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Case Scenario: Local Anesthetic Systemic Toxicity after Combined Psoas Compartment–Sciatic Nerve Block

Analysis of Decision Factors and Diagnostic Delay

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HIP fractures are common in elderly individuals, accounting for the majority of fracture-related medical care costs and mortality in patients over the age of 50 yr.[1] In the United States, the age-standardized annual incidence of hip fractures is estimated to be 150 to 250 per 100,000 per year, with higher rates observed in women.[2] Affected patients often present with multiple comorbidities, posing significant challenges to the anesthesiologist.

Peripheral nerve blocks have gained popularity for anesthetic management of procedures involving the lower extremity, both as a complement to general anesthesia and as an alternative to neuraxial anesthesia. Combined psoas compartment–sciatic nerve block (CPCSNB) is a technique used to provide adequate surgical anesthesia to the ipsilateral lower extremity during operative repair of hip fracture.[3,4] CPCSNB is theoretically associated with less of the sympathetic blockade and vasodilatation characteristic of neuraxial anesthesia and has successfully been performed in patients with severe aortic stenosis.[5]

Despite these advantages, CPCSNB is not without risk. The psoas compartment is formed by the psoas muscle, the anterior fascia of the psoas muscle, and the quadratus lumborum posteriorly; it contains the lumbar plexus (ventral rami of L1–4) and is the desired distribution of local anesthetic spread.[6] Epidural spread has been reported after psoas compartment blockade, with an incidence of up to 27% in adults and 92% in children depending on the approach used.[7–10] Auroy *et al.*,[11] in a major survey of regional anesthesia complications in France, reported one case of cardiac arrest, one case of seizure, and two cases of respiratory failure associated with cephalad diffusion of local anesthetic in the epidural or intrathecal space during psoas compartment blockade. The possibility of intravascular injection or systemic absorption from the epidural venous plexus places the patients at risk for local anesthetic systemic toxicity (LAST).

We report a case of LAST after CPCSNB in an elderly patient presenting for operative repair of a hip fracture. The time to onset of LAST signs and symptoms was prolonged, and patient-specific factors confounded the diagnosis. Delayed diagnosis and treatment may have contributed to the patient's eventual adverse outcome. We discuss the cognitive factors contributing to a delay in LAST diagnosis, with an emphasis on broadly applicable principles of clinical decision making and diagnostic error. A brief review of LAST clinical presentation and treatment is also presented.

Case Scenario

An 88-yr-old woman (weight 45 kg and American Society of Anesthesiologists physical status IV) was scheduled for an urgent surgical treatment of a right hip fracture after a mechanical fall. Medical history included hypertension, coronary artery disease, peripheral vascular disease, cerebrovascular disease, hypothyroidism, renal artery stenosis, and subdural hematoma in the past. The patient reported presyncope with systolic blood pressures less than 150 mmHg; her baseline systolic blood pressures were between 160 and 180 mmHg as documented by her cardiologist. The patient walked two thirds of a mile slowly each day without difficulty. Surgical history was significant for evacuation of subdural hematoma (4 yr before), two-vessel coronary artery bypass grafting (10 yr before), bilateral renal artery bypass grafting (10 yr before), cardiac stent placement to the left anterior descending coronary artery (12 yr before), and bilateral carotid endarterectomies (15 yr before) without any known anesthesia complications. Medications included metoprolol, amlodipine, losartan,

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hydrochlorothiazide, baby aspirin, and levothyroxine. Baseline electrocardiogram showed sinus bradycardia at 51 beats/min with occasional premature atrial complexes (fig. 1). A transthoracic echocardiogram performed 5 months before revealed a left ventricular ejection fraction of 55 to 60%, moderate aortic stenosis (valve area = 1.1 cm sq), and moderate to severe mitral regurgitation without evidence of pulmonary hypertension. A carotid Doppler study obtained 1 month before did not yield evidence of obstructive disease.

To avoid hemodynamic fluctuations secondary to neuraxial or general anesthesia, surgical anesthesia was planned *via* right-sided CPCSNB. A psoas compartment block was selected to ensure that all components of the lumbar plexus were anesthetized, reducing the likelihood of a failed block and subsequently the need for general anesthesia. Effective neural blockade of the hip joint must include the femoral, sciatic, and superior gluteal nerves.[12] Therefore, a sciatic block was also included. Local anesthetic doses were selected to minimize the chance of inadequate surgical anesthesia and the need to convert to general anesthesia.

