different strain of the *Chlamydia trachomatis* infection has given rise to a less common infection that spreads through the lymphatics: lymphogranuloma venereum (LGV). LGV often causes inguinal lymphadenopathy. Rectal LGV infections can cause a painful proctitis that is associated with rectal discharge or, in severe cases, proctocolitis. In MSM, the infection has been linked to high-risk sexual practices. The recommended treatment length for LGV is 21 days with doxycycline (the usual course for the more common *C. trachomatis* infection is 7 days).

STIs with *Mycoplasma genitalium* have also increased recently. Screening is recommended only in symptomatic individuals and should include susceptibility testing. Resistance to azithromycin and moxifloxacin, both standard treatments, has increased in recent years.

Zika virus has been recognized as an STI since its emergence in 2008. Infections with Zika have shown maternal-fetal transmission; the fetal infection causes microcephaly and other brain anomalies. The WHO recommends that people infected with Zika use condoms or refrain from sex for at least 3 months for men and 2 months for women and that women of reproductive age avoid pregnancy for 2 months after a suspected or confirmed infection. Similarly, the Ebola virus can be sexually transmitted through the semen of male survivors. The WHO recommends that male survivors of Ebola be offered monthly semen testing and that those with positive tests abstain from sex or use condoms until testing is negative on two separate occasions.

Syphilis remains a global problem. Rates have significantly increased in MSM in the last decade, especially among those receiving pre-exposure prophylaxis against HIV. Syphilis rates have also increased generally, increasing the rate of congenital infections. Because of the potentially similar appearance of the anogenital ulcerations in primary syphilis to other infections, cotesting should be performed. To avoid congenital infections, testing should be completed during the first trimester of pregnancy.

New or re-emerging STIs represent an ongoing health problem. With increases in travel, online connections, and technology, controlling the spread of STIs will continue to be a challenge. Access to health care and testing is a priority for controlling these infections. A multi-pronged approach is also needed to control emerging STIs and should include testing, education, and the development of new vaccines and treatments, with cooperation between governments, the private sector, and health care communities.

Headache Presentations in the Emergency Department

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

Objectives

On completion of this article, you should be able to:

- Differentiate between primary and secondary headaches.
- List the differential diagnosis of secondary headaches.
- Explain how to diagnose the causes of secondary headaches.

Raam R, Tabatabai RR. Headache in the emergency department: avoiding misdiagnosis of dangerous secondary causes, an update. *Emerg Med Clin North Am*. 2021 Feb;39(1):67-85.

KEY POINTS

- The likelihood of a secondary headache being from a dangerous cause can be gathered from a thorough history as well as neurologic and ophthalmologic examinations.
- ACEP's clinical policy recommendations can be used to decide which patients with headaches can be diagnosed based on a bedside assessment and which need further testing.
- In patients with headaches that peak in intensity within 1 hour, SAH can be safely ruled out by using the Ottawa SAH rule or noncontrast CT (within 6 hours of symptom onset). If results are negative and clinical suspicion persists, CT angiography or lumbar puncture can then be used to rule out SAH.
- Nonopioid medications are the preferred treatment for acute primary headache. Specific secondary headache conditions require other interventions.

Headaches are a common reason that people present to the emergency department. Headaches can be classified as either primary or secondary. Primary headaches are more common, more benign, and include tension-type headaches, migraines, and cluster headaches. Secondary headaches are attributed to an underlying disorder that can be life-threatening: an aneurysm, a dissection, an infection or inflammation, or a space-occupying lesion; their presentations are variable and atypical. Fortunately, secondary headaches are relatively rare and often respond to the same analgesic agents used to treat more benign headaches. Emergency physicians can use diagnostic approaches and clinical policy recommendations to better differentiate a primary headache from the more dangerous secondary type.

Raam and Tabatabai describe an initial approach to the undifferentiated headache patient that includes assessing the patient's stability, addressing pain management, and ruling out secondary headache causes without overutilizing diagnostic testing. The authors also highlight the clinical features, diagnostic tests, interventions, and 14 conditions for emergency physicians to include in the differential diagnosis (*Table 1*).

