The Second ASRA Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine

Executive Summary 2015

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Abstract: Neurologic injury associated with regional anesthetic or pain medicine procedures is extremely rare. The Second American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine focuses on those complications associated with mechanical, ischemic, or neurotoxic injury of the neuraxis or peripheral nervous system. As with the first advisory, this iteration does not focus on hemorrhagic or infectious complications or local anesthetic systemic toxicity, all of which are the subjects of separate practice advisories. The current advisory offers recommendations to aid in the understanding and potential limitation of rare neurologic complications that may arise during the practice of regional anesthesia and/or interventional pain medicine.

What's New: The Second American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine updates information that was originally presented at the Society's first open forum on this subject (2005) and published in 2008. Portions of the second advisory were presented in an open forum (2012) and are herein updated, with attention to those topics subject to evolving knowledge since the first and second advisory conferences. The second advisory briefly summarizes recommendations that have not changed substantially. New to this iteration of the advisory is information related to the risk of nerve injury inherent to common orthopedic surgical procedures. Recommendations are expanded regarding the preventive role of various monitoring technologies such as ultrasound guidance and injection pressure monitoring. New clinical recommendations focus on emerging concerns including spinal stenosis and vertebral canal pathologies, blood pressure management during neuraxial anesthesia, administering blocks in anesthetized or deeply sedated patients, patients with preexisting neurologic disease, and inflammatory neuropathies. An updated diagnostic and treatment algorithm is presented.

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In 2005, the American Society of Regional Anesthesia and Pain Medicine (ASRA) convened a group of experts to develop a practice advisory on neurologic complications associated with regional anesthesia and pain medicine. That initiative resulted in a series of articles published in 2008.[1–6] Consistent with ASRA's commitment to update its practice advisories as new knowledge emerges, the Society convened its second practice advisory in 2012 with the same goal, "to provide information for practitioners of regional anesthesia and pain medicine regarding the etiology, differential diagnosis, prevention, and treatment of neurologic complications."[4] As before, the current practice advisory focuses on neurologic injuries apart from those caused by hemorrhagic or infectious complications or local anesthetic systemic toxicity, which are the subjects of other ASRA-sponsored practice advisories.[7–9] This executive summary condenses findings and recommendations from subtopics of the second practice advisory, which reflects both the proceedings of the conference and interval updates. Practitioners are encouraged to read the supporting articles that accompany this summary; they contain the details on which individual recommendations are based.[10–16]

"Consistent with a recent editorial call to focus practice advisory and consensus conference updates on new material,[17] most supporting articles for individual topics considered by this advisory are built on 2 components. First, to provide perspective, those topics and associated recommendations for which no substantially new knowledge has emerged are reviewed briefly. To provide consistency across time or when appropriate, text and especially recommendations are presented essentially *verbatim* from those of our original work. The second component focuses on topics that have significantly new information to add to our previous understanding and/or that we felt deserved more extensive discussion than was provided in the first iteration of this advisory."[13] Completely new to the second practice advisory is an in-depth presentation of baseline nerve injury risk inherent to common elective orthopedic surgical procedures.[11,12,14] With the growth of registries and their impact on determining accurate and contemporary incidences of complications, the panel added expertise in large epidemiologic studies. Similarly, emerging concerns relating to various ischemia-related neuraxial injuries led to the addition of expert neuroanesthesiologists.

METHODS

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

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convened on March 16, 2012, at the Society's 37th Annual Regional Anesthesiology and Acute Pain Medicine meeting in San Diego, California. The ASRA Continuing Medical Education Committee and Board of Directors approved the first and second advisories. Lead members of the advisory panel presented their summaries in a daylong open forum at the annual meeting. Those advisory panelists are listed as authors of this executive summary; additional writers of the individual supporting documents are recognized in the acknowledgments and as individual authors on their articles. Primary panelists were chosen based on their demonstrated expertise in various issues related to neurologic injury and/or guideline creation. As with our first practice advisory, "panelists received no compensation for their contributions nor did any declare a conflict of interest pertinent to the topic" (Dr Hadzic's disclosure appears in the attributions). Panelists were charged with performing an extensive review of the literature, summarizing and presenting their findings at the conference, and producing an article based on their scholarly work. During the San Diego conference, panelists and attendees discussed several issues related to neurologic injury in open forum format. All subsequent recommendations were reviewed and approved by members of the panel. Manuscripts were first peer reviewed internally by at least 3 members of the advisory panel and subsequently peer reviewed externally using this journal's standard peer review process.[4]

Individual supporting articles[10–16] describe the specific search methodology used to research that topic. In general, standard search engines and cross-referenced citations provided the literature basis for the updated material contained within this review.

As paraphrased from our 2008 review, "The strength of scientific evidence that is used to arrive at these recommendations is not easily measured by traditional stratification methodologies such as the Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence."[18] We have used this methodology to rate the level of evidence wherever possible (Appendix 1). However, because of the extreme rarity of the specific complications that are addressed in this article, traditional methodologies such as randomized controlled trials or meta-analyses rarely exist and are unlikely to exist in the future. Our recommendations are therefore based on methodologies that are necessarily less robust, such as anatomic or pathophysiologic studies of human cadavers or animals, nonrandomized trials, retrospective series, case reports, and/or expert opinion. The grading of recommendations offered by this practice advisory has been modified from an American College of Cardiology/American Heart Association construct[19] that classifies the strength of guidelines for perioperative cardiac evaluation[3,13] (Appendix 2).

"Readers of this manuscript are reminded that practice advisories are created when data on a subject are limited or nonexistent. Advisories rely on limited clinical and animal data and, as such, the synthesis and interpretation of data by 1 group of experts may differ from conclusions by another set of equally qualified experts. Thus, practice advisories represent a level of recommendation that is less than that offered by standards or clinical practice guidelines.[20] The recommendations contained herein do not define standard of care. They are not intended to replace clinical judgment as applied to a specific patient scenario. Importantly, in this imperfect setting of controversial topics, limited data, and bias inherent to expert opinion, the Panel consistently tended towards conservative recommendations. These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge of specific complications advances."[4,13]

INCIDENCES OF NEUROLOGICAL INJURY

The incidence of *peripheral nerve injury* (PNI) has remained stable in recent decades, despite the introduction of ultrasound guidance.[21] The reported frequency of long-term neurologic symptoms after peripheral nerve block using ultrasound guidance[22–24] is virtually identical to that reported a decade earlier when peripheral nerve stimulation (PNS) was the primary nerve localization tool.[25,26] In both cases, the reported rate of long-term injury is in the 2 to 4 per 10,000 block range. Conversely, accumulating evidence suggests a rising incidence of some catastrophic *neuraxial* complications associated with regional anesthetic and interventional pain medicine procedures. Whether these observations signal an absolute increase in complication rates is unclear. The reported increase in neuraxial complications may reflect more robust registries and improved reporting mechanisms that allow capture of large population data from single countries and institutions and/or databases from health insurers or national quality assurance records.[22,27–35] It is also possible that incidences have increased as practitioners extend the limits of neuraxial blockade to sicker, older, and frailer patients who are at an increased risk from their comorbidities. Furthermore, perioperative nerve injury incidence data pertinent to either peripheral or neuraxial injury can vary widely between reports for a myriad of reasons, including 1) definition of the complication, 2) duration of follow-up, 3) associated risk factors specific to the cohort studied, 4) robustness of data recording (eg, retrospective vs prospective; registries vs quality assurance databases vs insurance company records vs self-report; single institution vs continent-wide); and 5) discriminating the cause of injury (eg, anesthetic vs surgical vs patient vs a combination; transient vs permanent).

Incidence of Neuraxial Injury

Neuraxial complications are extremely rare, but when they occur, they often result in life-altering injuries. For instance, there were 127 serious complications in more than 1.7 million neuraxial anesthetics performed during the 1990s in Sweden; 85 (67%) of which resulted in permanent injury.[28] The relative occurrence of complications from this report is presented in Table 1. From a medicolegal perspective, closed claims analysis shows that spinal hematomas are the most common cause of neuraxial injuries that proceed to litigation, and these injuries are often permanent. Conversely, infectious complications have a higher likelihood of at least partial recovery.[36]

The incidence of neuraxial injury associated with regional anesthetic techniques varies widely—so much so that it is extremely difficult to cite a meaningful overall risk for injury. Indeed, incidence can even vary among cohorts within the same study. To illustrate this point, the previously noted Swedish study reported vastly different incidences of spinal hematoma—from a risk of 1:200,000 in young women having obstetric epidural blockade to a risk of 1:22,000 in elderly women undergoing hip fracture repair to 1:3600 for those undergoing knee arthroplasty.[28] With regard to infectious complications, risks tend to rise in immunocompromised patients, with prolonged epidural catheterization, when the proceduralist unknowingly harbors virulent nasopharyngeal pathogens and does not wear a mask, and/or when practitioners breach aseptic technique.[7,28,37–40]

Table 2 lists studies reported since 1990 that document incidences of neuraxial injury (often combining hematoma, infection, direct spinal cord injury, etc). These studies point to several common themes. First, the risk of hematoma is higher with epidural than with subarachnoid techniques. Second, the risk of neuraxial injury increases when there are associated coagulation abnormalities (whether from disease or intended anticoagulation), increased

TABLE 1. Relative Frequency of Complications in 1.7 Million Neuraxial Blocks

	Epidural Blockade	Combined Spinal-Epidural Blockade	Spinal Blockade	Continuous Spinal Blockade	Total
Spinal hematoma	21	4	7	1	33
Cauda equina syndrome	8	4	18	2	32
Purulent meningitis	5	1	20	3	29
Epidural abscess	12	—	1	—	13
Traumatic cord lesions	8	—	1	—	9
Cranial subdural hematoma	3	—	2	—	5
Paraparesis	3	—	1	—	4
Other	2	—	—	—	2
Total	62	9	50	6	127

Eight cases of spinal hematoma were associated with thoracic epidural blockade and 17 cases with lumbar epidural blockade.
Data from Moen et al.[28] Used with permission.

age, or female sex. Furthermore, concurrent spinal stenosis or some preexisting neurologic diseases may worsen injury severity in the presence of neuraxial hemorrhage or infection. Third, risk is lower for obstetrical and higher for orthopedic surgeries. Fourth, risk varies when segregated by final outcome (temporary vs permanent vs death).