The patient consented and was brought to the operating room. A timeline of subsequent events is presented in figure 2. Routine perioperative monitors were placed and continuously monitored as recommended by the guidelines of the American Society of Anesthesiologists. With the patient in the supine position, a right radial arterial line was inserted. Initial vital signs included arterial blood pressure 140/91 and heart rate 78 beats/min. The patient was placed in the left lateral decubitus position for block placement. A posterior psoas compartment block, as previously described by Chayen *et al.*,[13] was performed with a 20-gauge 6-inch insulated Stimuplex® needle (B. Braun Medical, Melsungen, Germany) and a nerve stimulator. The needle was inserted along the transverse process of L4 and then directed cephalad into the lumbar plexus sheath, approximately 5 to 6 cm deep from skin (fig. 3). Patellar ascension by quadriceps femoris

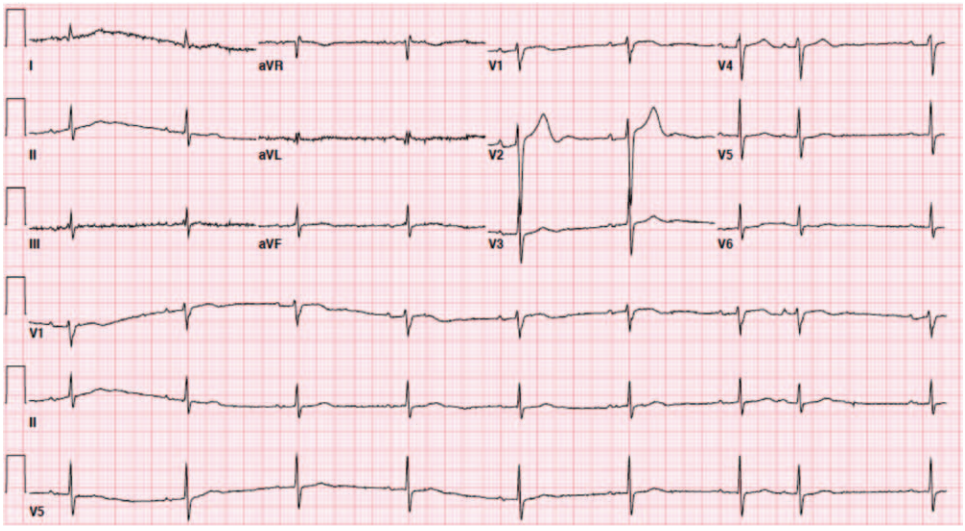

Fig. 1. Baseline electrocardiogram. An electrocardiogram obtained on the morning of surgery revealed sinus bradycardia at 51 beats/min with occasional premature atrial complexes.

Fig. 2. Timeline of operating room events. Approximately 15 min after completion of a right-sided combined psoas compartment–sciatic nerve block, the patient became unresponsive and experienced a grand mal seizure. Cardiac arrhythmias commenced 20 min after seizure onset. The patient was declared dead 1.5 h after the onset of neurologic symptoms despite initiation of advanced cardiac life support and lipid emulsion therapy. IV = intravenous.

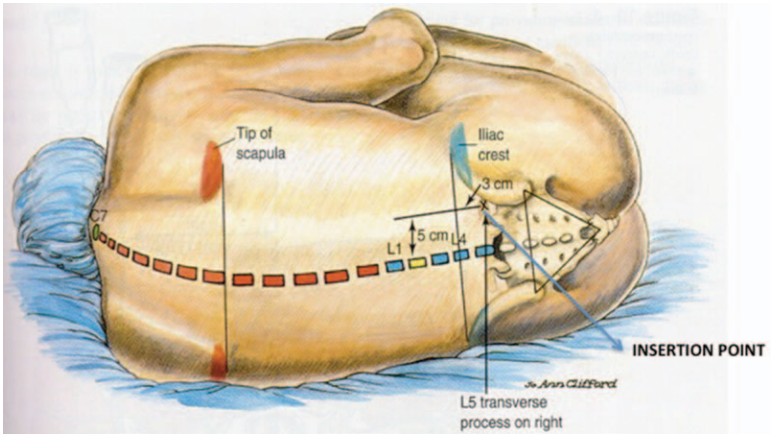

Fig. 3. Psoas block technique. The landmarks and technique for performing the posterior psoas compartment block (also known as the "lumbar paravertebral block") are depicted in this image. The psoas compartment is formed by the psoas muscle, the anterior fascia of the psoas muscle, and the quadratus lumborum posteriorly; it contains the lumbar plexus (ventral rami of L1–4) and is the desired distribution of local anesthetic spread. This block is indicated for unilateral lower limb surgery. Reproduced, with permission, from Brown DL: Atlas of Regional Anesthesia. 1999, pp 89. Copyright Saunders.[71]

muscle twitch was elicited at a current greater than 0.5 mA. After a negative aspiration test, 10 ml of 0.25% bupivacaine with 1:200,000 epinephrine and 15 ml of 1.5% mepivacaine plain were incrementally injected through the needle with negative aspiration for blood and cerebrospinal fluid every 3 ml. Mepivacaine was selected for faster onset of surgical blockade, with the addition of bupivacaine for postoperative analgesia, given its longer duration of action.

