ASRA Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine

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Neurologic complications associated with regional anesthesia and pain medicine practice are extremely rare. The ASRA Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine addresses the etiology, differential diagnosis, prevention, and treatment of these complications. This Advisory does not focus on hemorrhagic and infectious complications, because they have been addressed by other recent ASRA Practice Advisories. The current Practice Advisory offers recommendations to aid in the understanding and potential limitation of neurologic complications that may arise during the practice of regional anesthesia and pain medicine. *Reg Anesth Pain Med 2008;33:404-415.*

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The American Society of Regional Anesthesia and Pain Medicine (ASRA) convened a group of experts to develop a Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine. The goal of this Practice Advisory is to provide information for practitioners of regional anesthesia and pain medicine regarding the etiology, differential diagnosis, prevention, and treatment of neurologic complications. This Practice Advisory focuses on neurologic injuries apart from those caused by hemorrhagic[1] or infectious[2-6] complications, both of which have been the subject of other recent ASRA-sponsored Practice Advisories. The current report is a summation of the Practice Advisory's findings and recommendations. Anesthesiologists are strongly encouraged to read the manuscripts that accompany the present summary document, because they contain the details upon which recommendations are based. The accompanying manuscripts represent most of the subtopics discussed at the conference.

Methodology

The ASRA Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine was convened on April 23, 2005 at the ASRA Annual Meeting in Toronto, Ontario, Canada. The project was approved by the ASRA Education Committee and Board of Directors. The panelists were chosen by ASRA based on demonstrated expertise in issues related to neurologic injury, and included all of the authors of this manuscript in addition to a malpractice attorney.* Panelists received no compensation for their contributions to the Practice Advisory, nor did any declare a conflict of interest pertinent to the topic. Panelists were charged with

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performing an extensive review of the literature, summarizing and presenting their findings at the conference, and producing a manuscript based on their scholarly work. During the Toronto conference, panelists and attendees discussed several issues related to neurologic injury in an open forum format. All subsequent recommendations were reviewed and approved by members of the panel. Manuscripts were first peer reviewed internally by 3 members of the expert panel and subsequently peer reviewed externally using this journal's standard review process.

The recommendations contained within this Practice Advisory represent the opinions of a small group of expert panelists and are based upon their clinical experience, review of limited scientific literature (anatomic and physiologic studies of animals and human cadavers, case reports, retrospective case series, and non-randomized trials), and open forum discussion. Importantly, in this imperfect setting of controversial topics, limited data, and bias inherent to expert opinion, the Panel consistently tended towards making conservative recommendations. We acknowledge that other experts analyzing the same information may arrive at recommendations different than ours. The recommendations contained herein are not intended to define standard practice or to ensure the avoidance of adverse outcomes. Furthermore, the recommendations are subject to change as new information becomes available. Recommendations from the Practice Advisory are not intended to replace clinical judgment, and specific risk-to-benefit discussions as they pertain to individual patients.

Because neurologic injuries related to anesthesia and pain medicine practice are extremely rare, standard tools of evidence-based medicine such as randomized controlled trials, meta-analysis, and prospective human studies rarely exist—and are unlikely to be available in the future. Therefore, recommendations contained within this Practice Advisory could not be easily graded based on traditional stratification methods, such as those used by the United States Agency for Health Care Policy and Research.[7] Consequently, the Panel chose to stratify its recommendations based on a simplified schema used by other medical specialties facing similar circumstances (Table 1).[8]

Table 1. Strength of Recommendations

Classification	
I	Animal and/or human evidence, and/or general agreement of expert opinion, support the effectiveness and usefulness of the recommendation.
II	The weight of conflicting evidence and/or the weight of expert opinion support the usefulness of the recommendation.
III	The usefulness of the recommendation is limited by absent or conflicting evidence and/or divergent expert opinion.

NOTE. This classification system is significantly modified from the American College of Cardiology/American Heart Association construct for classifying strength of evidence.[8]

Overview of Anesthesia-Related Neurologic Injury

Incidence

Because of the infrequency at which anesthesia- and pain medicine-related neurologic injuries occur, it is extremely difficult to obtain reliable and consistent incidence data. Medicolegal and insurance-based data are biased by the very presence of injury, whereas underreporting may bias clinical-based data. Therefore, medicolegal data such as that provided by the American Society of Anesthesiologists (ASA) Closed Claims Project may overestimate the occurrence of injury, while clinical studies potentially underestimate the true incidence. Academic regional anesthesiologists are reasonably accurate in estimating the incidence of permanent neuropathy from neuraxial or peripheral blocks.[9] However, it is perhaps worrisome that the risk of permanent injury is only included in 42% to 77% of their informed consent discussions with patients.[9,10]

Recent clinical data from Sweden suggest that the frequency of hematoma is 1.3 to 2.7 per 100,000 (95% confidence interval [CI]) neuraxial anesthetics.[11] Neuraxial infectious complications (epidural abscess and meningitis) range from 0 infections in over 70,000 epidural and spinal anesthetics[12] to 1 abscess per 1,930 epidural anesthetics.[13] Hematoma and infectious complications are relatively common as compared with conditions such as anterior spinal artery syndrome (ASAS), and direct needle trauma. For instance, no cases of ischemic spinal cord injury were reported in over 70,000 neuraxial anesthetics performed in France over a 10 month period.[12] Only 12% of neuraxial injuries in the ASA Closed Claims Database were associated with ASAS or spinal cord infarction; only 6 of 821 neuraxial claims involved suspected direct spinal cord trauma.[14] In contrast to the often transient nature of peripheral nerve injuries, most neuraxial injuries are permanent. In fact, permanent nerve injury has been shown to range from 15% in French surveillance studies[12] to 80% to 100% in the ASA Closed Claims Database—with the frequency being highly dependent on the type of neural lesion.[14]