To illustrate how incidence data can vary depending on how they are collected and what specific population they reflect, consider the following approximations as presented in Table 2. Preexisting neurologic disease may affect overall injury incidence: patients with spinal canal pathology or some preexisting neurologic diseases (especially diabetes mellitus) may experience a transient or permanent new neurologic deficit, or worsening of an existing deficit, in 0.3% to 1.1% of neuraxial anesthetics.[49,50,58] Conversely, in the general population, the incidence of neuraxial injury from any cause is much less, ranging from less than 0.001% to 0.07%. If one defines serious neuraxial complications based on the need for emergency decompressive surgery, injury incidence ranges from less than 0.01% to 0.05%. Indeed, when propensity scoring was used to remove important baseline differences between patients who underwent intermediate- to high-risk noncardiac surgery with either epidural or general anesthesia, there was actually no difference in the necessity for decompressive laminectomy at 30 days.[67] Overall, 3 studies point to an approximate 1:8000 incidence of laminectomy after neuraxial blockade.[27,52,67] Still another way to view incidence data is by using pessimistic versus optimistic estimates. The United Kingdom National Health Service has estimated the risk of paraplegia or death from neuraxial techniques from a pessimistic 1.8:100,000 (95% confidence interval [95% CI], 1.0–3.1) to an optimistic 0.7:100,000 (95% CI, 0–1.6). Similarly, the risk of permanent injury (but not death or paraplegia) ranged from a pessimistic 1:5800 adult epidural anesthetic blocks to an optimistic 1:12,200.[27] Thus, incidence data from neuraxial injury vary widely in accordance with those circumstances that frame the reporting process.

Incidence of PNI

Similar to neuraxial injuries, the reported incidence of PNI associated with regional anesthesia and pain medicine techniques is quite variable. In addition to those factors mentioned for neuraxial injury, the type of peripheral nerve block and its use relative to other blocks may influence injury rate. Because proximal nerves contain a higher proportion of neural tissue as compared with connective tissue,[68] it has been speculated that proximal nerve blocks are riskier than more distal approaches. However, there are no convincing data to confirm or refute this notion.[22,26,35,69] Evidence strongly suggests that the choice to use a regional anesthetic technique (neuraxial, peripheral, or combined) for total joint arthroplasties does not inherently increase the risk for neurologic injury when compared with general anesthesia alone.[70–72] A large retrospective study has also shown that peripheral nerve blocks are not an independent risk factor for perioperative nerve injury.[73]

Table 3 details the incidences of neurologic outcomes associated with peripheral nerve blockade reported since 1997. Consistent with previous reviews,[35,100] early transient postoperative neurologic symptoms (PONSs) are very common in the first days to month after peripheral nerve blockade. However, the incidence is reduced sequentially with time—0% to 2.2% at 3 months, 0% to 0.8% at 6 months, and 0% to 0.2% at 1 year. Importantly, PNIs are not all block related. For perspective, the overall incidence of perioperative nerve injury in more than 380,000 operations conducted for 10 years at a single institution was 0.03%; perioperative nerve injury was associated with hypertension and smoking but not peripheral nerve block.[73]

In summary, the incidence of perioperative nerve injury is extremely difficult to pinpoint with any degree of accuracy. We have instead chosen to present several different approaches to incidence reporting. The incidence of injury after neuraxial blockade is extremely low, but the injuries are often permanent. Conversely, PONSs after peripheral nerve blockade are common but rarely result in long-term or permanent injury. Complicating this analysis are examples of how individual hospital systems can influence patient outcomes when practices are vigilant, evidence based, and use rapid diagnosis and early treatment.[28,32,64] This implies that decreased injury rates and better patient outcomes are attainable when hospitals develop systems that signal risk factors for neuraxial complications (such as concurrent anticoagulation) or devise emergency diagnostic and therapeutic pathways for when a potentially reversible neuraxial injury is suspected.

NEUROLOGIC COMPLICATIONS OF ELECTIVE ORTHOPEDIC SURGERIES

New to this practice advisory is a series of articles[11,12,14] that explore the rate of neurologic complications related to common elective orthopedic surgical procedures. Knowledge of these injuries and their mechanisms is beneficial for the perioperative physician to ascertain potential etiologies for perioperative neural

TABLE 2. Serious Neurologic Complications After Neuraxial Blockade—As Reported Since 1990

Author, Year	Type	N	Complication (n)	Incidence (%)	Potential Risk Factors	Comment/Outcome
Scott and Hibbard, 1990[41]	E	505,000	Permanent disability (5)	0.001		Postal questionnaire, data from 203 obstetric units
Dahlgren and Tornebrandt, 1995[42]	S, E	17,733	Hematoma (3)	0.03 (E)	Impaired coagulation	Paraplegia in 9232 epidural techniques
Wulf, 1996[43]	S, E	1,334,506	Hematoma (6) Serious complications (34)	0.0005 0.005	Impaired coagulation and anticoagulant therapy, ankylosing spondylitis	Risk of hematoma estimated from analysis of case reports/series where denominator could be estimated; however, in total, 51 case reports identified 1966–1985
Giaufré et al, 1996[44]	E, C	15,013	Neurologic complication	0	—	Pediatric cohort, caudal most frequently performed CNB
Aromaa et al, 1997[34]	S, E	720,000	Hematoma (5)	0.005 (S) 0.005 (E)	Spinal canal stenosis, preexisting neurological or vascular disease	Reports from a no-fault insurance scheme. 25 and 9 serious complications from S and E, respectively, occurred, including paraplegia (5), paraparesis (1), CES (2), other permanent deficits (8) for S and E combined
Auroy et al, 1997[25]	S, E	71,053	Radiculopathy (24) CES (5) paraplegia (1)	0.007*	Paresthesia during puncture, pain during injection, intraoperative, hypovolemic hypotension	All presented within 48 h and resolved within 3 mo except for paraplegia (1 patient), radiculopathy (3 patients), CES (1 patient). There were no hematomas
Wang et al, 1999[32]	E	17, 372	Abscess (9)	0.05	Immune status, prolonged catheterization, delayed diagnosis	Poor neurological outcome in 4 of 9 patients: paraplegia (2), paraparesis (2), operative intervention required in 0.01%
Auroy et al, 2002[26]	S, E	76, 630	Peripheral neuropathy (11) CES (3)	0.007†	Lidocaine > bupivacaine; paresthesia during puncture	9 of 14 complications including 3 CESs occurred in nonobstetric population (n = 41, 000). 3 complications persisting at 6 mo
Horlocker et al, 2003[45]	E	4298	Neurologic complication (0)	0.08§	—	Lumbar epidural placement under general anesthesia
Moen et al, 2004[28]	S, E	1, 260, 000	Hematoma	0.006§	Orthopedic surgery, epidural anesthesia, spinal canal stenosis	Higher risk with female sex, age, degenerative change in vertebrae. Lower risk with obstetrics
Lee et al, 2004[36]	E	821	Hematoma, abscess	—	Hematoma associated with coagulopathy in 72% of cases	Closed claims analysis, denominator unknown. Hematoma is most common cause (57%) of nonobstetric injury, worse outcome compared with infection
Ruppen et al, 2006[46]	E	1,370,000	Hematoma (6) Epidural infection (11) Persistent neurological injury (3)	0.0006 0.0009 0.0004	—	Obstetric anesthesia/analgesia, results pooled from 27 studies from 1966 to 2005
Ruppen et al, 2006[47]	E	14,105	Hematoma (0)	0.02§	—	Data pooled from 12 studies of cardiac, thoracic, and vascular surgery
DeVera et al, 2006[48]	E	579	Neurologic complication	0	—	All CNB performed in anesthetized children