No paresthesias were elicited, and vital signs were unchanged. Immediately after, a right sciatic nerve block *via* the paragluteal approach was then performed under ultrasound guidance and nerve stimulation using a 20-gauge 6-inch Stimuplex® needle. Foot eversion was elicited at a current of 0.5 mA or more. Fifteen milliliter of 1.5% mepivacaine plain was injected in similar incremental doses with negative aspiration throughout. Fentanyl 25 μg IV was administered during block placement for pain management. Total time for block placement was 20 min. Vital signs remained unchanged, and the patient was without complaints. She was then placed supine for the operation.

Fifteen minutes after the conclusion of the block placement, during surgical positioning, the patient became unresponsive to verbal or tactile stimuli and was noted to have a fixed gaze. Vital signs remained unchanged from baseline, and no complaints or clinical signs preceded the loss of responsiveness. Given the patient's extensive history of vascular disease, initial concern was for cerebrovascular accident. The attending surgeon was called to the room to discuss the patient's evolving clinical status. Approximately 5 min later, while discussing the change in neurologic status with the attending surgeon, the patient displayed bilateral convulsions consistent with a grand mal seizure. Midazolam 2 mg IV was administered, seizure activity ceased, and the patient was immediately intubated. Arterial blood pressure was 135/75 and heart rate was 82 beats/min, essentially still unchanged. The surgical procedure was cancelled and the patient was to be transferred to the intensive care unit for further evaluation, neurology consultation, and monitoring. However, the intensive care unit was unable to accept the patient immediately, and the patient remained in the operating room awaiting intensive care unit bed availability. Twenty minutes later, approximately 40 min after the completion of block placement, the patient developed severe bradycardia with a heart rate of 30 beats/min and varying degrees of heart block. Electrocardiogram data were unavailable to be printed due to an operating room monitor printer malfunction. Atropine 0.4 mg IV was administered, with an increase in the heart rate to 50 beats/min. However, within 1 min, the patient deteriorated into pulseless electrical activity and the advanced cardiac life support (ACLS) algorithm was initiated. Epinephrine 1 mg IV was given as chest compressions were initiated. Multiple rounds of epinephrine, atropine, and a dose of vasopressin were administered according to the ACLS pulseless electrical activity protocol. The diagnosis was re-evaluated, and given the now-apparent combination of neurologic and cardiovascular symptoms, LAST was suspected and a lipid emulsion 20% bolus was initiated at 1.5 ml/kg IV followed by an infusion at 0.25 $ml.kg^{-1}.min^{-1}$ as per American Society of Regional Anesthesia (ASRA) guidelines.[14] Two repeat boluses of lipid emulsion were given and the infusion rate was doubled due to persistent cardiovascular collapse. Cardiopulmonary bypass was not immediately available. The patient was unable to be resuscitated after 1 h of ACLS and lipid emulsion administration. She was declared dead 1.5 h after the onset of her grand mal seizure.

Discussion

Cognitive Factors in Clinical Decision Making

The general preference to judge decisions and actions on the eventual outcome (which may have been grave in this patient whether or not lipid rescue was instituted at the first

sign of altered mental status) is called "outcome bias."[15] In the biomedical literature, publication bias (also known as positive-outcomes bias) occurs when authors are less likely to submit and editors are less likely to accept articles that do not describe a positive outcome or effect.[16–18] This form of bias has been described in anesthesia journals with high clinical trial impact that are used by many clinicians to guide future medical decision and policy making.[19] The mental tendency to avoid discussion of cases with negative outcomes should not prevent us from learning important lessons about LAST specifically and medical decision making in general. Confronting diagnostic errors, openly discussing adverse events, and formulating recommendations for quality improvement are all critical to limiting future errors and improving overall patient safety.