In the early postoperative period, mild paresthe-

sias may be present in up to 15% of patients that undergo peripheral nerve block.[15] Most of these symptoms resolve within days to weeks, with over 99% completely resolving by 1 year.[16,17] Serious neurologic injury reported in a large prospective study occurred in 2.4 per 10,000 peripheral nerve blocks.[18]

Risk Factors Unrelated to Anesthesia

Proper evaluation of perioperative nerve injuries includes a search for causes unrelated to anesthetic technique. The plethora of factors that can contribute in whole or in part to perioperative neural injury underlies the difficulties encountered in both the academic study and clinical evaluation of this phenomenon. In brief, patient-specific risk factors for perioperative nerve injury include pre-existing neurologic disorders, diabetes mellitus, extremes of body habitus, male gender, and advanced age. Surgical risk factors include direct surgical trauma or stretch, compressive dressings or casts, tourniquet inflation, hematoma or abscess formation, perioperative inflammation, and improper patient positioning.[17]

ASA Closed Claims Perspective

Excluding obstetric and pain management cases, the ASA Closed Claims Database (1980-1999) showed that neuraxial blocks were associated with temporary nerve injury in 38% and permanent nerve injury in 26% of cases with complications reported to the database. Of those neuraxial injuries believed to be block-related (41%), 45% were attributed to the block technique, including direct needle or catheter damage to the neuraxis or adjacent nerves. Most permanent injuries involved the lumbosacral nerve roots or the thoracolumbar spinal cord. Over half of the neuraxial injuries were caused by an epidural hematoma, with the remaining injuries being caused by assorted conditions such as ASAS, epidural abscess formation, or meningitis.[14]

Of all claims associated with neuraxial chronic pain management, 25% involved nerve damage. Injuries associated with treatment for chronic pain were most likely to result from an infectious cause, with hematoma and direct needle injury occurring less frequently. The most striking finding stemming from the ASA analysis of chronic pain claims was that use of local anesthetic and/or opioid during epidural steroid injection was associated with 9 deaths or brain damage, while there were no deaths or brain damage when local anesthetic and/or opioid was not used as part of the neuraxial injectate. The authors warn that injection of neuraxial local anesthetic and/or opioid for pain treatment in the ambulatory setting should be accompanied by the same close monitoring, and the ability to perform resuscitative maneuvers that are available to those patients receiving neuraxial local anesthetic and/or opioid in the operating room or obstetric settings.[19,20]

Most claims involving peripheral nerve injury were for temporary injury (56%) with half of the deficits believed to be block-related. The brachial plexus is the most commonly injured peripheral nerve structure in the Closed Claims Database, followed by the median, ulnar, and radial nerves. Lower extremity nerve injuries are rare in the Closed Claims Database, most likely reflecting the less frequent practice of lower extremity regional anesthesia. A notable increase in claims involving eye blocks performed by anesthesiologists has occurred since 1980.[21] The most serious injuries from peripheral nerve or facet blocks placed for chronic pain involved blocks performed in the neck or near the neuraxis that ultimately injured neuraxial structures.[20]

Pathophysiology of Neuraxial Injury

Neuraxial injury may involve the spinal cord, spinal nerve roots, spinal nerves, or spinal vasculature. With the exception of obvious compressive lesions such as an epidural hematoma or abscess, the etiology of neuraxial injuries is rarely apparent. Neuraxial injuries are typically linked to needle- or catheter-related mechanical damage to the neural or vascular components, to space-occupying lesions competing for limited cross-sectional area within the spinal canal, to ischemia, or to drug-related neurotoxicity.

Direct needle or catheter trauma to the spinal cord may be associated with inaccurate determination of vertebral levels, anatomical variation in the terminal portion of the conus medullaris, incompletely fused ligamentum flavum, or progressive (caudad to cephalad) posterior-to-anterior epidural space narrowing. Laterally directed needles intended to enter the dorsal epidural space may injure spinal nerves or vasculature near the medial aspect of the intervertebral foramina, while needles advanced medially during transforaminal injection may injure these same structures within or just lateral to the intervertebral foramina. Direct trauma is further complicated by inconsistent and unreliable signals when needles or catheters contact or enter the spinal cord. The spinal cord has no sensory receptors and sensory input from the meninges is inconsistent. This may explain, in part, reported cases in which needle entry into the spinal cord was not recognized even in awake patients.