Dangerous Causes of Secondary Headaches
AACG
Bacterial meningitis
CAD • ICAD • VAD
Cerebral infarction
CO poisoning
CVT
GCA
IIH
Occult trauma
Preeclampsia
Pituitary apoplexy
RCVS
SAH
Space-occupying lesion

TABLE 1. Differential diagnosis for secondary headaches

When gathering a patient's history, physicians should focus on the headache's characteristics (eg, time of onset, time-to-peak intensity, and quality), modifying factors, and associated symptoms. A sudden, severe headache with maximal intensity at onset (ie, a thunderclap headache) deserves special attention: It is a red flag symptom that indicates a subarachnoid hemorrhage (SAH). The classic thunderclap headache's peak time is usually within seconds to minutes but, according to the literature, can take up to 1 hour. Although a hallmark of SAH, thunderclap headaches are sometimes absent in SAH patients and can also be associated with other causes of secondary headaches (ie, cerebral venous thrombosis [CVT], cervical artery dissection [CAD], acute angle closure glaucoma [AACG], pituitary apoplexy, and reversible cerebral vasoconstriction syndrome [RCVS]). Dangerous headache etiologies can also be associated with headaches that are slow in onset (as with CVT) or recurrent (as with idiopathic intracranial hypertension [IIH]).

Headaches that have a positional quality, such as those that occur in supine position, or headaches that are worse in the morning or evening, may be associated with conditions that increase intracranial pressure, such as space-occupying lesions. Modifying factors can also

provide clues to a specific cause. For example, giant cell arteritis (GCA) and AACG are associated with increasing age, especially patients aged 50 years and older. IIH is most likely to occur in obese women in their 20s and 30s. Pituitary apoplexy and preeclampsia should be high on the differential diagnosis for pregnant patients with headaches, especially when they are past 20 weeks' gestation. Space-occupying lesions should be suspected in any patient with a history of malignancy.

Medication use, specifically anticoagulants or oral contraceptives; immune status; and events that preceded headache onset are other important considerations in determining the cause. Bacterial meningitis and CVT can occur after head and neck infections. SAH or CAD can occur after physical exertion, coughing, or any activity that acutely elevates arterial pressure. CAD can also be preceded by blunt cervical trauma or chiropractic manipulation. Carbon monoxide (CO) poisoning should be suspected in headache patients who were recently exposed to smoke inhalation, engine exhaust, or inadequate ventilation of heating sources, especially when multiple household members are ill.

Associated symptoms also provide clues to the cause. Fever can be seen in bacterial meningitis and GCA; neck pain or stiffness in bacterial meningitis, CAD, and SAH; visual disturbances in GCA, CVT, IIH, AACG, preeclampsia, and pituitary apoplexy; and focal neurologic deficits in SAH, CVT, space-occupying lesions, and CAD (anterior circulation symptoms are seen with internal carotid artery dissection [ICAD], and posterior circulation symptoms are seen with vertebral artery dissection [VAD]). Some secondary headache causes have unique features: GCA is associated with jaw claudication and temporal artery abnormalities (eg, tenderness and swelling).

The physical examination should include detailed neurologic and ophthalmologic examinations that focus on mentation levels, new neurologic signs, and ocular abnormalities. Completely normal examination results are more common in benign conditions but can also be seen in headaches with dangerous etiologies. The presence of an altered mental status or focal neurologic deficits warrants further workup for secondary headache causes. Nuchal rigidity, jolt accentuation, and positive Kernig and Brudzinski signs suggest bacterial meningitis, but their absence does not rule out the condition. Ocular abnormalities include monocular vision loss in GCA and intracranial atherosclerotic disease, transient or persistent visual acuity changes or vision loss in IIH, papilledema in IIH and CVT, and associated cranial nerve palsies in CVT and pituitary apoplexy. In cases of AACG, patients can have isolated monocular pain, conjunctival injection, a mid-fixed dilated pupil, decreased visual acuity, and an intraocular pressure (IOP) greater than 21 mm Hg (but typically at least 30 mm Hg), which establishes the diagnosis.