Role of Cognitive Factors in Delayed Diagnosis. Diagnostic errors reflect the complex interplay of clinical, systems, and cognitive factors, with cognitive error playing a role in up to three quarters of diagnostic errors.[20] Importantly, cognitive error refers to decision-making processes, and excludes errors made due to lack of knowledge or novel clinical situations.[21] Although the exact incidence of diagnostic error is not known in anesthesiology, experts estimate the rate to be approximately 15% in general, and higher in circumstances of atypical or nonspecific presentations, as well as when there are distracting comorbid conditions.[20,22,23] Decision making is even more vulnerable to error during acute clinical decompensation because of the time-pressured, high-stakes evolution of the complication. Uncertainty and stress such as in this case are known to increase the likelihood of medical error.[24]

Postevent debriefing with the anesthesiologists involved in this case revealed several important influencers of decision making (anchoring and representativeness) that deserve consideration, and have broad applicability in many anesthesiology situations. First, the amount of time that passed between block placement and the onset of symptoms (>15 min) did not fit the classic presentation of LAST. In the medical literature, the mean time to LAST symptom onset is less than 1 min and 75% of cases present within the first 5 min after injection.[25] Classic prodromal signs were not present, and hemodynamic changes occurred significantly after the change in mental status. In addition, the patient's cardio- and neurovascular risk factors (*i.e.*, aortic stenosis, presyncope, stroke history) were of foremost concern in the minds of the anesthesiologists during preoperative planning and patient counseling. As such, other plausible causes for isolated altered mental status came more readily to mind than the seemingly less-likely possibility of delayed absorption from the epidural venous plexus. On the onset of the patient's symptoms, these cardio- and neurovascular concerns led to a well-described phenomenon in clinical decision making known as anchoring. Anchoring is defined as "the tendency to fixate on specific features of a presentation too early in the diagnostic process, and to base the likelihood of a particular event on information available at the outset."[15] In this case, anchoring on neurovascular possibilities may have contributed to a delay in the diagnosis. In addition to anchoring, the case was lacking in a very important decision-making influence known as the representativeness heuristic described by Nobel Prize winners Tversky and Kahneman,[26] world experts in the psychology of judgment and decision making. Representativeness heuristic describes the importance of the degree of similarity between a current set of data and the "standard" data—in this case, classic LAST presentation, including prodromal and cardiovascular symptoms. This lack of representativeness with the classic presentation of LAST in terms of both symptoms and timeline may have also contributed to a delay in diagnosis.

The tendency to perceive this case and ultimate diagnosis as being more predictable than it was as the emergency was unfolding is called hindsight bias. Mistakes have been described as a cognitive experience of "now" and "then": the "now" of medical error has the benefit of hindsight, whereas the "then" of decisions and actions are influenced by circumstances of incomplete or uncertain knowledge, as the future is evolving into existence.[27] As the true diagnosis reveals itself over time, a seemingly correct action "back then" is becoming an incorrect action "now."[28] This phenomenon is important to consider when evaluating clinical cases for educational value (*e.g.*, morbidity and mortality conference) and professional or medico-legal implications (*e.g.*, root-cause analysis or litigation).

Although the influence of cognitive error on anesthesiology practice has not been definitely quantified, it may be substantial. The majority of diagnostic errors are at least partially attributable to cognitive mistakes in terms of decision-making or clinical reasoning strategies.[29] Strategies for counterbalancing the influence of bias, heuristic, and the other numerous subconscious influencers of decision behavior have been proposed.[21,22,30,31] Although definitive evidence for the effectiveness of these strategies is still scarce,[32] some studies have demonstrated that metacognitive "debiasing" strategies improve diagnostic accuracy,[33–35] and that errors associated with intuitive judgments can be repaired by deliberate use of analytical strategies.[36] There has been an increased interest over the last decade in further understanding this psychology of decision making, and the role and effectiveness of strategies to enhance diagnostic accuracy and improve patient safety.[37]

Cognitive Aids for LAST Management. A simulation-based study by Neal *et al.*[38] compared the effectiveness of LAST management by residents randomized to a checklist group (checklist adapted from ASRA guidelines) or a no-checklist group. The group with the checklist outperformed the control group on both medical management skills (7 prevention and diagnostic items and 21 treatment items) as well as performance of important nontechnical skills (task management, team working, situation awareness, and decision making). The authors of this study propose that simulation is the ideal setting to learn and practice LAST management, as it is fortunately rare, and

many anesthesiologists may otherwise never be exposed to a life-threatening LAST case in their careers.