Hebl et al, 2006[49]	S, E	567	New neurologic deficits (2)	0.4	Cohort–preexisting peripheral neuropathies	Exacerbation of diabetic neuropathy (1) causing urinary retention; lumbar plexopathy (1) symptoms improving at 1 y
Hebl et al, 2006[50]	S, E, CSE	139	New neurologic deficits (0)	0.3†	Cohort–preexisting CNS disorders	—
de Sèze et al, 2007[51]	S, E	966,000–1,064,504	Neurologic complication (12)	0.001	Mechanisms of injury: hemorrhage (3), direct trauma (2), associated anomaly (2), ischemia (1), uncertain (4)	Cohort of patients admitted to spinal cord injury units. Sequelae—paraplegia (1), monoparesis (2), injury to single nerve (2), bladder/sphincter dysfunction (5), other (2)
Cameron et al, 2007[52]	E	8210	Hematoma, abscess	0.1	—	Operative intervention 0.01%. There were no permanent neurologic deficits
Christie and McCabe, 2007[53]	E	8100	Hematoma (3) Abscess (6) Meningitis (3)	0.04 0.0007 0.04	Immune status, low-molecular-weight heparin	Operative intervention (0.05%). Complete recovery in patients with meningitis, 5 of 6 with abscess and 1 of 3 with hematoma. 3 patients had permanent neurologic deficits
Pöpping et al, 2008[54]	E	14, 223	Hematoma (3), Abscess (2), Meningitis (1)	0.04	Lower limb surgery, elderly female patients	Operative intervention (0.007%). Permanent neurologic deficit (urinary incontinence) in 1 patient with abscess
Cook et al, 2009[27]	E, S, CSE, C	707, 455	Paraplegia/death (13) Permanent injury (30) Permanent harm (postoperative E)	0.002‡ 0.04 0.02	Postoperative epidural analgesia, CSE	"Pessimistic" incidences reported in this table. 30 complications used for "pessimistic" incidences including abscess (8), hematoma (5), nerve injury (7), ischemia (4). 22 of 54 patients made complete recovery
Li et al, 2010[55]	E	125,821	Hematoma	0.002	Emergency surgery, bacterial infection	—
Ecoffey et al, 2010[56]	C, E, S	10, 556	Neurologic complication	0	—	Pediatric regional anesthesia, minor events of duration 48 h to 9 mo
Wallace et al, 2010[57]	E	415	Abscess (2)	0.48	Cohort–open abdominal aortic aneurysm repair	6 patients required MRI
Hebl et al, 2010[58]	S, E	937	Neurologic complication (10)	1.1	Cohort– spinal canal pathology, including spinal stenosis and lumbar disk disease	Deficits coincided with operative side in 5 of 6 patients having unilateral surgery, difficulty separating etiologies—surgical, anesthetic, or evolution of spinal pathology
Liu et al, 2011[59]	E	4365	Hematoma (0)	0.069§	—	4365 patients had uncomplicated removal of epidural catheters despite INRs ranging from 1.5 to 5.9
Volk et al, 2012[31]	E	33,142	Hematoma (6)	0.02		General surgical population
Polaner et al, 2012[30]	All	9156	Neurologic complication	0.02‖	—	Pediatric regional anesthesia

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TABLE 2. *(Continued)*

Author, Year	Type	N	Complication (n)	Incidence (%)	Potential Risk Factors	Comment/Outcome
Sviggum et al, 2012[60]	S	12,465	Neurologic complication	0.04	Chlorhexidine gluconate skin asepsis did not increase risk of complications	All complications resolved by 30 d
Bateman et al, 2013[61]	E	62,450	Hematoma (7)	0.01	Anticoagulant guidelines not adhered to, perioperative epidural analgesia	All complications occurred in patients with perioperative E, no complications in 79,837 obstetric patients
Hemmerling et al, 2013[62]	E	16,477	Hematoma (3)	0.02	Risk comparison with other medical and nonmedical activities	Cohort comprises all publications between 1966 and 2012
Pitkänen et al, 2013[29]	S, E, CSE	1,372,000	Neuraxial hematoma (13)	0.0001 (S) 0.004 (E) 0.006 (CSE)	Anticoagulant guidelines not adhered to, spinal canal stenosis	10-y-long nationwide study from no-fault insurance system in Finland. Sequelae–paraplegia (4), paraparesis (4), incontinence (2), CES (1), recovery (1)
Ehrenfeld et al, 2013[63]	E	43,200	Hematoma (6)	0.01	Perioperative anticoagulation	Cases identified using multiple search strategies, lower extremity weakness present in all cases. Sequelae–paralysis (1), paraparesis (2), recovery (3)
Pumberger et al, 2013[64]	E, S	100,027	Hematoma (8)	0.008	Perioperative anticoagulation	Total hip and knee arthroplasty
Kang et al, 2014[65]	E	5083	Hematoma (1)	0.02		Nonobstetric case load
Gulur et al, 2015[66]	E	11,600	Hematoma (2)	0.02	Abnormal coagulation	Risk 1 in 315 patients with abnormal coagulation

*Incidence 3 months; †Incidence 6 months postoperatively; ‡No complications occurred, upper limit of 95% confidence level reported; §There were no deaths or complications with sequelae lasting more than 3 months, upper limit of 95% confidence level presented; ‖Incidence of final outcome reported.

E indicates epidural anesthesia; S, spinal anesthesia; C, caudal anesthesia; CSE, combined spinal-epidural anesthesia; CNB, central neuraxial block; N, denominator; n, number of events.

TABLE 3. Incidence of Neurologic Outcomes Associated With Peripheral Nerve Blockade—As Reported Since 1997

Author, Year	PNB Type	Technique Used	N	Neurologic Outcome	Incidence (%) (time)*	Potential Risk Factors	Comment
Giaufré et al, 1996[44]	UL, LL	-	4090		0	-	No complication reported after PNB
Auroy et al, 1997[25]	All	-	21,278	Radiculopathy	0 (3 mo)	Paresthesia during puncture, pain during injection	Transient radiculopathy in 0.02%
Fanelli et al, 1999[69]	UL, LL	NS	3996	Neurological complication	0.03 (3 mo)	Tourniquet inflation pressure >400 mm Hg	Transient neurologic dysfunction in 1.7%. All resolved by 6 mo
Borgeat et al, 2001[74]	ISB	NS	521	Plexus lesion	0.2 (9 mo)	Sulcus ulnaris and carpal tunnel syndromes	Neurologic features present in 7.9%, 3.9%, and 0.9% at 1, 3, and 6 mo; serial EMGs performed
Hebl et al, 2001[75]	Ax	NS, LM	100	PONS	6	Bupivacaine (0.375%): an independent risk factor	Anesthetic (GA or Ax block) did not affect neurological outcome after UT
Weber and Jain, 2002[76]	ISB	NS	218	Neurologic complication‡	0.5 (2 y)	Pain during ISB	Retrospective chart review, permanent injury in 1 patient
Auroy et al, 2002[26]	All	NS, LM	50,223	Neurologic complication‡	0.014 (6 mo)	Popliteal SNB (0.3%), paresthesia during PNB	50,223 PNB, 12 complications in total, 7 present at 6 mo
Bergman et al, 2003[77]	Ax, CPNB	NS, LM	405	Neurologic complication‡	0.5	Profound sensorimotor deficits–poor recovery (1 patient)	2 of 4 patients with new deficits were related to anesthesia
Capdevila et al, 2005[78]	CPNB	NS	1416	Neurologic complication‡	0 (3 mo)	Anesthetized during PNB	Incidence 0.21% in early postoperative period. All resolved by 3 mo
Candido et al, 2005[79]	ISB	NS	693	Neurologic sequelae	0.1 (3 mo)	Paresthesia at needle insertion, ISB site pain or bruising at 24 h	Neurologic sequelae present in 3.3%, 0.1% at 1, 3 mo
Liguori et al, 2006[80]	ISB	NS, MP	218	PONS	0 (12 mo)	PONS: 10.1% with NS, 9.3% with MP	Median duration of PONS, 2 mo. Resolved within 1 y
Bishop et al, 2006[81]	ISB	NS	277	Neuropathy	0	—	Transient sensory neuropathies all resolved (5 wk)
Ben-David et al, 2006[82]	Ax	TA	336	Neurologic complication‡	0.3	Nerve injury: 7.5% with PNB performed under GA vs 2.6% with sedation	All complications resolved except for 1 permanent injury
Faryniarz et al, 2006[83]	ISB	NS	133	Neuropraxia	0 (2 mo)	—	Detailed perioperative neurological assessment, all events transient (1.4%)
DeVera et al, 2006[48]	UL, LL	NS	1529	PONS	0 (1 mo)	Duration of tourniquet inflation	Persistent paresthesia after FNB, resolved by 1 mo
Wiegel et al, 2007[84]	CPNB	NS	1398	Neurologic complication‡	0.07	—	Retroperitoneal hematoma led to long-term femoral neuropathy
Lenters et al, 2007[85]	ISB	NS, MP	3172	Neurologic complication‡	0.2–0.4 (6 mo)	Volume of practice	Incidence of serious, long-term PNB-related injury higher than other studies
Pöpping et al, 2008[54]	CPNB	—	3111	Neurologic complication	0 (4 wk)	Incidence 0.06%, complete recovery within 4 wk	Difficulty distinguishing anesthetic from nonanesthetic etiology after ISB
Christ et al, 2009[86]	ISB	NS	273	Neurologic complication‡	0 (6 mo)	Superficial cervical plexus involvement: 7.7% at 24 h, 1.8% at 1 mo	All deficits resolved by 6 mo