After the history and physical examination, patients with acute headaches should be risk stratified. According to the American College of Emergency Physicians' (ACEP's) 2019 clinical policy, the Ottawa SAH rule is a highly sensitive decision rule that should be used to rule out SAH in headache patients with normal neurologic examinations and peak headache severity within 1 hour of pain onset (level B recommendation).

Serum laboratory workup has limited diagnostic utility in most cases of secondary headaches but can be useful for specific conditions. An elevated erythrocyte sedimentation rate ≥50 mm/hr is part of the diagnostic criteria for GCA; elevated C-reactive protein levels and platelet counts can also increase GCA's likelihood but may also be normal in positive cases. D-dimer testing has been studied in patients with CVT and has been found to have variable diagnostic accuracy that limits its usefulness. A diagnosis of preeclampsia can be established in pregnant patients with headaches through the presence of proteinuria, thrombocytopenia, renal insufficiency, or impaired liver function. Findings of hypoglycemia and hyponatremia can be signs of pituitary apoplexy. A diagnosis of CO poisoning can be established through co-oximetry that reveals an elevated CO level.

A 2008 ACEP clinical policy addresses which headache patients require neuroimaging. An emergent noncontrast head CT is required for headache patients with new sudden-onset severe headaches; with new abnormal findings on neurologic examination; or with HIV and a new type of headache (level B recommendations). An urgent noncontrast head CT, which can be arranged before discharge home, is recommended for headache patients older than 50 years who have a new headache but normal neurologic examination findings (level C recommendation).

ACEP's 2019 clinical policy recommends a normal noncontrast head CT (minimum third-generation scanner) within 6 hours of symptom onset in headache patients with normal neurologic examinations to rule out nontraumatic SAH. Importantly, however, a normal noncontrast head CT does not evaluate for most of the dangerous headache causes. For example, AACG is diagnosed based on an IOP assessment, and GCA and preeclampsia diagnoses do not require neuroimaging based on their specific diagnostic criteria from other specialty organizations. Other diagnoses require more advanced neuroimaging. CAD requires CT or MR angiography of the head and neck. CVT and IIH (to exclude alternative causes with IIH) require CT or MR venography of the head. Pituitary apoplexy and space-occupying lesions are diagnosed by MRI. Lastly, bacterial meningitis, IIH, and SAH require lumbar puncture to establish the diagnosis. CT angiography has an increasing role in the diagnostic workup for SAH, which is reflected in ACEP's clinical policy recommendation to perform lumbar puncture or CT angiography to safely rule out SAH in adult patients who are still at risk of SAH after a negative noncontrast head CT (level C recommendation).

Therapy should target treating the pain and the specific identified cause. ACEP recommends nonopioid medications to treat acute primary headaches (level A recommendation); it also recommends that physicians refrain from using the pain response to therapy as the sole diagnostic indicator of an acute headache's underlying etiology (level C recommendation). Raam and Tabatabai go into more detail on the therapies and interventions for specific dangerous causes of secondary headaches.

Early Anticoagulant Reversal After Trauma

By Kelechi Umoga, MD, MBA; and
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Objective

On completion of this article, you should be able to:

- Discuss the management of trauma patients who use anticoagulant medication.

Peck KA, Ley EJ, Brown CV, et al. Early anticoagulant reversal after trauma: a Western Trauma Association critical decisions algorithm. *J Trauma Acute Care Surg*. 2021 Feb 1;90(2):331-336.

KEY POINTS

- A combination of physical examination, imaging, and laboratory testing should be used to identify trauma patients with severe bleeding.
- Management of trauma patients on anticoagulants should include consideration of medication removal or reversal as well as surgical or procedural intervention.
- Each class of anticoagulants has unique mechanisms, reversal agents, and laboratory values that can be used for medication monitoring.