As the study by Neal *et al.* demonstrated, use of a checklist improved performance. Other cognitive aids exist, and there are no data to suggest the superiority of one over another as of yet. Perhaps, more important than which aid is used is the convenience and accessibility of such an aid and how it is used.[39,40] We recommend a copy of the ASRA guidelines and/or another cognitive aid for management of LAST be readily available in every location where regional anesthesia is performed, as well as secured to an emergency box containing lipid emulsion. The recommendation to have a set of emergency procedures, checklists, or an emergency manual present in the care area (*i.e.*, operating room, procedure suite, and many more) or attached to a specialized treatment kit (*i.e.*, malignant hyperthermia kit, LAST kit) is becoming increasingly adopted, with emphasis on effective implementation.*

Nontechnical Skills and Crisis Resource Management. Not yet universal, but becoming more widely appreciated and adopted, are the core "nontechnical skills" of effective emergency management, also called *crisis resource management*.[41–43] These skills include early mobilization of resources, effective distribution of workload, communication, leadership and followership, and decision making. Some important tenants of decision making include allocation of attention that minimizes distractions, prevents task saturation, and recruits the participation of helpers. Another important concept is the anticipation of future patient states, and early implementation of "back-up" plans. Sharing these anticipated states and plans is an important component of team *situation awareness (e.g., sharing "what is happening now" and "what is likely to happen next")*.[44] A specific benefit to shared situation awareness is the opportunity for other team members to offer input, whether on diagnosis and treatment, or on potential environmental vulnerabilities (*i.e.*, limited resources on off-hours or in remote locations, and many more). Increased training and practice *via* simulation is a nationwide trend.

In 2008, Smith *et al.*[45] presented a case of successful resuscitation of bupivacaine-induced cardiac arrest by anesthesia providers who had recently completed simulation training involving a nearly identical scenario. In the debriefing, the care providers indicated that their rapid recognition of the diagnosis and prompt initiation of lipid emulsion therapy were strongly influence by the crisis resource management skills learned in simulation. New data suggest that emergencies may be better managed if one team member is delegated the task of "reader" (*i.e.*, one person consults the cognitive aid and reads the steps to the code leader, ensuring no steps are missed).[46] Studies in both simulated and real operating room settings demonstrated a decrease in missed critical management elements when a checklist was available and consulted.[47–49] Research going forward should focus on identifying best formats and implementation strategies of cognitive aids for use during emergencies.

Review of LAST

Having addressed influences on decision-making behavior and emergency management principles, we will now briefly review the incidence, presentation, and treatment of LAST.

Incidence. The estimate of clinically significant LAST after peripheral nerve blocks ranges from 7.5 to 20 occurrences per 10,000 blocks performed.[50] Unfortunately, the true incidence of LAST is difficult to determine as occurrences of transient neurologic symptoms or cardiovascular effects may be underrepresented in published data. Although Di Gregorio *et al.*,[25] in a review of 93 published cases of LAST from 1979 to 2009, found only one report of death from LAST, an analysis of data from 1980 to 2000 in the American Society of Anesthesiologists Closed Claims Database found LAST to be associated with 7 of 19 claims for death or brain damage after eye and peripheral nerve blocks.[51] As closed claims do not represent all events, but only those resulting in litigation, this suggests that adverse outcomes are underreported in the literature.

Risk of LAST after Psoas Compartment Blockade. In 2002, Macaire *et al.*[52] performed a large retrospective study of 4,319 psoas compartment blocks performed at 42 centers in the United States, France, Belgium, and Switzerland. The incidence of local anesthetic spread into the epidural space ranged from 1 to 10%. There were 25 inadvertent spinal anesthetics (11 cases of total spinal anesthesia and 1 death), 13 intravascular injections (3 cases of seizure and 1 cardiac arrest), 4 cases of delayed toxicity, and 13 cases of inappropriate catheter paths.

Psoas compartment blocks have greater potential for local anesthetic systemic absorption when compared with other peripheral nerve blocks due to the highly vascular nature of the muscle bed in which the lumbar plexus is embedded. The psoas compartment block is also considered a paravertebral blockade of the lumbar region as the paravertebral space lies in continuity with the epidural space. Injection of local anesthetic with high injection pressures (>20 psi) may result in unintentional bilateral blockade and an increased risk of neuraxial blockade.[53] Administration of larger local anesthetic volumes increases the likelihood of epidural spread.[54] Both bilateral psoas compartment and neuraxial blockade may result in hemodynamic instability from sympathetic blockade. In elderly patients, particularly those with pre-existing hypovolemia or general debilitation, cardiovascular collapse may ensue.

Aspirating the needle or catheter before each injection and administering local anesthetic in 3 to 5 ml aliquots is advised in the ASRA Practice Advisory on LAST, and may be useful in limiting intravascular injection.[14] However, arrhythmias have been reported after psoas compartment block despite a negative aspiration test and the use of divided doses.[55]

Clinical Presentation of LAST. Local anesthetic systemic toxicity is classically described in textbooks as a clinical

* Two leading examples. Available at: http://emergencymanual.stanford.edu (accessed October 22, 2013) and http://www.project-check.org (accessed October 22, 2013).

progression from prodromal symptoms (agitation, tinnitus) to seizures, and provided sufficiently high blood levels are reached, ventricular arrhythmias, and cardiac arrest (table 1). Symptoms typically begin immediately after intravascular injection or systemic local anesthetic uptake. However, a review of the literature over the last 3 decades shows that not all cases of LAST fit into this model.