Actual injection into the spinal cord appears to more consistently elicit a painful response, most likely because of pressure-related stimulation of afferent neurons.[22]

Another mechanism leading to neuraxial injury is the presence of a mass lesion that compresses the spinal cord within the fixed cross-sectional area of the spinal canal. Intradural or extradural compression of the cerebrospinal fluid (CSF) or the spinal cord itself, especially when it develops rapidly, may generate pressures sufficient to compromise blood flow and cause ischemia or infarction. Hematoma and abscess are relatively common mass lesions that are of sufficient size to impair spinal cord function. In contrast, abnormal epidural fat, tumor, hypertrophic ligamentum flava, bony overgrowth of the vertebral canal or foramina, temporary mass effect from local anesthetic, or a relative change in cross-sectional area secondary to various surgical positions may occur less often. Although these conditions have the potential to compress the neuraxis, their primary importance lies in further reducing available spinal canal cross-sectional area should a more acute process such as an epidural hematoma occur.[22]

Although isolated case reports describe what is speculated to be local anesthetic-induced spinal injury in presumably normal individuals, local anesthetics are rarely neurotoxic when administered in recommended concentrations and dosages. The potential for toxicity is heightened when mechanical damage to the spinal cord or neural fibers damages their normally protective connective tissue barriers, when injection or catheter insertion physically disrupts the structural integrity of the spinal cord, or when vasoconstrictors impede local anesthetic clearance. Some neuraxial components may theoretically be more susceptible to local anesthetic neurotoxicity—such as the cauda equina because it is partially unmyelinated and has a large surface area, and the spinal nerve roots contained within the dural root cuffs because they lack the mechanical and metabolic protection afforded peripheral nerves.[22]

Vascular injury within the neuraxis during regional anesthesia or pain medicine is also extremely rare and arguably more difficult to understand. Although hypotension and vasoconstrictors are often cited as the "diagnosis of exclusion" of unexplained perioperative spinal cord injury, neither factor seems to be supported by physiologic principles. Spinal cord blood flow (SCBF) is autoregulated within the same physiological range as the brain. Therefore, blood pressure within the normal autoregulatory range has no adverse effect on SCBF. There are no human data to support diminution of SCBF from vasoconstrictors such as epinephrine.[23] Spinal cord blood supply can be tenuous, particularly to the anterior cord and the lower thoracic and lumbosacral segments. Although mechanical damage to the arterius radicularis magnus could compromise spinal cord circulation, this vessel and the anterior spinal artery system are quite distant from needles used for neuraxial and perineuraxial pain procedures.[22] However, transforaminal approaches may have a higher potential for encountering major spinal arteries as they traverse the intervertebral foramen.[24]

In summary, the pathophysiology of neuraxial injury involves various, and perhaps combined mechanical, ischemic, and neurotoxic insults. Although a definitive etiology is apparent in the case of hematoma or infection, the link between specific factors and most other neuraxial injuries are associative—rather than causative—in nature. Our inability to prospectively identify patients at risk suggests that most of these injuries are neither completely predictable nor preventable. Furthermore, serious injuries are known to occur in healthy patients who have received competent and standard care.

Pathophysiology of Peripheral Nerve Injury

Similar to neuraxial injury, peripheral nerve injury is commonly linked to trauma from needles or catheters, ischemia, drug toxicity, compression, or neural stretch. Central to prognosis is whether or not the axon is preserved. Neuropraxic lesions, which damage the myelin sheath but preserve the axon, are typically associated with compressive or stretch injuries and are perhaps more likely to resolve. Conversely, if the axon is completely disrupted, recovery is slower and more likely to be incomplete. The double crush theory[25] and some clinical evidence[16,26] suggest that patients with pre-existing peripheral nerve injury—even if subclinical—are more likely to sustain further nerve damage if a second subclinical or obvious injury occurs.[27]

Permanent peripheral nerve injury is not completely preventable—even in healthy patients receiving competent, standard care. Nerve injury theory suggests that more than 1 insult is often necessary to cause damage. Peripheral nerve injury appears to require the breach of connective tissue barriers such as the perineurium that surrounds individual nerve fascicles and protects them from the external milieu. Disruption of the perineurium from needle or catheter trauma is remarkably difficult to accomplish. Animal studies and experience with ultrasound-guided nerve localization has shown that nerves tend to move away from approaching nee-

dles. When nerves are impaled, the needle may pass harmlessly into or through connective tissue, which constitutes up to 70% of a nerve's cross-sectional area.[28] However, if the fascicle is penetrated, neurons are exposed to local anesthetics that can cause time- and concentration-dependent injury. Vasoconstrictors play a role by limiting local anesthetic clearance and thereby enhancing the time-dependent component of injury. Decreased neural blood flow from edema or mass effect can also potentiate cytotoxicity. In summary, peripheral nerve injury associated with regional anesthesia is likely caused by a combination of insults to the nerve's internal milieu. However, the exact sequence and relative importance of these insults remain unknown.[29]

Diagnosis and Treatment

Suspected compressive lesions of the neuraxis require rapid diagnosis and treatment. The likelihood of full or partial recovery in these circumstances rapidly diminishes as time to decompression approaches or exceeds 8 hours.[1] In most cases, magnetic resonance imaging (MRI) is the preferred imaging modality for spinal canal pathology, although diagnosis should not be delayed if only computed tomography (CT) is available.