Introduction

Trauma evaluation, management, and outcomes in adult patients are often complicated by anticoagulation use, which primarily consists of vitamin K antagonists (VKAs), direct oral anticoagulation medications, and therapeutic low-molecular-weight heparins (LMWHs). This article summarizes the 2020 Western Trauma Association algorithm and guidelines for trauma patients who are — or may be — using anticoagulant medications.

Assess Degree of Injury and Bleeding

The extent of traumatic injury and bleeding should be rapidly assessed using the standard Advanced Trauma Life Support algorithm. Depending on patient-specific circumstances, this assessment often includes physical examination, imaging, and laboratory testing. Together, these tools are used to identify patients who have or may have severe bleeding, which the article defines as the "need for urgent/emergent operation or intervention, need for immediate transfusion, presence of hemorrhagic shock or hemorrhage into a critical organ or space including major intracranial, ocular, spine, cavitary, or extremity injuries."

Management of Anticoagulated Patients Without Severe Injury or Bleeding

These patients should be managed with simple hemostatic measures including direct pressure, pressure dressings, and suture control, when relevant, and should be monitored with serial physical examinations, laboratory tests, and imaging, as indicated.

Management of Anticoagulated Patients With Severe Injury or Bleeding

Management of severe bleeding in anticoagulated patients must involve removal or reversal of the anticoagulant in addition to the standard management of hemorrhagic shock (ie, appropriate surgical or procedural interventions and emergent resuscitation and transfusions). Care should be taken to avoid trauma-induced coagulopathy, and physicians should monitor for and address any hypothermia, thrombocytopenia, or acidosis.

Management of Specific Anticoagulant Medications

VKAs Such as Warfarin

VKAs disrupt the hepatic synthesis of factors II, VII, IX and X as well as proteins C and S, with the degree of anticoagulation measured by PT and INR. Anticoagulation by these agents is corrected through replacement of the deficient factors, typically with prothrombin complex concentrate (PCC) — four-factor PCC is the preferred agent. Other PCC options include three-factor PCC (factor IX complex) and activated PCC (anti-inhibitor coagulant complex). Fresh frozen plasma is a less expensive alternative, but it requires more time (for crossmatching and thawing) and large volumes for INR correction, which can lead to volume overload.

Direct Thrombin Inhibitors Such as Dabigatran

Dabigatran competitively binds the active site of thrombin, preventing thrombin-mediated conversion of fibrinogen to fibrin. Since dabigatran is heavily cleared by the kidneys, it can potentially be removed by hemodialysis. The only FDA-approved reversal agent for dabigatran is idarucizumab, a monoclonal antibody that binds dabigatran. It can be given as two successive doses of 2.5 g IV each for a total of 5 g. Although the most accurate tests to track dabigatran's effect — dilute thrombin time and ecarin clotting time — are not readily available, thrombin time and PTT can be used with some limitations. Thrombin time is extremely sensitive to dabigatran, and so a normal thrombin time reliably excludes clinically relevant dabigatran levels. By contrast, a prolonged PTT suggests the presence of dabigatran, but a normal value does not exclude it.

Factor Xa Inhibitors Such as Apixaban and Rivaroxaban

Factor Xa inhibitors directly inhibit factor Xa, resulting in decreased conversion of prothrombin to thrombin. The anti-Xa level is useful in determining the amount of clinically relevant anti-Xa drug present and is most reliable when calibrated to the specific drug. The only FDA-approved reversal agent for factor Xa inhibitors is andexanet alfa, a recombinant inactive protein with a structure similar to endogenous factor Xa that competitively binds and sequesters factor Xa inhibitors. It is administered in two different dosing levels depending on the specific factor Xa inhibitor taken, the dose taken, and the timing of the last dose. The lower dose is a bolus of 400 mg IV given at 30 mg/min followed by an infusion of 480 mg given at 4 mg/min for up to 120 minutes. The higher dose is a bolus of 800 mg given at 30 mg/min followed by an infusion of 960 mg given at 8 mg/min for up to 120 minutes. When the dose and timing of a factor Xa inhibitor are unknown, the higher-dose regimen is recommended. Four-factor PCC can also be used for management of severe bleeding in the setting of factor Xa–inhibitor use, although mortality with this option remains high.