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TABLE 3. *(Continued)*

Author, Year	PNB Type	Technique Used	N	Neurologic Outcome	Incidence (%) (time)*	Potential Risk Factors	Comment
Fredrickson and Kilfoyle, 2009[87]	BP, FNB, SNB	US	1010	PNI	0.6 (6 mo)	Paresthesia during PNB	Most PNI unrelated to PNB
Liu et al, 2009[88]	ISB	US	230*	PONS	0.8–1.1 (1 wk)	—	No difference in PONS, US compared with NS
Welch et al, 2009[73]	All		380,680*	PNI	0.03	EA, GA, hypertension, diabetes mellitus, tobacco use, surgical specialty	Retrospective study using 3 databases including QI database
Barrington et al, 2009[22]	All	US, NS, LM	8189	Neurologic complication‡	0.02 (6 mo)	Comorbidities: vascular disease, lumbar stenosis, radiculopathy, neuropathy	Systematic postoperative follow-up. No significant difference: US vs NS techniques
Davis et al, 2009[89]	ISB	US	200	Neurologic deficits	0	—	Transient neurological deficits (1%)
Perlas et al, 2009[90]	SCB	US	510	Neurologic deficits	0	—	0.4% reported transient numbness in fingers
Sharma, 2010[91]	FNB	NS	729*	Femoral neuropathy/neuritis	0.14 (12 mo)	Neuropathy: 0.7% with FNB, 0.4% with no FNB	1 patient after FNB had residual sensory symptoms at 12 mo
Ecoffey et al, 2010[56]	UL, LL, Trunk	Not stated	20, 576	Neurologic complication	0	Pediatric study	Femoral distribution hypoesthesia (iliofascial block) resolved <48 h
Liu et al, 2010[92]	ISB, SCB	US	1169	PONS	0.4	—	No permanent injuries
Jacob et al, 2011[71]	LL	NS, LM	12,329*	PNI	0.79 (3 mo)	Tourniquet time and bilateral surgery	PNI was not associated with PNB or type of anesthesia
Jacob et al, 2011[70]	LL	NS, LM	12,998*	PNI	0.72 (3 mo)	Age, female, surgical duration, posterior approach	PNI was not associated with PNB or type of anesthesia
Misamore et al, 2011[93]	ISB	NS	910	Neurologic complication‡	0.8 (6 mo)	Diffuse mild brachial plexopathy confirmed on EMG	Radial nerve palsy (n = 1), mild forearm/hand paresthesias (n = 5), Horner syndrome (n = 2)
Singh et al, 2012[94]	ISB	US	1319	Neurological complication	0 (4 mo)	Brachial plexitis (3 cases) related to underlying comorbidities	Digital numbness (0.6%), all resolved by 4 mo, ulnar neuropathy (1 case) resolved
Sviggum et al, 2012[72]	ISB	NS, LM	1569	PNI	2.2 (3 mo)	ISB did not increase the risk of PNI. GA used as primary anesthetic in 1569 patients	Complete resolution of symptoms in 97% of patients after TSA
Sites et al, 2012[33]	All	US	12,668	PONS	0.09 (6 mo)	ISB and shoulder surgery	PONS defined as sensory/motor dysfunction >5 d
Orebaugh et al, 2012[24]†	UL, LL	US, NS	9069	Neurologic complication‡	0.04 (6 mo)	No significant difference: US vs NS techniques	1 sensorimotor deficit persisted >1 y after FNB
Polaner et al, 2012[30]	All	US, NS	5761	Neurologic complication	0 (3 mo)	Possible exacerbation of preoperative symptoms after LPB	Pediatric regional anesthesia
Hara et al, 2012[95]	SNB	US	325	Neurologic complication‡	0	Unintentional intraneural injection occurred in 16.3%	No clinical evidence of nerve injury
Henningsen et al, 2013[96]	SNB	US	97	Neurologic complication	0 (6 mo)	Infrapatellar branch involved in 84% (surgical etiology)	Neurologic examination of patients after TKA
Lecours et al, 2013[97]	ICB	US	627	Neurologic complication‡	0.2 (1 y)	1 patients had biceps weakness >1 y	4 patients with features potentially related to ICB

Rohrbaugh et al, 2013[98]	ISB	US or PNS	15,014	Neuropathy	0.03 >6 mo	—	All sitting position, sensory neuropathy, 1 phrenic nerve injury (0.07%)
Nye et al, 2013[99]	CLPB	PNS	213 PONS		2.8 (>6 mo)		Hip arthroplasty cohort

*Indicates elapsed postoperative time period when incidence calculated; PNB, peripheral nerve or plexus block; N, number of PNB procedures or *Number of patients receiving all anesthetic types (GA and regional); CPNB, continuous peripheral nerve block; ISB, interscalene block; ICB, infraclavicular block; Ax, axillary brachial plexus block; BP, brachial plexus; FNB, femoral nerve block; FIB, fascia iliaca block; PCB, psoas compartment block; SNB, sciatic nerve block; UL, upper limb PNB; LL, lower limb PNB; NS, nerve stimulator; LM, landmark; CLPB, continuous lumbar plexus block; TA, transarterial; MP, mechanical paresthesia; US, ultrasound; PNI, new perioperative nerve injury due to any cause; PONS, postoperative neurologic symptom (in distribution of PNB); GA, general anesthesia; EA, epidural anesthesia; EMG, electromyography; QI, Quality improvement; UT, ulnar transposition; TSA, total shoulder arthroplasty; SaNB, saphenous nerve block.

†Results of smaller cohort published in 2009, included in 2012 publication; ‡PNB thought to be the cause.

deficits, which might include surgical, anesthetic, and patient-related factors (Table 4). In consultation with the operating surgeon and neurologist, the knowledgeable anesthesiologist might facilitate global awareness of possible injury mechanisms, which in turn may optimize postoperative diagnostic and therapeutic interventions. Despite this optimistic goal, determining causation in the setting of concurrent surgery and regional anesthesia is often challenging because of confounding factors such as double-crush injury and/or the technical limitations of diagnostic imaging and neurophysiologic testing. Furthermore, orthopedic surgery literature rarely designates nerve injury as a primary outcome, is often retrospective, and therefore lacks sufficient granularity to fully understand the mechanism of injury. These limitations likely result in underreporting. Thus, although the literature affords a glimpse into the "overall baseline nerve injury" associated with specific surgeries, precise determination of causation is often speculative.

Similar to anesthesia-related injuries, the vast majority of neural injuries associated with orthopedic procedures are transient, yet the rate of long-term injury is of consequence. Most injuries result from a short list of perioperative causes such as direct nerve trauma, positioning, stretch, retraction, or compression from hematoma or dressings. What follows is a brief summary of well-recognized injuries specific to surgery type. To more completely understand this topic, we urge study of the supporting articles and their excellent accompanying illustrations.[11,12,14]

Shoulder Surgery

The frequency and etiology of nerve injury associated with shoulder surgery vary by surgical approach. Arthroscopic shoulder surgeries are associated with nerve injury ranging from less than 0.1% to 10%,[11] most of which are caused by surgical traction to improve exposure or by arthroscopic portal placement. Shoulder surgeries performed in the lateral decubitus position are associated with transient neuropraxia affecting the operated limb in up to 10% of patients, especially when documented by intraoperative somatosensory evoked potentials.[101] Portal placement too close to typical nerve pathways is particularly risky for axillary or musculocutaneous nerve injury. These same nerves are at risk during open (nonarthroscopic) shoulder surgeries, but the cause is more likely surgical traction to the arm. Open rotator cuff surgery is associated with mostly transient injuries (<2%), but open shoulder stabilization procedures increase injury frequency up to 8.2%.[102] Anatomic total shoulder replacement is most often associated with diffuse brachial plexus injuries, which may occur transiently in up to 17% of patients. Patients with stiff shoulders or prior shoulder surgery are at an increased risk.[103] The 0.6% to 3.6% incidence of nerve injury associated with reverse total shoulder replacement[11] is 11-fold higher than that reported for anatomic shoulder replacement and is primarily related to the permanent arm lengthening associated with that procedure.[104]

Elbow Surgery

Surgery of the elbow is particularly hazardous because of the minimal soft tissue protection available to the multiple nerves that traverse the joint. Ulnar neuropathy persists in up to 10% of elbow replacement patients.[105] Up to 4.2% of elbow arthroscopies are associated with transient iatrogenic nerve injury[106] in part because portals are placed blindly in a nerve-rich area.