Diagnosis of suspected peripheral nerve injury is guided by presenting symptoms, history, and physical examination. *Complete or progressive neural deficits* should prompt urgent evaluation by a neurologist or peripheral nerve surgeon. *Mild and/or resolving symptoms* without objective evidence of neural deficit typically indicate excellent prognosis and require only patient reassurance. If symptoms fail to progressively improve, neurological consultation should be sought in 2 to 3 weeks. *Incomplete lesions with evidence of moderate or severe deficit* are an indication for early neurological consultation and consideration of neurophysiologic testing (nerve conduction studies and electromyography) or MRI imaging of the nerve(s). Neurophysiologic testing can help quantify nerve damage and, together with MRI, can establish injury location. Although neurophysiologic changes are most apparent 14 to 21 days after injury, earlier testing may be indicated to rule out pre-existing (including bilateral) disease, establish baseline, and aid in prognosis. After initial evaluation, incomplete and unresolved lesions should be followed up in 3 to 5 months. Improvement and evidence of reinnervation suggest further conservative management. However, no improvement or reinnervation might prompt referral to a peripheral nerve surgeon, although there is no consensus with regards to when an injured nerve warrants surgical exploration.[27]

Recommendations of the Practice Advisory Panel

As previously noted, the following recommendations are based on existing scientific literature and expert opinion, and tend toward conservative interpretation of this information. They are intended to promote understanding of neurologic complications associated with regional anesthesia and pain medicine. However, the recommendations cannot ensure the absence of adverse outcomes nor should they supersede physician judgment in specific clinical situations. The strength of each recommendation is stratified according to the evidence-based grading scheme described in Table 1.

Neuraxial Injuries

Neuraxial injuries may be limited by possessing a detailed knowledge of those anatomic conditions that place the spinal cord, spinal nerves, or spinal vasculature at risk for mechanically induced injury from needles, catheters, improper positioning, space-occupying lesions, or drug-induced neurotoxicity. When neurologic injury is suspected, diagnosis and treatment must proceed without delay to avoid adverse or incomplete recovery. Recommendations are listed in Table 2.

Peripheral Injuries

Although peripheral nerve injuries may be reduced by minimizing trauma to neural fibers, no nerve localization or monitoring technique has been shown to be clearly superior in terms of reducing the frequency of clinical injury. These techniques include paresthesia-seeking, peripheral nerve stimulation, defined minimal or maximal milliamperage for acceptance of a motor response,[30,31] ultrasound guidance, or monitoring of injection pressures.[31-35] Ultrasound guidance, advances in peripheral nerve stimulation,[36] and pressure monitoring in particular are relatively new technologies; therefore, clinical experience and scientific study regarding their potential role in injury avoidance are limited.[37] In patients with pre-existing clinical or suspected subclinical peripheral nerve injury, consideration should be given to modifying the regional technique to minimize the introduction of additional potential neural insults. Reducing the dose, concentration, or potency of local anesthetic, or eliminating or reducing the concentration of vasoconstrictive additives are potential considerations, based on moderately extensive animal data.[17,23] Limited human data neither support nor refute this recommendation. The diagnosis and prognosis of peripheral nerve injury largely depends on the

Table 2. Recommendations: Limiting, Diagnosing, and Treating Neuraxial Injury

Limiting injury

- Misidentification of vertebral level, unrecognized lateral needle placement or deviation, abnormal caudad termination of the spinal cord, or failure of the ligamentum flavum to fuse in the midline may contribute to direct needle injury to the spinal cord. Clinicians are advised to be aware of these anatomic conditions, particularly in patients with challenging surface anatomy. (Class I)
- Clinicians are advised to be aware of and to avoid conditions that have been linked to the formation of epidural hematoma or epidural abscess, as noted in previous ASRA Practice Advisories. Such conditions include concurrent or imminent anticoagulation, the use of multiple anticoagulants, improper aseptic technique, and needle placement during untreated active infection.[1,3] (Class I)
- Patients with known tumor in the epidural space should undergo neuraxial imaging studies to define the extent of tumor mass. If the tumor is close to the planned site of epidural solution injection, alternative methods of anesthesia or analgesia should be considered. (Class II)
- Surgical positioning and specific space-occupying extradural lesions (e.g., severe spinal stenosis, epidural lipomatosis, ligamentum flavum hypertrophy, or ependymoma) have been associated with temporary or permanent spinal cord injury in conjunction with neuraxial regional anesthetic techniques. These conditions are particularly relevant when they coexist with an epidural hematoma or abscess. Awareness of these conditions should prompt consideration of risk vs. benefit when contemplating neuraxial regional anesthetic techniques. (Class II)
- Initial dosing or redosing of subarachnoid local anesthetic in excess of the maximum recommended dose may increase the risk of spinal cord or spinal nerve root neurotoxicity and should be avoided. (Class I)
- Epidural anesthetic procedures using the thoracic approach are neither safer nor riskier than using the lumbar approach. (Class I)
- The use of local anesthetic and/or opioid during neuraxial block for chronic pain treatments in the ambulatory setting should be accompanied by the same close monitoring and ability to perform resuscitative maneuvers that are available to those patients receiving neuraxial local anesthetic and/or opioid in the operating room. (Class I)

Diagnosis and treatment

- Magnetic resonance imaging (MRI) is the diagnostic modality of choice for suspected neuraxial lesions. Computed tomography (CT) should be used for rapid diagnosis if MRI is not immediately unavailable, especially when neuraxial compression injury is suspected. (Class I)
- Diagnosis of a compressive lesion within or near the neuraxis demands immediate neurosurgical consultation for consideration of decompression. (Class I)

severity of symptoms upon presentation. Recommendations are listed in Table 3.