LMWHs Such as Enoxaparin

LMWH (enoxaparin for the purposes of this guideline) binds and activates antithrombin, which inhibits factor Xa and, to a lesser extent, factor IIa. Like with factor Xa inhibitors, the anti-Xa level is useful for monitoring the amount of clinically relevant anti-Xa drug present. The recommended dose depends on the amount and timing of the enoxaparin administration. Protamine sulfate is recommended at 1 mg for every 1 mg of enoxaparin given within the prior 8 hours and at 0.5 mg for every 1 mg of enoxaparin given more than 8 hours ago. The intravenous doses should be given slowly, and the maximum recommended single dose is 50 mg in any 10-minute interval to avoid hypotension and anaphylaxis-like reactions.

Assessment for Ongoing Bleeding

Ongoing bleeding should be reassessed with repeated physical examinations, serial laboratory tests, and imaging, if indicated. If bleeding persists despite attempts with reversal agents and appropriate surgical intervention, reversal agents can be redosed or alternative agents considered.

Areas of Controversy and Existing Knowledge or Research Gaps

Additional research is needed to further refine the algorithm and study anticoagulation in acutely injured patients. The authors specifically note areas of controversy, such as the thrombotic risks associated with anticoagulation reversal, the timing of anticoagulation reinitiation, and the role of advanced testing such as thromboelastography and rotational thromboelastometry in anticoagulated patients.

The LLSA Literature Review

Shoulder Dislocations

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

Objectives

On completion of this article, you should be able to:

- Explain how appropriate shoulder reduction techniques are selected.
- Name the most successful shoulder reduction techniques for each type of shoulder dislocation.

Gottlieb M. Shoulder dislocations in the emergency department: a comprehensive review of reduction techniques. *J Emerg Med*. 2020 Apr;58(4):647-666.

KEY POINTS

- Shoulder dislocations are a common presentation in the emergency department. Physicians should be familiar with the different reduction techniques for this condition.
- There are multiple shoulder reduction techniques. Each has advantages, disadvantages, and varying success rates.
- The reduction technique chosen will depend on the type of shoulder dislocation, the patient, the physician, and factors specific to the health care system.
- Slow and guided movements should be pursued over rapid or forceful movements. If the first attempt fails, physicians should consider an alternative maneuver.

Joint dislocations are common orthopedic emergencies; shoulder dislocations, in particular, are among the most often seen presentations. Shoulder dislocations are classified as anterior, posterior, or inferior based on the position of the humeral head relative to the glenoid fossa. There are multiple reduction techniques available to achieve anatomic alignment, and the choice depends on the type of shoulder dislocation being reduced. Gottlieb provides a comprehensive review of the 26 major shoulder reduction techniques, describing each technique and its modifications in detail with pictorial representations; the review also highlights the success rates, advantages, and disadvantages of each technique.

Factors related to the patient, physician, and health system also influence which shoulder reduction technique is chosen. Patient factors to consider include body habitus, pain tolerance, comorbidities, and sedation risk factors. Other factors related to the patient include the body positions they can tolerate during the reduction; whether this is a first-time or recurrent dislocation; and where the reduction will be performed (eg, in the field or a hallway bed of the emergency department). Physician factors include the physician's experience with reductions and how many people are available to assist with the reduction. Health system factors include the emergency department's census, available resources, and time constraints.

Two variables associated with higher rates of failed reduction are (1) delays in emergency department presentation and reduction attempts and (2) repeated reduction attempts. Repeated reduction attempts also increase the risk of neurovascular injuries. Thus, important aspects to emergency care include performing shoulder reductions as soon as possible and striving for a successful reduction on the first attempt. Emergency physicians must also know multiple shoulder reduction techniques in case the first attempt is unsuccessful; however, data that compare specific techniques are limited.