Hip Surgery

The frequency of nerve injury after total hip arthroplasty (THA) varies widely but generally falls in the 1% range.[12] The cause of these injuries is attributed to compression from retractors, traction from intraoperative hip dislocation and manipulation, or excessive leg lengthening. The common peroneal branch of the

sciatic nerve is most frequently injured during THA (0.08%–3.7%)[107]; injuries to the femoral and superior gluteal nerves occur less often. Transient injury to the lateral femoral cutaneous nerve is frequent (15%–88%) after the anterior approach to THA.[108,109] Two conditions uniquely increase the risk of nerve injury associated with primary THA—developmental dysplasia sometimes requires leg lengthening, which increases the risk 4-fold,[110] whereas revision THA increases the risk 3-fold.[111] The incidence of nerve injury associated with hip arthroscopy ranges from 0.4% to 13.3%[12] and carries with it a unique set of traction-associated risks to the pudendal nerve (from longitudinal traction against the pudendal post) or to the sciatic and femoral nerves.[12]

Knee Surgery

The incidence of major nerve injury after total knee arthroplasty (TKA) ranges from 0.3% to 9.5%.[12] The upper end of this incidence range represents injury to the common peroneal nerve, which is particularly at risk in those patients with severe valgus deformity (>12 degrees), flexion contractures (>10 degrees), prolonged tourniquet times (>120 minutes), or preexisting neuraxial neuropathy (spinal stenosis or lumbar radiculopathy). Disruption of the infrapatellar branch of the saphenous nerve and/or the cutaneous nerves of the thigh is quite common but tends to resolve within 2 years. Arthroscopic knee surgeries are associated with frequent (up to 25%) sensory loss to the anterior knee.[112] Similarly, paresthesia from injury to the infrapatellar and sartorial branches of the saphenous nerve is common (up to 75%) after arthroscopic anterior cruciate ligament repair.[113] Inside-out techniques for arthroscopic medial meniscus repair are associated with saphenous nerve injury from direct trauma or suture entrapment.

TABLE 4. Evidence Statements Regarding Anesthetic, Patient, and Surgical Factors That Contribute to Perioperative PNI

Anesthetic Factors

- Postoperative neurological features are more likely to be related to patient and surgical factors than to be related to peripheral nerve blockade (Level 3)
- Peripheral nerve injection injury with local anesthetic is greatest when the injection is intrafascicular in location. This is likely related to:
  - Exposure of axons to vastly higher concentrations of local anesthetics compared with extraneural application of anesthetics and
  - Mechanical damage to the perineurium and associated loss of the protective environment contained within the perineurium (Level 3)
- Intrafascicular injections are associated with higher opening injection pressures and risk of PNI compared with perineural injection (Level 3)
- Local anesthetic toxicity is time and concentration dependent (Level 3)
- Epidural and general anesthetics, but not PNB, have been associated with PNI. Furthermore, PNB is not associated with PNI after TKA, THA, or TSA (Level 2)

Patient Factors

- The presence of a preoperative neurologic deficit or neural compromise theoretically places a patient at increased risk of perioperative PNI (Level 4)
- The ulnar nerve at the elbow and the common peroneal nerve are at increased risk of PNI (Level 3)

Surgical Factors

- Tourniquet neuropathy can be associated with marked clinical deficits and pathological changes on electromyography. The duration of inflation and pressure are important factors contributing to its severity (Level 2)
- Surgical procedures have unique risk profiles (Level 2)
- Inflammatory mechanisms for PNI are recognized and exhibit features that are physically and temporally remote from PNB (Level 4)

Levels of evidence are based on the 2011 Oxford construct.[18]

PNB indicates peripheral nerve block; TSA, total shoulder arthroplasty.

TABLE 5. Recommendations: Factors That May Limit Neuraxial Injury

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

Anatomic Factors

- 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 of the spinal cord. Clinicians are advised to be aware of these anatomic conditions, particularly in patients with challenging surface anatomy *(eg, as may occur with obesity, kyphoscoliosis, and other conditions)*. Ultrasonography or fluoroscopy could be considered as an adjunct for accurate determination of vertebral level in these challenging patients (Class I).
- Surgical positioning, severe spinal stenosis, and specific space-occupying extradural lesions (eg, epidural lipomatosis, ligamentum flavum hypertrophy, synovial cysts, 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 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).
- For patients receiving neuraxial injection for treatment of pain (eg, cervical epidural injection of steroids via an interlaminar route), radiologic imaging studies such as computed tomography or MRI 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).

Physiologic Factors

- 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 American Society of Regional Anesthesia and Pain Medicine Practice Advisories. Such conditions include concurrent or imminent anticoagulation, the use of multiple anticoagulants, improper aseptic technique, and needle placement during untreated active infection (Class I).[7,8,38,39]

Recommendations contained within Table 5 have been modified minimally from our 2008 advisory.[3] Significant changes are in *italics*.

Levels of evidence are based on the 2011 Oxford construct.[18]

Foot and Ankle Surgery

Elective foot and ankle surgery using arthroscopy or involving joint replacement is a relatively new field. Literature related to

nerve injury in these patients is sparse and mostly retrospective. Iatrogenic injury, especially to cutaneous nerves, seems to be relatively common, albeit mostly well tolerated by patients unless the sensory deficit involves the plantar aspect of the foot.[14] Adequate surgical exposure for ankle arthroscopy places all nerves that cross the ankle joint at risk for traction neuropraxia. Cutaneous nerves of the foot are at risk from portal placement or direct surgical trauma during the anterior arthroscopic approach, ankle replacement, or open triple arthrodesis ankle fusion. Fortunately, persistent defects are rare (0.2% at 10 years).[114] Total ankle arthroplasty carries an overall nerve injury rate of 1.3%[115] and most commonly involves the peroneal nerve if the anterior approach is used. Cutaneous nerve sensory deficits after hallux valgus deformity (bunion repair) are poorly documented, and their reported incidence ranges widely.[14]

Recommendations

- Awareness of the causation, location, and frequency of nerve injuries associated with elective orthopedic surgery might assist the anesthesiologist in diagnosis and treatment of perioperative nerve injury. Actual discrimination between surgical, anesthetic, and patient factors is often difficult (Class I).
- Differential diagnosis should include prolonged use of a pneumatic tourniquet (>120 minutes), which has been associated with nerve injury. These injuries often present as diffuse sensorimotor deficits (Class I).
- Consider delaying placement of regional blocks if assessment of postoperative nerve function is important for the surgeon (Class III).

ANATOMY AND PATHOPHYSIOLOGY OF NEURAXIAL INJURY

Since our 2008 practice advisory,[3,4] we have expanded recommendations on 5 specific topics that relate to the anatomy and pathophysiology of spinal cord injury associated with regional anesthesia and pain medicine: spinal stenosis, blood pressure control during neuraxial anesthesia, neuraxial injury subsequent to transforaminal techniques, cauda equina syndrome (CES)/local anesthetic neurotoxicity/arachnoiditis, and performing regional anesthetic or pain procedures in patients receiving general anesthesia or deep sedation.[13,116] Recommendations that remain unchanged from 2008 are summarized in Table 5.

Spinal Stenosis

After gaining attention shortly before the creation of our 2008 advisory,[28,51] evidence has continued to accumulate that suggests an increased risk of spinal cord injury after neuraxial techniques are performed in patients with spinal canal pathology, especially spinal stenosis.[29,58] These studies suggest a slightly increased rate (compared with institutional norms) of new or worsening neurologic deficits in those patients with *known* spinal canal pathology who undergo spinal anesthesia.[58] Conversely, studies also report the *unexpected* discovery of spinal stenosis when (especially elderly women) patients undergo neuroimaging during diagnostic workup for spinal hematoma and CES.[28] It remains unclear if these observations represent cause and effect or simply associate spinal stenosis with the complication. Alternatively, the injuries could have been caused by surgical factors, natural progression of the underlying spinal pathology, or a combination thereof. From a pathophysiologic perspective, spinal stenosis may contribute to spinal injury by reducing the vertebral canal cross-sectional area, thereby inducing spinal cord ischemia via compressive mechanisms and/or by limiting the clearance or free distribution of local anesthetic within the neuraxis, thereby contributing to neurotoxicity.[13] Although the preponderance of these injuries have been associated with epidural or combined spinal-epidural techniques,[28] injuries have also been associated with spinal anesthesia.[58,116]

As supported by a few large population studies and a multitude of case reports and series,[13] the advisory panel speculates that patients with spinal stenosis may be especially vulnerable to

TABLE 6. Recommendations: Patients With Spinal Stenosis

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- Spinal stenosis represents a continuum of spinal canal encroachment by hypertrophied ligamentum flavum, bony overgrowth, and/or degenerative changes such as from osteoporosis or herniated nucleus pulposus. Patients with spinal canal pathology (eg, spinal stenosis, lumbar disk disease) may have clinical or subclinical evidence of a preexisting neurologic deficit because of neural compromise from the disease state. However, even moderately severe spinal stenosis is not always symptomatic; many patients (or their health care providers) are unaware that they have the condition (Class I).
- When neuraxial anesthesia is complicated by the development of mass lesions within the spinal canal (eg, hematoma or abscess), resultant postoperative neurologic complications may be more likely or more severe in patients with spinal stenosis or other obstructive spinal canal pathology, including changes brought on by patient positioning (Class I).
- In patients with known severe spinal stenosis or symptoms suggestive thereof, we recommend that risk-to-benefit be considered before performance of neuraxial anesthesia because of the association of spinal stenosis with neurologic complications in the setting of neuraxial blockade. If neuraxial blockade is performed, we recommend heightened perioperative vigilance for symptoms suggestive of neural compromise (Class II).
- There is no firm linkage to injury if spinal stenosis is at a site distant from the level of neuraxial block placement (Class III).
- If neuraxial anesthesia is planned, the practitioner may consider reducing the total mass (volume × concentration) of local anesthetic in an effort to reduce segmental spread, local anesthetic neurotoxicity (which is related to concentration), and/or facilitate neurologic assessment by earlier block resolution. Although we are unaware of routinely administered volumes of local anesthetic being associated with injury in patients with spinal stenosis, reports have postulated linkage between high volumes and neuraxial injury in the setting of other mass lesions such as epidural lipomatosis (Class III).
- The literature has established an association between spinal stenosis and injury after neuraxial blockade, most often affecting patients in whom the diagnosis of spinal stenosis was made during workup for the injury. There is no clear evidence that spinal stenosis per se caused these injuries (Class II).
- Currently, it is unclear whether the development of new or worsening neurologic symptoms after neuraxial anesthesia or analgesia is caused by surgical factors, the anesthetic technique, the natural progression of spinal pathology, or a combination of these factors (Class II).