Regional Anesthesia and the Patient With Pre-Existing Neurologic Disease

Pre-existing disorders of the central nervous system (CNS) and peripheral nervous system, such as multiple sclerosis, amyotrophic lateral sclerosis, and postpolio syndrome, present challenges to patients and anesthesiologists who desire to use neuraxial anesthetic techniques. Because these diseases involve damage to the CNS, the concern is that perioperative stress or further mechanical trauma, or drug-induced toxicity could exacerbate the underlying disease process or lead to a relapse of symptoms. The rarity of these diseases results in a paucity of data

Table 3. Recommendations: Limiting, Diagnosing, and Treating Peripheral Nerve Injury

Limiting injury

- There are no animal or human data to support the superiority of one nerve localization technique—paresthesia, nerve stimulation, ultrasound—over another with regards to reducing the likelihood of nerve injury. (Class I)
- Animal data have linked high injection pressures to subsequent fascicular injury, but there are no human data that confirm or refute the effectiveness of injection pressure monitoring for limiting nerve injury. (Class II)
- There are no human data to support the superiority of one local anesthetic or additive over another with regards to reducing the likelihood of neurotoxicity. (Class I)
- Patients with diseased or previously injured nerves (e.g., diabetes mellitus, severe peripheral vascular disease, or chemotherapy) may theoretically be at increased risk for block-related nerve injury. Although isolated case reports have described new or progressive neurologic deficits after regional anesthetic techniques in patients with multiple sclerosis or previous exposure to chemotherapy, clinical experience can neither refute nor confirm these concerns. Based on limited animal data, consideration may be given to avoiding more potent local anesthetics, reducing local anesthetic dose and/or concentration, and avoiding or limiting vasoconstrictive additives in these patients. (Class II)
- If damage to protective tissue barriers such as the perineurium is suspected from an abnormally painful paresthesia or pain on injection of local anesthetic, further injection should be halted immediately, and the needle repositioned. (Class I) Consideration may be given to aborting the block procedure so as to avoid further deposition of local anesthetic and additive. (Class III)

Diagnosis and treatment

- Complete absence of nerve function beyond the duration of the anesthetic or the progression of neurologic deficit(s) should prompt urgent neurological or neurosurgical consultation and evaluation. (Class I)
- Incomplete lesions associated with moderate-to-severe neural deficit should prompt neurologic consultation and evaluation for consideration of electrophysiological studies and/or radiologic imaging. Consideration should be given to bilateral examination and early studies to establish baseline, pre-existing lesions, and prognosis. (Class I)
- Nerve lesions that fail to resolve 2 to 5 months after initial neurological evaluation should prompt consideration of neurosurgical consultation. (Class II)

Table 4. Recommendations: Performing Regional Anesthesia in Patients With Pre-Existing Neurologic Deficits

Pre-existing peripheral neuropathy
- Patients with chronic diabetes mellitus, severe peripheral vascular disease, multiple sclerosis, or previous exposure to chemotherapy (e.g., cisplatin or vincristine) may have clinical or subclinical evidence of a pre-existing peripheral neuropathy. Peripheral nerve block may theoretically increase the risk of new or progressive postoperative neurologic complications in these patients. However, existing data can neither confirm nor refute this theory in clinical practice. Under these clinical conditions, a careful risk-to-benefit assessment of regional anesthesia to alternative perioperative anesthesia and analgesia techniques should be considered. (Class II)

Pre-existing central nervous system disorders
- Definitive evidence indicating that neuraxial anesthesia or analgesia may increase the risk of new or progressive postoperative neurologic complications in patients with pre-existing central nervous system disorders (e.g., multiple sclerosis, postpolio syndrome) is lacking. However, under these clinical conditions, a careful risk-to-benefit assessment of regional anesthesia to alternative perioperative anesthesia and analgesia techniques should be considered. (Class II)

Spinal stenosis or mass lesions within the spinal canal
- When neuraxial anesthesia is complicated by the development of mass lesions within the spinal canal (e.g., hematoma or abscess), resultant postoperative neurologic complications may be more likely or more severe in patients with pre-existing severe spinal stenosis or other obstructive spinal canal pathology. In patients with known severe spinal stenosis or mass lesions within the spinal canal, a careful risk-to-benefit assessment of regional anesthesia to alternative perioperative anesthesia and analgesia techniques should be considered. In these patients, high local anesthetic volume neuraxial techniques (i.e., epidural anesthesia) may be associated with a higher risk of progressive mass effect when compared with low volume techniques (i.e., spinal anesthesia). (Class II)
- For patients receiving neuraxial injection for treatment of pain (e.g., cervical epidural injection of steroids via an interlaminar route), radiologic imaging studies such as computed tomography or magnetic resonance imaging should be used to assess the dimensions of the spinal canal, and this information should be considered in the overall risk-to-benefit analysis, as well as guiding the selection of the safest level for entry. (Class II)

Overall approach to patients with pre-existing neurologic deficits
- Patients with pre-existing neurologic disease may be at increased risk of new or worsening injury regardless of anesthetic technique. When regional anesthesia is thought to be appropriate for these patients, modifying the anesthetic technique may minimize potential risk. Based on a moderate amount of animal data, such modifications may include using a less potent local anesthetic, minimizing local anesthetic dose, volume, and/or concentration, and avoiding or using a lower concentration of vasoconstrictive additives. Limited human data neither confirm nor refute these modifications. (Class II)