In the largest review to date, a wide range of times to the onset of signs of toxicity was reported, with a median time after single injection of 52.5 s (25 to 75%, 30 to 180 s).[25] In 25% of cases, symptom onset occurred at 5 min or more after local anesthetic administration. The greatest time interval between local anesthetic injection and signs of systemic toxicity was 60 min. Neurologic symptoms occurred in 89% of cases, but were isolated (no cardiovascular symptoms) in only 45% of reports. Seizure was the most common sign of neurotoxicity, occurring in 68% of cases. Classically described prodromal signs such as perioral numbness, dysarthria, and dizziness were actually *uncommon* and in aggregate occurred in only 16% of patients. Cardiovascular toxicity was reported in 55% of patients and occurred in conjunction with central nervous system signs in 44%. Bradyarrhythmias were most common and, together with tachycardia and pulseless electrical activity, represented approximately half of reported signs of cardiovascular toxicity.

Alternative Diagnoses. Although practitioners should maintain a low threshold for diagnosing LAST, there are multiple other potential causes of altered sensorium and/or hemodynamic collapse in the orthopedic patient (table 2). Alternative diagnoses strongly considered in our case scenario included: cerebrovascular accident/transient ischemic attack, metabolic derangements, thrombotic pulmonary embolus, and acute myocardial infarction.

The patient's altered mental status presented 15 min after block placement and was quickly followed by grand mal seizure. Any acute change in mental status in a patient with significant history of cerebrovascular disease or risk factors warrants consideration of a new cerebrovascular insult.

Table 1. Signs and Symptoms of Local Anesthetic Systemic Toxicity[25,72–74]

Central Nervous System Toxicity	Cardiovascular Toxicity
Subjective symptoms • Agitation • Auditory changes • Difficulty focusing • Dizziness/lightheadedness • Metallic taste • Tinnitus • Abrupt onset of psychiatric symptoms *Objective signs* • Coma • Muscle tremors • Seizures • Respiratory arrest	*Direct cardiac effects* • Depression of sinus node pacemaker activity • Depression of rapid phase of depolarization in Purkinje fibers and ventricular muscle • Depression of cardiac contractility *Peripheral vascular effects* • Low concentration—vascular smooth muscle vasoconstriction • High concentration—vascular smooth muscle vasodilation

Table 2. Causes of Altered Sensorium or Hemodynamic Compromise in Orthopedic Patients[75,76]

Causes of Altered Sensorium or Hemodynamic Compromise in Orthopedic Patients
Acute decompensation of valvular disease
Acute myocardial infarction
Alcohol use and withdrawal
Anaphylaxis
Bilateral pneumothorax
Brain injury or abnormality (including cerebrovascular accident or transient ischemic attack)
Central nervous system infections
Contrast agents
Epilepsy
Fever (children)
Illicit drug use and withdrawal
Medications (analgesics, antibiotics, immunomodulators, local anesthetics, psychotropics, theophylline)
Metabolic disorders (electrolyte abnormalities, inborn errors of metabolism, liver and/or kidney failure, pyridoxine deficiency)
Paroxysmal movement disorders (acute dystonic reactions, hemifacial spasms, nonepileptic myoclonus)
Sepsis
Thrombotic pulmonary embolus

Noncontrast computed tomography of the head is the initial imaging modality of choice and allows for differentiation between hemorrhagic and ischemic disease.[56]

Seizures are most frequently observed in the setting of sodium disorders, glucose disorders, hypocalcemia, or hypomagnesemia. Acid/base derangements may also be implicated. Potassium imbalances rarely cause central nervous system symptoms although they may promote fatal cardiac arrhythmias.[57]

Thrombotic pulmonary embolus is estimated to occur in up to 24% of patients after hip fracture repair.[58] Hypotension, tachycardia, hypoxemia, and decreased end-tidal carbon dioxide are all described in patients with pulmonary embolus; acute altered mental status may result from hypoxemia and cerebral ischemia in the setting of reduced cardiac output. Sinus tachycardia and atrial arrhythmias are the most common findings on electrocardiogram. Transesophageal echocardiography may yield evidence of right ventricular dilation and is useful for establishing alternative diagnoses.

Myocardial infarction may lead to hemodynamic instability and, *via* cerebral hypoperfusion, cause altered mentation. The electrocardiogram may reveal evidence of S-T or T-wave abnormalities. Echocardiography is useful for evaluation of ejection fraction, wall motion abnormalities, and valvular anomalies. Biochemical markers are unlikely to acutely reveal evidence of myocardial infarction but are useful to trend over time.