neuraxial injury in the concurrent settings of preexisting neuraxial disease, non-neutral positions during the perioperative period (eg, hyperlordosis or extreme lateral flexion), or other conditions that compete with the spinal cord for space within the vertebral canal, for example, epidural hematoma or abscess, spinal arachnoid cyst, or ankylosing spondylitis (Fig. 1). When the diagnosis of moderate-to-severe spinal stenosis is known, we recommend consideration of the risk versus benefit of a neuraxial technique. If such a technique is chosen, we suggest increased vigilance for signs of postoperative neurologic compromise. Finally, we acknowledge that significant spinal stenosis is common (19% prevalence in patients in their sixties[118]) and often unrecognized by both patients and their health care providers. The majority of patients with spinal stenosis tolerate neuraxial blockade without clinically apparent injury. Nevertheless, the panel advises that increased reporting of neuraxial injury in the setting of spinal stenosis should elevate the anesthesiologist's awareness of this disease process. Our recommendations regarding spinal stenosis are presented in Table 6.

Blood Pressure Control During Neuraxial Anesthesia

The current advisory places increased emphasis on the importance of avoiding prolonged hypotension during neuraxial anesthetics (>20%–30% below baseline mean arterial pressure [MAP] especially for 20 minutes or longer).[13] We base this recommendation on evolving knowledge that the lower limit of autoregulation (LLA) for cerebral and spinal cord blood flow (SCBF) is likely higher than previously believed and ongoing case reports and medicolegal experience wherein patients have suffered spinal cord ischemia or infarction in the setting of prolonged hypotension or hypoperfusion.

Perioperative spinal cord ischemia or infarction is an extremely rare event that is most often associated with specific surgeries (aortic, cardiac, spine). Other risk factors for spinal cord infarction include those classically recognized for vascular disease, that is, atherosclerosis, hypertension, and tobacco abuse. An insult to the spinal cord circulation that is sufficient to cause ischemia or infarction implies either mechanical injury to the spinal vasculature, an embolic event, or hypoperfusion, as may occur during prolonged periods of hypotension. Recent data and opinion suggest that the LLA for SCBF is likely closer to a MAP of 60 to 65 mm Hg rather than the classically understood MAP of 50 mm Hg.[119–122] Moreover, direct and surrogate measures of the LLA for cerebral blood flow in humans suggest that the LLA varies widely among subjects and, contrary to common belief, is usually not related to or predicted by baseline blood pressure.[121] There exists a "physiologic reserve" between the LLA and the blood pressure at which cellular injury or death actually occurs. Clinical experience suggests that the vast majority of patients whose blood pressure is low during a neuraxial technique do not suffer spinal cord ischemic injury most likely because 1) the blood pressure is not critically low for that individual (ie, the blood pressure is higher than that patient's LLA or within their physiologic reserve) and/or 2) limited duration at the lower blood pressure. However, case reports also reveal that an extremely small subset of patients either have a higher set point for their personal LLA and/or cannot withstand prolonged periods of "low-normal" blood pressure. Moreover, the risk for ischemic injury is likely increased in these patients when hypotension is interposed with other factors that may compromise SCBF, such as vascular stenosis, embolic phenomena, non-neutral spinal column positioning (eg, hyperlordosis, extreme lateral flexion, or lithotomy), hypocapnia, raised intrathoracic pressure, and/or surgical retraction.

The extreme rarity of perioperative ischemic spinal cord injuries makes it impossible to assume cause and effect in those patients identified with concurrent periods of hypotension particularly when the degree of hypotension is not extreme and/or of extreme duration. Nevertheless, because the chance for recovery after spinal cord infarction is dismal and the ability to predict an individual patient's LLA is clinically difficult if not impossible, the panel "recommends that anesthesiologists strive to maintain blood pressure within 20% to 30% of baseline and that persistent hypotension be treated."[13] If an ischemic injury is suspected, immediate neuroimaging is necessary to rule out a potentially treatable condition, such as spinal hematoma or abscess. If such a condition is excluded, the panel recommends normalizing or increasing the patient's blood pressure to high-normal range and considering cerebrospinal fluid (CSF) drainage. The role of corticosteroids specifically for anesthesia or pain medicine–related injuries is unknown. The use of corticosteroids may be beneficial in instances of direct spinal cord trauma from interventional procedures. Conversely, the known linkages to worsened neurologic outcome from direct corticosteroid-induced neurotoxicity and indirect hyperglycemia lead us to recommend avoiding corticosteroids when spinal cord ischemia is suspected. In either case, maintain normoglycemia by using insulin in those patients with elevated glucose levels. These decisions are best made in consultation with neurological colleagues. Recommendations for the diagnosis and treatment of spinal cord ischemia or spinal cord infarction are presented in Table 7.

Transforaminal Pain Medicine Procedures

Our 2008 practice advisory[4] made recommendations regarding the then emerging awareness of catastrophic neurologic injuries associated with transforaminal pain medicine procedures. In the interim, a collaboration took place between the US Food and Drug Administration Safe Use Initiative and a group with representation from specialties with expertise in interventional treatment of spinal disorders.[123] This initiative puts forth a series of expert opinions meant to improve patient safety during the provision of transforaminal procedures. In addition, a number of case reports and small series continue to describe infarctions of the spinal cord, brainstem, cerebrum, or cerebellum after both cervical[124,125] and lumbar[126,127] transforaminal injections. More evidence for the role of particulate steroids in these injuries has come forth, including reports that the effectiveness of nonparticulate steroidal preparations, such as dexamethasone, may be similar to that of particulate preparations.[128–130] Our previous recommendations regarding transforaminal injections have been modified based on these studies plus the US Food and Drug Administration Safe Use Initiative and are presented in Table 8.

CES, Local Anesthetic Neurotoxicity, and Arachnoiditis

Since the 2008 practice advisory,[3,4] there has been relatively little new data on CES, local anesthetic neurotoxicity, and arachnoiditis—topics that we have loosely combined because of commonality to a presumed etiology that involves neural tissue toxicity. Recommendations specific to these entities are summarized in Table 9.

Cauda Equina Syndrome

Injury to the cauda equina manifests as bowel and bladder dysfunction with various degrees of bilateral lower extremity weakness and sensory impairment. There are multiple etiologies for CES, ranging from neural element compression from hematoma, abscess, or herniated intervertebral discs to poorly understood