Patients with previous spinal surgery
- Prior spinal fusion or spinal corrective surgeries are not a contraindication to neuraxial anesthesia or analgesia. In these patients, spinal anesthesia may be technically easier to perform and more reliable than epidural anesthesia. A review of radiologic imaging and/or the use of fluoroscopy are recommended to refine the approach to the neuraxis. (Class II)

that are often conflicting. For instance, an isolated case report describes a patient with postpolio syndrome who did not develop progression of his neurologic symptoms after spinal anesthesia.[38] Small case series note an increase in the relapse rate of multiple sclerosis after spinal anesthesia in surgical patients[39] vs. a statistically similar incidence of relapse rates in women who received neuraxial anesthesia and analgesia for obstetric indications.[40] A retrospective investigation of 139 patients with pre-existing CNS disease (multiple sclerosis, postpolio syndrome, traumatic spinal cord injury, etc.) who underwent neuraxial anesthesia revealed no subsequent exacerbation of disease process (0.0%-0.3%, 95% CI).[41] Another retrospective study of neuraxial anesthesia in patients with pre-existing sensorimotor neuropathy or diabetic polyneuropathy noted the onset of new or progressive neurologic deficit in 0.4% (0.1% to 1.3%, 95% CI) of patients—an incidence that is higher than expected within the general population.[42] However, the existing literature neither confirms nor refutes the safety of neuraxial anesthesia in patients with CNS or peripheral nervous system neurologic disorders, nor does it definitively address the relative safety of spinal vs epidural anesthesia or analgesia in these patients. Recommendations regarding patients with pre-existing CNS disorders are listed in Table 4.

Peripheral nerve block may also be problematic in patients with pre-existing clinical or suspected subclinical neurologic disease from diabetes mellitus, neurotoxic chemotherapeutic agents (e.g., vincristine or cisplatin), or in patients who are scheduled to undergo surgery on a nerve within the expected distribution of neural block. Although wide clinical experience suggests that neural block in these patients rarely exacerbates pre-existing nerve injury, animal data and isolated human reports give some cause for concern. For instance, diabetic rats are more prone to the neurotoxic effects of local anesthetic.[43] Patients undergoing ulnar nerve transposition are at no increased risk of postoperative neural deficit regardless of whether they receive general or regional anesthesia. However, neural deficits that did occur within the regional anesthesia group were associated with either an ulnar nerve paresthesia or motor response during block placement.[44] In addition, 2 case reports describe patients with presumed subclinical neuropathy from cisplatin[26] and multiple sclerosis[37,45] who developed a new neural injury after uncomplicated brachial plexus block. Similar to CNS disease, the

literature is unable to definitively support or refute the use of regional anesthesia in patients with pre-existing peripheral neuropathy. Recommendations for these patients are listed in Table 4.

Patients with a history of prior spinal surgery present unique technical challenges for neuraxial regional techniques. Various spine stabilization and fusion procedures can involve autologous bone grafts, screws placed into pedicles, and anterior or posterior instrumentation. Most instrumentation does not alter the architectural integrity of the posterior spinal elements. Therefore, neuraxial anesthesia or pain medicine procedures are frequently possible in these patients.[46] Plain radiographs or fluoroscopy can be beneficial in planning or executing neuraxial techniques within these patients. Furthermore, imaging may decrease the frequency of multiple attempts at block placement or unsuccessful identification of the epidural space.[47] Because of surgically induced epidural space scarring, local anesthetic spread may be abnormal in these patients; thus spinal anesthesia may be the preferred neuraxial technique when appropriate.[48] Prior lumbar spine surgery may also increase the risk of paraplegia associated with transforaminal epidural steroid injections (Table 4).[49,50]

In summary, existing scientific literature and expert opinion can neither confirm nor refute an adverse effect of regional anesthesia in patients with pre-existing neurologic disease. However, most existing data suggest that any increased risk, if present, is likely of minimal magnitude. More importantly, patients with pre-existing neurologic disease may develop new or progressive deficits during the perioperative period independent of anesthetic choice — from surgical factors, perioperative stress, or their underlying comorbidity.

Regional Anesthesia in Anesthetized or Heavily Sedated Patients

One of the most controversial areas of regional anesthesia and pain medicine practice is whether or not it is advisable to perform blocks in patients that are either anesthetized (under general anesthesia) or sedated to the point of being unable to recognize and/or report any sensation that the physician would interpret as atypical during block placement *(hereafter referred to as heavy sedation)*. This seemingly simple question is indeed tremendously complex. Central to its answer is whether or not the subjective sensations that herald systemic local anesthetic toxicity or impending neural injury are specific and/or sensitive enough to constitute reliable, consistent warning signs. If these symptoms are indeed reliable, do they substantively differ depending on the patient's degree of wakefulness? Finally, should recommendations regarding block placement in anesthetized or heavily sedated patients differ based on patient age, block site, or risk-to-benefit ratio?