Treatment of LAST. Effective treatment of LAST requires understanding of the differences between LAST resuscitation and other cardiac arrest scenarios. ASRA, the American Heart Association, and the Association of Anesthetists of Great Britain and Ireland all generally recommend airway management as a first priority, followed by treatment of seizure with benzodiazepine, and then initiation of lipid emulsion therapy, all while performing effective cardiac compressions and basic life support (fig. 4).[14] Key differences between traditional ACLS and LAST management are highlighted below.

Medications. Small initial doses of epinephrine (10 to 100 μg IV) are recommended for the treatment of hypotension.[14] This is because epinephrine may promote cardiac arrhythmias, especially in high doses. In addition, a rodent model of bupivacaine overdose showed an impairment of lipid-based resuscitation after a single IV injection of epinephrine 10 μg/kg.[59] Vasopressin, calcium channel blockers, and β-blockers are all not recommended. Use of vasopressin for treatment of LAST is associated with pulmonary hemorrhage in animal studies.[60] Propofol use is not recommended due to its low lipid content (10%) and direct cardiodepressant effects.[14] In our case scenario, the diagnosis of LAST was not immediately evident and another (*e.g.*, primary cardiac) cause of severe arrhythmia could not be excluded. Thus, full ACLS doses of epinephrine were initially administered despite recommendations for lower doses in the setting of LAST.

Lipid Emulsion. Lipid emulsion 20% should be given as a bolus (1.5 ml/kg) and continued as an infusion of 0.25 ml kg^{-1} min^{-1}. The bolus may be repeated up to two times and the infusion rate may be doubled to 0.5 ml kg^{-1} min^{-1} if cardiovascular collapse is persistent. Timing should not be conservative (*i.e.*, waiting for traditional ACLS to prove ineffective).[14] Although early administration at the first sign of neurologic or cardiovascular symptoms may result in overtreatment of the great proportion of patients who will not go on to have severe toxicity, the risks of treatment are generally well tolerated. Potential, but uncommon, risks could include: allergic reaction, fluid overload, and hypertriglyceridemia.[61,62] Hemoglobin and methemoglobin measurements may be falsely increased, as lipid emulsion may interfere with

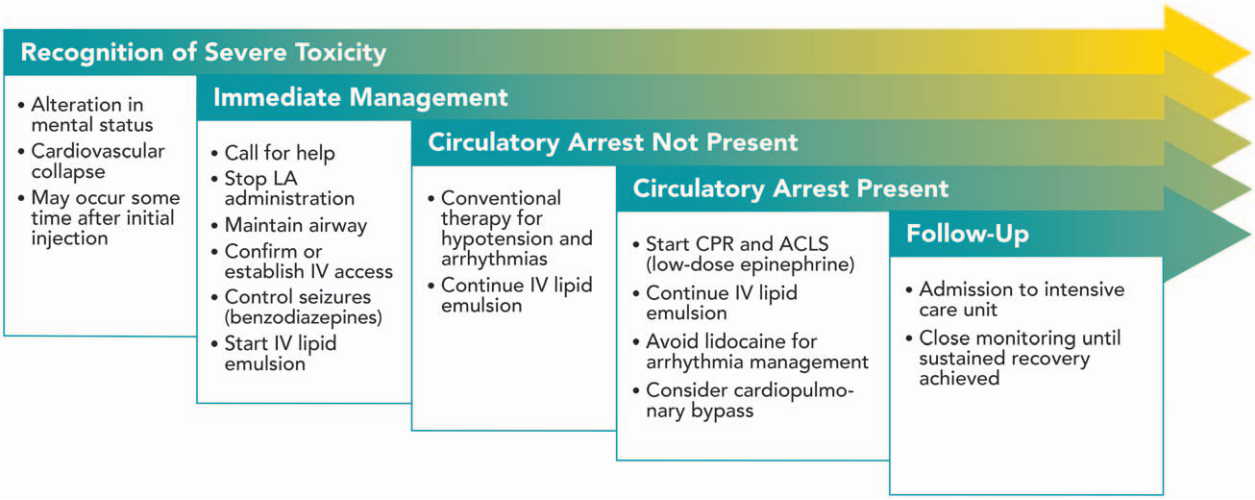

Fig. 4. Management of local anesthetic systemic toxicity. Early recognition and mobilization of resources are crucial for effective treatment of local anesthetic emergencies. Lipid emulsion therapy should be instituted at the first sign of neurologic or cardiovascular symptoms. High-dose epinephrine should be avoided as it may promote cardiac arrhythmias and impede the efficacy of lipid rescue. ACLS = advanced cardiac life support; CPR = cardiopulmonary resuscitation; IV = intravenous; LA = local anesthetic.