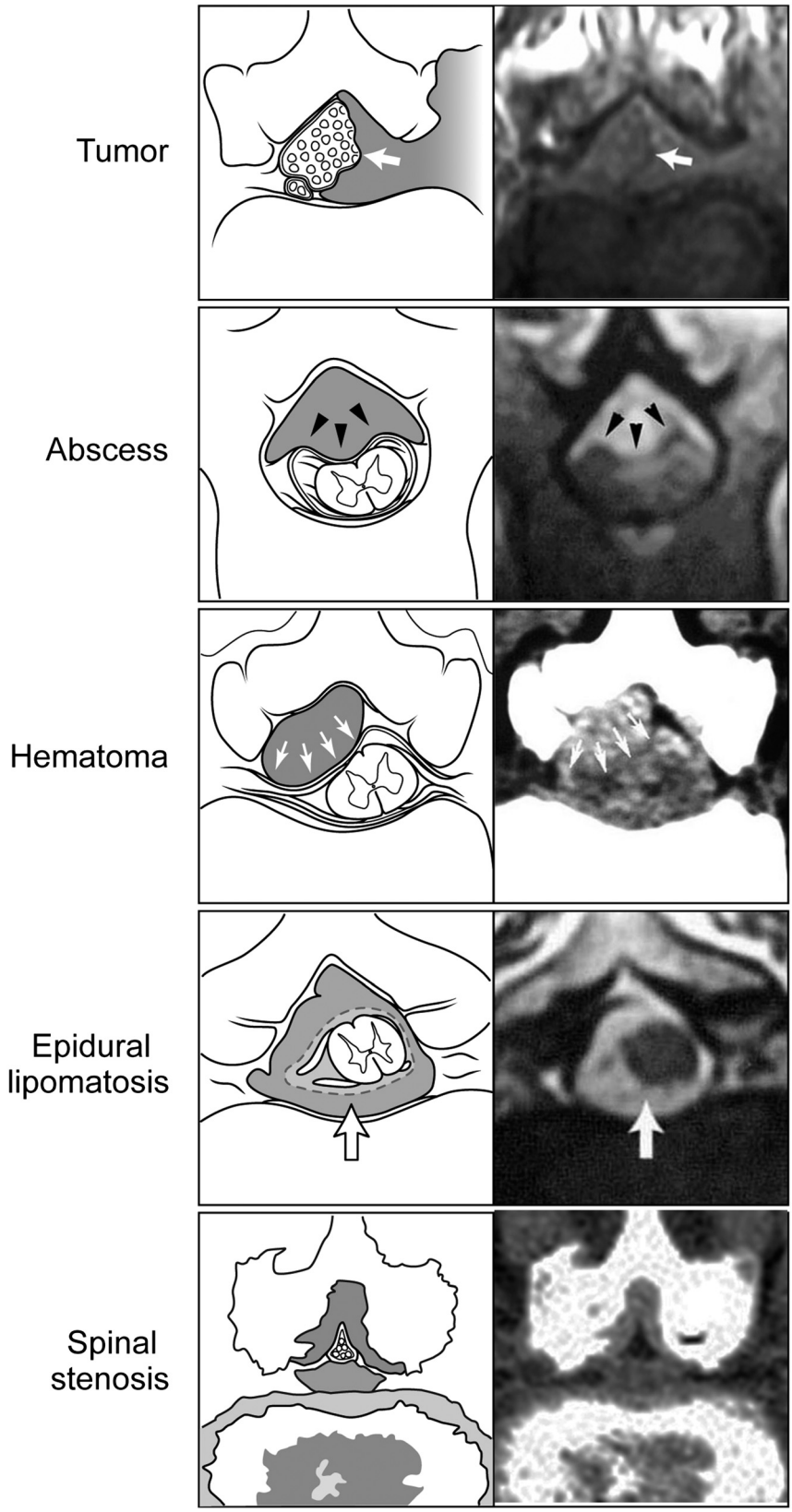

FIGURE 1. Extradural mass lesions. Note how various conditions can reduce spinal canal cross-sectional area and either directly compress the spinal cord or the cauda equina (arrows) or increase epidural space or cerebrospinal fluid pressures through their mass effect. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell, Complications in Regional Anesthesia and Pain Medicine.[117]

TABLE 7. Recommendations: Blood Pressure Control During Neuraxial Anesthesia

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- Local anesthetics, adjuvants, and their combination have variable effects on SCBF. Reduction of SCBF in the presence of local anesthetics and adjuvants typically mirrors reduction in metabolic demand secondary to spinal cord anesthesia. There is no evidence that either intravenous or intrathecal epinephrine or phenylephrine adversely affect SCBF (Class I).
- Our understanding of the LLA of SCBF has evolved recently, based on inferences gained from cerebral LLA studies. Rather than the previously accepted cerebral LLA at a MAP of 50 mm Hg in humans, many experts now believe the cerebral LLA in unanesthetized adults is 60 to 65 mm Hg MAP. There is wide variability of LLA among subjects. Preexisting hypertension seems to be a poor predictor of LLA except at the extremes of hypertension, for example, systolic pressure >160 mm Hg (Class II).
- Case reports attest to an extremely small subset of patients who have sustained cerebral or spinal ischemia associated with periods of severe or prolonged low blood pressure. These rare events stand in stark contrast to the common perioperative occurrence of relative hypotension that does not result in spinal cord ischemia. Presumably, injury does not manifest in most patients because of a physiologic reserve that exists between the LLA and blood pressure thresholds below which neurologic injury occurs (Class III).
- When the LLA of SCBF is approached, specific patient conditions may increase the risk of injury. Such conditions include reduced blood oxygen carrying capacity, impairment of SCBF from obstructing anatomic lesions, and/or increased spinal cord CSF pressure (Class I).
- In the absence of compelling reasons to manage a patient otherwise, we recommend that blood pressures during neuraxial anesthesia be maintained in normal ranges or at least within 20% to 30% of baseline MAP. When MAP goes below these parameters, we recommend that it not be allowed to persist at those levels. Although these recommended parameters are arbitrary, they are inferred based on large population studies that have linked both degree and duration of hypotension to perioperative cerebral, renal, or myocardial injury (Class II).
- When neuraxial anesthesia or analgesia is followed by unexpectedly prolonged sensory or motor blockade, recrudescence of weakness or sensory changes after initial block resolution, or neural blockade outside of the expected distribution of the intended procedure, the anesthesiologist must rule out reversible causes in an expedient manner. At the physician's judgment, this may entail a reduction or discontinuation of local anesthetic infusion and reexamination of the patient within an hour or immediate neuroimaging to exclude a compressive process (hematoma or abscess). If imaging is ordered, MRI is preferable to CT, but the diagnosis should not be delayed if only CT is available. However, if CT rules out a compressive lesion, subsequent MRI will be necessary if spinal cord ischemia is suspected (Class I).
- If imaging rules out an operable mass lesion and spinal cord ischemia is suspected, practitioners should ensure at least normal blood pressure or consider inducing high-normal-range blood pressure. The efficacy of CSF pressure modulation via lumbar drains in anesthesia/interventional pain medicine–related spinal cord ischemia is unknown, but the technique is widely used to treat surgery-related spinal ischemia and seems safe in the setting of ischemic spinal cord injury (Class III).
- The role of corticosteroids in anesthesia-related injuries is unknown. Corticosteroids may have a beneficial effect after direct spinal cord trauma resulting from interventional procedures. However, the potential benefits for these patients should be balanced against the associated risk of corticosteroid-associated hyperglycemia, that is, hyperglycemia worsens brain (and presumably, spinal cord) ischemic injury. We do not recommend the use of corticosteroids for ischemic spinal cord injury. Definitive diagnosis and treatment are best determined in consultation with neurology or neurosurgery colleagues (Class III).

presentations associated with normal clinical settings. Known risk factors for anesthetic-related CES are supernormal doses of intrathecal local anesthetic and/or the maldistribution of local anesthetic spread within the intrathecal space. In recent years, reported cases of CES have been associated with previously undiagnosed spinal stenosis.[25,26,28,51] In theory, a tight spinal canal may lead to pressure-induced spinal cord ischemia or limit normal local anesthetic distribution within the intrathecal sac, thereby exposing the cauda equina to high drug concentrations. Either of these conditions could promote local anesthetic neurotoxicity and could be exacerbated by additional compromise of the spinal canal, as may occur with non-neutral surgical positioning. In addition to these pathophysiologic explanations for CES, there seems to exist a subset of patients who suffer CES after receiving a standard neuraxial anesthetic. The advisory panel speculates that these patients might represent an extremely rare subset of patients who are predisposed to neurotoxicity from clinically appropriate doses of local anesthetic and/or who develop neural inflammation in response to the local anesthetic, adjuvant, needle trauma, surgical positioning, or factors unrelated to the anesthetic.[13] Table 9 presents our recommendations regarding CES, which include risk-to-benefit consideration of neuraxial anesthesia in patients with known severe lumbar spinal stenosis, and to avoid exceeding the maximum recommended dose of intrathecal local anesthetic in the setting of a failed, partial, or maldistributed spinal anesthetic.

Local Anesthetic Neurotoxicity

Controversy remains as to whether transient neurologic symptoms (TNS) after spinal anesthesia are a forme fruste of local anesthetic neurotoxicity. Regardless, since the 2008 advisory, further clinical experience has come forth concerning TNS and intrathecal 2-chloroprocaine (2-CP).[131,132] These studies suggest that the risk of TNS is very low when using 40 to 50 mg intrathecal 2-CP. Spinal 2-CP remains off-label in the United States; in 2013, a 1% 2-CP solution was approved for intrathecal use in Europe. Although the risk of TNS from 2-CP is low, there are insufficient data for the advisory panel to make recommendations with regard to 2-CP and CES. Indeed, 1 patient who received 2-CP in a recent study developed a transient case of incomplete CES that was confirmed by positive nerve conduction study and electromyography.[132]

Arachnoiditis

New to this iteration of the practice advisory is a discussion regarding arachnoiditis. This poorly understood diffuse inflammatory reaction of the meninges is classically associated with nonanesthetic conditions, such as infection, trauma, contrast media, or multiple back surgeries. Cases of arachnoiditis that stem directly from a neuraxial anesthetic, if they exist, are extremely rare and most likely related to an idiosyncratic reaction to an unknown provocation. Nevertheless, concern has recently been

TABLE 8. Recommendations: Transforaminal Injection Techniques

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- To avoid direct injection into critical structures, final position of an immobile needle during transforaminal injection should be confirmed by injecting contrast medium under real-time fluoroscopy and/or digital subtraction imaging, using adequate radiologic views, before injecting any substance that may be hazardous to the patient (Class III).
- Because of the significantly higher risk of catastrophic neurologic injuries associated with cervical transforaminal injections, particulate steroids should not be used in therapeutic cervical transforaminal injections (Class III).
- Although the risk of neurologic injury is markedly lower when performed at lumbar levels, a nonparticulate steroid (eg, dexamethasone) should be used for the initial injection in lumbar transforaminal epidural injections (Class III).
- Particulate steroids can be considered under some circumstances for lumbar transforaminal injections, for example, after failure to respond to treatment with a nonparticulate steroid (Class III).