Based on Gottlieb's review, *Table 1* summarizes the major shoulder reduction techniques and their reported success rates. The table also references each technique's targeted anatomic location, the positioning the technique requires, and the number of operators needed to perform each technique. For example, a patient with an anterior shoulder dislocation is able to sit upright but is unable to lie in bed. Only one physician is available to perform the shoulder reduction. An appropriate technique for this scenario is the Bokor-Billman technique, which has been reported to have no complications and a 100% success rate. In another example, a patient with an anterior shoulder dislocation is able to lie prone, and one physician is available but has strict time constraints. According to the table, the Stimson maneuver would be an appropriate reduction technique.

Some techniques — the Cunningham, Davos/Aronen, FARES, and GONAIS — have the advantage of requiring no sedation in selected patients. Techniques such as the Davos/Aronen, GONAIS, and the modified Milch can be taught as self-reduction techniques, which is especially useful for patients with recurrent shoulder dislocations or patients who require reduction in places outside of the emergency department. Scapular manipulation has several modifications to its original prone technique, making it flexible in terms of patient positions and the number of operators needed.

Gottlieb cautions that several reduction techniques have been associated with higher risks of injury. For example, the Hippocratic method for reduction is no longer recommended because the axillary pressure exerted during this technique increases the risks of a humerus fracture and neurovascular injury. The modified Kocher technique that uses axial humeral traction, the Nicola method, and the traction-countertraction technique have also been associated with injuries. Although expertise in all shoulder reduction techniques is not realistic, emergency physicians should know how to perform the most successful shoulder reductions for each type of shoulder dislocation and should avoid techniques with the highest risk of complications. Additionally, they should know how to select an appropriate reduction technique based on a patient's presentation and should tailor their approach to patient, physician, and health system limiting factors.

Anatomic Location (% Dislocations)	Patient Position or Position of Comfort	Operators Required	Technique	Reported Success Rates
Anterior dislocation (96.4%)	Sitting upright	One operator	Bokor-Billmann technique	100%
			Cunningham technique	100%
			Chair method	96.6%-100%
			Nicola method	88.6%-100%
			Davos method/ Aronen technique	60%-86%
			Modified seated Spaso method	79.4%, Matsumoto et al modification
		Two operators	Legg reduction maneuver	Data lacking
	Supine	One operator	Elbow technique	100%
			Janecki forward elevation maneuver	92.6%-100%
			FARES method	85.7%-100%
			Milch technique	69.2%-100%
			Kocher technique	68%-100%
			Spaso method	66.7%-100%
			Zahiri technique	84.6%
			Hippocratic method	72.5%-100%, no longer recommended
		Two operators	Traction-countertraction method	91.5%-100%
		Three operators	Double traction method	90%-100%
	Prone	One operator	Modified prone Milch techniques	100%, Lacey and Crawford modification 90%, McNair modification
			Scapular manipulation	78.4%-100%
		No operator	Stimson technique	28% first attempt, 91.3% overall
	Lateral decubitus (affected side facing ceiling)	One operator	Modified Nicola method	100%, Bhan and Mehara modification
		Two operators	Pendel method (also called Eskimo technique)	77.3%
	Standing	One operator	GONAIS method	Data lacking
	Any position	One operator	Axial traction with acromial fixation	100%
			External rotation maneuver (ERM)	78%-100%
		One or two operators	Modified scapular manipulation techniques	Data lacking for modified techniques
Posterior dislocation (3%)	Supine or sitting upright	One operator	DePalma "lever" method	Data lacking
			Caudal traction	Data lacking
	Sitting upright	Two operators	Wilson technique	100%, data limited
Inferior dislocation (0.6%)	Supine	One operator	Two-step maneuver	Data lacking
		Two operators	Traction-countertraction method	Data lacking

TABLE 1. Shoulder reduction techniques based on anatomic location, patient position, and number of operators required