spectrophotometric measurements.[63,64] Lipid emulsion infusion should be maintained for at least 10 min after cardiovascular restabilization, and observation for at least 12 h is recommended, as symptoms of toxicity can recur.[14]

ACLS. Prolonged effort may be required, and cardiopulmonary bypass may be indicated for refractory cases. Because these kinds of resources may take significant time to mobilize and ready, early consideration and anticipation of future patient states must be given a high priority. Defibrillation or pacing is not expected to be effective until lipid emulsion is administered. High-quality chest compressions are needed to circulate the lipid to the coronary vascular beds.[14]

Knowledge Gap. Technological Innovations. Several technological innovations may further improve the safety and efficacy of regional anesthesia. Ultrasound localization has enhanced understanding of needle–nerve relationships and allows for clear delineation of lumbar plexus anatomy as well as real-time views of block needle advancement and local anesthetic distribution during injection. Karmakar *et al.* performed lumbar plexus blocks on patients with American Society of Anesthesiologists physical status II to III undergoing emergency lower limb surgery. In three of five patients, the lumbar plexus nerve roots were identifiable by ultrasound in the posterior aspect of the psoas muscle. Improved nerve localization may allow for targeted administration of lower doses of local anesthetic medication, lessening the risk of LAST. Further research studies are needed to address this topic, as there is only limited data on the cost-effectiveness of ultrasound-guided peripheral nerve blocks as well as their safety and efficacy when compared with traditional methods.[65]

Pharmacologic Innovations. Bupivacaine is prepared as a 50:50 racemic mixture of two optically active enantiomers in levorotatory S(-)- and dextrorotatory R(+)- configurations. Stereoselectivity plays a key role in local anesthetic-induced cardiotoxicity; the R(+)- enantiomer is associated with greater potential for toxicity than the S(-)- enantiomer. Levobupivacaine and ropivacaine, pure S(-)- isomers, cause fewer negative cardiovascular effects *in vivo* when compared with racemic bupivacaine.[66] Similar cardiovascular effects were found when levobupivacaine and ropivacaine were administered intravenously at equal concentrations, milligram doses, and infusion rates in healthy human volunteers.[67] The reduced toxic potential of these two S(-)- enantiomers suggests their utility in clinical scenarios where the risk of LAST due to overdosing or unintended intravascular injection/absorption is high. Cost, availability, and local practice patterns may influence the use of these agents. These "systems" issues are also recognized as important influences on decision-making and error.[29]

Development of ultralong-acting local anesthetics may allow for administration of small drug doses, decreasing the risk of LAST associated with large volume drug administration. A recent report describes the development of a local anesthetic liposomal depot that allows for a four-fold increase in bupivacaine administration without corresponding increases in peak plasma concentration.[68]

The optimal formulation of lipid emulsion for treatment of LAST is still debated. Both long-chain triglyceride and long- and medium-chain triglyceride mixtures have successfully treated LAST. Ruan *et al.*[69] reported a greater local anesthetic extraction with long- and medium-chain triglyceride mixtures *in vitro*, whereas Li *et al.*[70] found a greater reversal of bupivacaine toxicity when using long-chain triglycerides *in vivo*. Further research is required to optimize the efficacy of lipid emulsion therapy.

Diagnostic Approach. Medical diagnosis cannot be left to the variability of whatever comes readily to mind based on previous experience and formal education (*e.g.*, residency training, conferences, and modern literature). A systematic approach is required, so that important diagnostic options are not missed in high-stakes, time-pressured, stressful conditions. Deliberate efforts should be made to consider common diagnoses, context-specific diagnoses, and rare but serious possibilities. Giving specific mental attention to each of these three categories minimizes the chance that an important diagnosis would not be considered. Regular practice prevents premature closure; therefore, we recommend engaging in this kind of thinking even when diagnoses seem to be obvious.

We conclude by emphasizing that although there are many possibilities for altered sensorium or hemodynamic compromise in orthopedic patients, particularly those who are elderly with neurologic and cardiac comorbidities, one must consider the diagnosis of LAST in any patient who exhibits altered mental status, neurologic symptoms, or cardiovascular symptoms after receiving local anesthetics, even if the presentation is quite delayed. Despite classic teachings, LAST is not usually associated with prodromal findings. Monitoring for at least 30 min after local anesthetic administration is recommended. We encourage consideration of diagnostic strategy and decision making as well as adoption of nontechnical and crisis resource management skills as part of daily anesthetic practice.

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Competing Interests

The authors declare no competing interests.

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