Avoiding systemic (cardiac or central nervous system) local anesthetic toxicity is predicated on early detection of intravascular injection of local anesthetic. This is accomplished using objective measures such as test doses or the awareness of subjective symptoms of local anesthetic toxicity—including auditory enhancement, circumoral numbness, or metallic taste. Seizures after local anesthetic injection into arteries directly supplying the brain occur too rapidly for any warning to be effective. However, seizures or cardiac signs consequent to tissue absorption typically happen after detection measures are complete. Because subjective signs of local anesthetic toxicity are unreliable even in mildly sedated patients,[51] only imperfect objective measures such as epinephrine-containing test doses[52] can potentially detect intravenous local anesthetic injection, regardless of patient wakefulness. Furthermore, anesthetic and sedative agents can lower the risk of systemic local anesthetic toxicity by raising seizure threshold and altering untoward hemodynamic manifestations of local anesthetic toxicity (Table 5).[53]

Patient wakefulness as a factor related to neuraxial or peripheral nerve injury is more complicated. Proponents for only performing blocks in patients that are mildly to moderately sedated argue that such patients are able to recognize and communicate to the anesthesiologist worrisome sensations or pain, which in turn may modify the anesthetic procedure and prevent or lessen the severity of injury. Proponents for performing blocks in anesthetized or heavily sedated patients argue that this practice promotes the benefits of regional anesthesia to a wider range of patients who may otherwise refuse the procedure because of anxiety, or may reduce the likelihood of unintentional movement during procedures near critical structures. The latter point is debatable, because disinhibited patients may also move at inopportune times. Furthermore, these proponents note that neural injury has been reported in both anesthetized and awake patients. There is no scientifically valid answer to this question; randomized controlled trials are unlikely because of the large numbers of patients that would be required for statistical validity. Existing animal and human data on this topic suggest the following: (1) the experience of a paresthesia or pain on injection during block placement is neither sensitive nor specific for nerve injury, even though it may be sensitive for needle-to-nerve proximity; (2) neuraxial and peripheral nerve injury has been reported both in awake patients who experienced

Table 5. Recommendations: Performing Regional Anesthesia in Anesthetized or Heavily Sedated* Patients

Limiting local anesthetic systemic toxicity
- The potential ability of general anesthesia or heavy sedation to obscure early signs of *systemic local anesthetic toxicity* is not a valid reason to forgo performing peripheral nerve or epidural blocks in anesthetized or heavily sedated patients. (Class I)

Limiting neural injury

Monitoring and prevention
- There are no data to support the concept that peripheral nerve stimulation or ultrasound guidance, and/or injection pressure monitoring reduce the risk of peripheral nerve injury in patients under general anesthesia or heavy sedation. (Class I)
- Because ultrasound-guided peripheral nerve block and pressure monitoring are relatively new technologies, this recommendation may change with the acquisition of more clinical experience and data.

Adult neuraxis
- Warning signs, such as paresthesia or pain on injection of local anesthetic, inconsistently herald needle contact with the spinal cord. Nevertheless, some patients do report warning signs of needle-to-neuraxis proximity. General anesthesia or heavy sedation removes any ability for the patient to recognize and report warning signs. This suggests that neuraxial regional anesthesia should be performed rarely in adult patients whose sensorium is compromised by general anesthesia or heavy sedation. (Class II)

Pediatric neuraxis
- The benefit of ensuring a cooperative and immobile infant or child may outweigh the risk of performing neuraxial regional anesthesia in pediatric patients undergoing general anesthesia or heavy sedation. The overall risk of neuraxial anesthesia should be weighed against its expected benefit. (Class II)

Interscalene blocks
- Case reports document spinal cord injury during the placement of interscalene blocks in patients under general anesthesia, which heightens concern associated with this practice. Interscalene blocks should not be performed in anesthetized or heavily sedated adult or pediatric patients. (Class I)

Adult peripheral nerve blocks
- Because general anesthesia or heavy sedation removes all opportunity for adults to communicate symptoms of potential nerve injury, peripheral nerve block should not be routinely performed in most adults during general anesthesia or heavy sedation. However, the risk-to-benefit ratio of performing peripheral nerve block under these conditions may improve in select patient populations (e.g., dementia, developmental delay, or when unintended movement could compromise vital structures). (Class II)

Pediatric peripheral nerve blocks
- Regardless of wakefulness, infants and children may be unable to communicate symptoms of potential peripheral nerve injury. However, uncontrolled movement may increase the risk of injury. Therefore, the placement of peripheral nerve blocks in children undergoing general anesthesia or heavy sedation may be appropriate after duly considering individual risk-to-benefit ratio. (Class II)

*Anesthetized refers to patients under general anesthesia. Heavy sedation is defined as the patient being sedated to the point of being unable to recognize and/or report any sensation that the physician would interpret as atypical during block placement.

no atypical sensation, and in those who experienced severe paresthesia or pain on injection (with or without subsequent injection of local anesthetic); and (3) awake patients most commonly suffer no injury regardless of the presence or absence of atypical sensation during nerve block placement. Thus, the presence of general anesthesia or heavy sedation eliminates patient recognition and/or report of abnormal sensation, but may or may not impact the actual occurrence of injury.

While acknowledging the conflicting literature relevant to this topic, the Panel's conservative opinion is that general anesthesia or heavy sedation removes all opportunity for the patient and/or physician to recognize, report, and respond to an atypical symptom during block placement. This opinion is in part based on a major unknown in anesthesia-related nerve injury—how often, when a patient reports an atypical sensation or the anesthesiologist perceives something atypical during block performance, does the anesthesiologist consciously or unconsciously modify technique, possibly avoiding injury? Therefore, the weight of the Panel's opinion is that regional anesthetic or pain blocks should not be performed in adults with concurrent general anesthesia or heavy sedation except in those circumstances when the physician and patient conclude that benefit clearly outweighs risk. The Panel further acknowledges that the risk of injuring an anesthetized, heavily sedated, or awake patient may differ as a function of block site. For instance, most reports of injury involve interscalene block in anesthetized or heavily sedated patients, thus the Panel makes a separate recommendation specific to interscalene block (Table 5). However, there are relatively fewer reports of injury to lower extremity nerves in anesthetized or heavily sedated patients.[54] Whether this variation in reported injury is a function of relative block frequency, practice patterns, or reflects an inherent difference in risk is unknown. Finally, data are limited with regards to the risk, if any, of performing peripheral nerve blocks in the setting of an incomplete proximal peripheral nerve or plexus block, or an unresolved neuraxial block. However, several studies have linked selective nerve "rescue blocks" to peripheral nerve injury.[55,56]

There is no localization or monitoring device, or approach to the neuraxis, that ensures protection from nerve injury. Some studies have compared paresthesia with peripheral nerve stimulation as

indicators of needle-to-nerve contact,[31,32] while another has compared paresthesia or peripheral nerve stimulation with ultrasound-guided nerve localization.[33] These studies clearly illustrate the differences between localization modalities, but fail to determine superiority. Importantly, none of these observations have been clinically linked to fewer neural injuries. The use of a peripheral nerve stimulator does not prevent nerve injury in anesthetized patients.[57] There are no data to establish the safety of performing ultrasound-guided blocks in anesthetized or heavily sedated patients. Similarly, recent data suggest that high pressures during the injection of intrafascicular local anesthetic is frequently, but not always, associated with neural injury in dogs,[34] and methods have been proposed to avoid high injection pressure.[35] In part because ultrasound and pressure monitoring are relatively new technologies, there are no human data to confirm or refute these findings. Finally, there is no clinical evidence in nonanesthetized patients, that approaching the epidural space at the lumbar level is more or less safe than at the thoracic level;[58,59] therefore, there is no reason to assume that either approach is inherently safer in the anesthetized or heavily sedated patient.

Recognizing the absence of incontrovertible clinical data and the conflicting nature of case reports and case series regarding neural injury as a function of patient wakefulness,[53] the Practice Advisory's recommendations are listed in Table 5.

Performing regional anesthesia or pain procedures in anesthetized or heavily sedated pediatric patients represents a distinct subset of recommendations, which in part recognizes that this represents standard practice for many anesthesiologists. The Panel acknowledges that there are no data to confirm or refute the concept that performing blocks in anesthetized or heavily sedated pediatric patients is inherently riskier or safer than doing so in adults. Particularly with infants and younger children, the ability to recognize and verbalize specific block-related sensations may be absent regardless of wakefulness. Conversely, a struggling child may well increase the risk of an untoward event during needle placement. Thus, the Practice Advisory recommends that performing neuraxial and peripheral nerve block in anesthetized or heavily sedated pediatric patients may constitute an acceptable benefit-to-risk ratio (Table 5). Although ultrasound can accurately determine the skin-to-ligamentum flavum distance in infants and children,[60] there is no clinical evidence that such preprocedural measurements will increase safety.

Table 6. Recommendations: Transforaminal Injection of Steroids

- To avoid direct injection into critical structures, final position of an immobile needle during transforaminal injection should be confirmed using anterior-posterior and lateral radiography. (Class III)
- After the final needle position is confirmed, injection of radiographic contrast under real-time fluoroscopy should be used to exclude intra-arterial needle location *before* injection of particulate steroid. When intra-arterial injection occurs, the needle should be removed without subsequent injection of steroid, and an alternate approach (e.g., interlaminar route) should be used. (Class III)
- When available, monitoring the injection using digital subtraction imaging technology is recommended. (Class III)

Transforaminal Injection of Steroids

Transforaminal injection of steroids, often used in the treatment of acute radicular pain, has been linked to cases of spinal cord infarction, cortical blindness, paralysis, and death.[24,50,61] The presumed mechanism of these complications involves unintentional needle entry into a small artery that traverses the intervertebral foramen to join the arterial supply to the spinal cord or posterior circulation of the brain. This can occur at various levels, including the vertebral artery anterior to the cervical intervertebral foramina, or the spinal medullary or radicular arteries within the foramina at variable levels within the cervical,[62,63] thoracic, lumbar, and sacral portions of the spine. Subsequent injection of particulate steroid preparations can result in occlusion of the distal arterioles within the spinal cord or brain and lead to infarction.[61] In vitro studies note that methylprednisolone has the largest particles, betamethasone the smallest, and dexamethasone has no particulate matter.[64] While evidence of unintended injection into perispinal vessels during transforaminal injection has been reported, direct evidence to confirm or refute the role of particulate steroids in causing subsequent neuronal injury is lacking (Table 6).

Summary

Neurologic complications associated with regional anesthesia and pain medicine are rare—particularly those complications that do not involve hematoma or infection. Understanding the pathophysiology and risk factors associated with neuraxial and peripheral nerve injury may allow anesthesiologists to minimize the number of adverse neurologic outcomes. Unfortunately, even with flawless care of otherwise healthy patients by well trained physicians, these complications are neither completely predictable nor preventable. This Practice Advisory offers a number of recommendations specific to common clinical scenarios encountered in everyday practice.

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