raised regarding the possibility of antiseptic solutions, particularly chlorhexidine/alcohol mixtures, causing arachnoiditis. The evidence for these concerns is circumstantial at best. Conversely, a retrospective cohort study of more than 12,000 patients reported no increased risk in neuraxial complications with the use of chlorhexidine as the skin disinfectant.[60] Furthermore, an in vitro study found chlorhexidine at clinically used concentrations no more cytotoxic that povidone-iodine and calculated that, if allowed to dry, any residual chlorhexidine carried by the block needle tip from skin to subarachnoid space would be diluted 1:145,000.[133] Based on the superiority of chlorhexidine as an antiseptic agent, the advisory panel stands with other national organizations in recommending it as the skin disinfectant of choice before neuraxial procedures.[7,27,134] Table 9 summarizes our recommendations, which include allowing chlorhexidine/alcohol mixtures to fully dry (2–3 minutes) before starting the procedure and maintaining complete physical separation of chlorhexidine (or any disinfectant solution) or its applicator devices from aseptic equipment so as to avoid drip or splash contamination of needles, syringes, or drugs.[13]

Procedures on Anesthetized or Deeply Sedated Patients

One of the more controversial recommendations from our previous advisory concerns performing regional anesthetics or interventional pain medicine procedures on patients receiving general anesthesia or who are "deeply sedated to the point of being unable to recognize and/or report any sensation that the physician would interpret as atypical during block placement."[1,4] This topic is a good example of how groups of equally qualified experts can analyze the same limited data set and arrive at different advices, as is the case with North American and European interpretations of this topic. In the interim since our last advisory, a number of large registries from the United States and Europe[30,56,135] have reaffirmed our previous recommendation that placing peripheral and neuraxial nerve blocks in anesthetized children seems not to increase injury above baseline risk estimates (which are derived mostly from studies of awake adults). Similarly, a report from the ASA Closed Claims study pointed to an apparent increased injury rate in those patients who underwent cervical interventional pain medicine procedures while anesthetized or deeply sedated.[124] We believe that this report also reaffirms our previous advice not to routinely perform regional anesthetic or interventional pain medicine procedures in anesthetized or deeply sedated adult patients. Despite the controversy surrounding this topic, the panel views wakefulness as yet another monitor of patient well-being during procedural interventions and as such suggests that wakefulness could be considered a component of vigilant patient care, just as ultrasound guidance, PNS, and expert observation are.[13] Recommendations for performing procedures on anesthetized or deeply sedated patients are presented in Table 10.

ANATOMY AND PATHOPHYSIOLOGY OF PNI

The pathophysiology and etiology of PNI associated with regional anesthetic techniques are exquisitely complex topics. Yet understanding these mechanisms is crucial if anesthesiologists are to develop risk avoidance strategies. Since the 2008 practice advisory,[4] further studies have added to our understanding of how peripheral nerve microanatomy influences PNI. Similar knowledge gains have occurred regarding the relative roles of nerve localization and monitoring technologies. Although the next section of this article will summarize existing and new knowledge

TABLE 9. Recommendations: CES, Local Anesthetic Neurotoxicity, and Arachnoiditis

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- 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. In addition, maldistribution (usually sacral) of local anesthetic spread should be ruled out before redosing single-injection or continuous subarachnoid blocks (Class I).
- The risks and benefits of neuraxial techniques should be considered in patients known to have moderate-to-severe spinal stenosis, especially if within the vertebral territory of the intended injection (Class II).
- The incidence of TNS after 40 to 50 mg intrathecal 2-chloroprocaine seems to be remarkably low. The number of 2-chloroprocaine spinal anesthetics reported in the literature is insufficient to determine the risk for CES or other manifestations of neurotoxicity (Class III).
- Physically and temporally separate disinfectant use from block trays and instruments during neuraxial procedures. Allow the solution to completely dry on skin before needle placement (2–3 min). Care should be taken to avoid needle or catheter contamination from chlorhexidine spraying or dripping, or from applicator device disposal, onto aseptic work surfaces (Class II).

TABLE 10. Recommendations: Performing Neuraxial Techniques in Anesthetized or Deeply Sedated* Patients

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- **Monitoring and Prevention:** There are *no data to support the concept that ultrasound guidance of needle placement reduces the risk of neuraxial injury* in patients under general anesthesia or deep sedation (Class II).
- **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 deep sedation removes any ability for the patient to recognize and report warning signs. This suggests that neuraxial regional anesthesia *or interventional pain medicine procedures* should be performed rarely in adult patients whose sensorium is compromised by general anesthesia or deep sedation. *Adult patients with specific conditions (eg, developmental delay, multiple bone trauma) may be appropriate exceptions to this recommendation after consideration of risk vs benefit (Class III).*
- **Pediatric Neuraxis:** The benefit of ensuring a cooperative and immobile infant or child *likely outweighs* the risk of performing neuraxial regional anesthesia in pediatric patients during general anesthesia or deep sedation. The overall risk of neuraxial anesthesia should be weighed against its expected benefit *(Class I).*

Recommendations contained within Table 10 have been modified from our 2008 advisory.[1] Significant changes are in *italics*.

**Anesthetized* refers to patients under general anesthesia. *Deep 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.

related to nerve injury pathophysiology, readers who desire a more complete understanding of this complicated topic are referred to the detailed supporting article contained within this series.[10]

Anatomic Considerations

Anesthesiologists are increasingly aware of the importance of peripheral nerve microanatomy as a key determinant of PNI risk. Nerve axons are bundled as fascicles and enveloped within the perineurium, which consists of layers of tightly fitting perineural cells that prevent diffusion of potentially toxic substances into the fascicle and also partially protect against mechanical injury. Multiple fascicles are surrounded by a permeable epineurium, which contains the fascicles plus various amounts of interfascicular connective tissues that occupies an ever-increasing proportion of the nerve's cross-sectional area as the nerve extends proximally to distally. This relative abundance of distal connective tissue explains why intraneural, but extrafascicular, needle tip placement is more likely to reside in a noncritical (ie, nonfascicular) portion of the nerve. Thus, neural microanatomy seems to correlate with ultrasound-enabled clinical observations that block needles were intraneural (subepineurium, but extraperineurium) more often than was previously assumed, but that this unanticipated occurrence was not associated with clinical evidence of PNI in most patients.[136]

Pathophysiology of PNI

The traditional mechanisms of PNI have been described in animal models as mechanical, injection, ischemic, and/or neurotoxic.

TABLE 11. Recommendations: Needle Tip Location, Choice of Local Anesthetic, and Nerve Localization Techniques

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

Needle Tip Location, Choice of Local Anesthetic, and Paresthesia

- Intraneural needle insertion does not invariably lead to functional nerve injury (Level 3)
- Intrafascicular needle insertion and injection should be avoided because it can cause histological and/or functional nerve injury (Level 2)
- Paresthesia during needle advancement or on injection of local anesthetic is not entirely predictive of PNI (Level 3)

Nerve Localization Techniques

- There are no human data to support the superiority of 1 nerve localization technique over another with regard to reducing the likelihood of PNI (Level 3)
- *Peripheral Nerve Stimulation*
  - Presence of an evoked motor response at a current of <0.5 (0.1 ms) indicates intimate needle-nerve relationship, needle-nerve contact, or an intraneural needle placement (Level 2)
  - Absence of a motor response at current of up to 1.8 mA does not exclude needle-nerve contact or intraneural needle placement (Level 3)
- *Injection Pressure* Monitoring
  - 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 PNI (Level 2)
  - Injection pressure monitoring can detect needle-nerve contact for interscalene brachial plexus block (Level 3)
  - The common practice of subjectively assessing injection pressure by "hand feel" is inaccurate (Level 3)
- *Ultrasound*
  - Ultrasound can detect intraneural injection (Level 2)
  - Current ultrasound technology does not have adequate resolution to discern between an interfascicular and intrafascicular injection (Level 2)
  - Adequate images of needle-nerve interface are not consistently obtained by all operators and in all patients (Level 2)

Levels of evidence are based on the 2011 Oxford construct.[18]

Forceful needle-to-nerve contact and/or injection into the nerve are believed to set in motion a series of events that might lead to ischemia or neurotoxicity. Needle trauma to or rupture of the perineurium is believed to negate the fascicle's protective environment, which then becomes a crucial contributory factor in determining the likelihood and severity of subsequent PNI. Direct application of (otherwise innocuous) local anesthetic to denuded axons can cause acute inflammatory reactions or neurotoxicity. Such insults are magnified in the setting of a disrupted perineurium[137,138] and prolonged exposure to the local anesthetic (as might occur with vasoconstrictive adjuvants, which reduce drug clearance). If the needle does not completely disrupt the perineurium, injection can transiently elevate intraneural pressure and lead to ischemia. Bleeding around the nerve or microhematoma within the nerve can also lead to ischemia. Lastly, nonspecific inflammatory responses can affect single or multiple nerves and at sites proximate to or distant from the surgical site. Such inflammatory changes have been observed during surgical nerve bypass procedures for permanent phrenic nerve injuries associated with interscalene block.[139]

Etiology of PNI

The etiology of PNI continues to evoke explanations that include anesthetic, surgical, patient-related, or a combination of factors thereof. The evidence for the significance of these factors is summarized in Table 4.

Anesthetic Risk Factors

Recent large studies fail to link peripheral nerve block as an independent risk factor for perioperative nerve injury either in the general operative setting[73] or in total joint arthroplasties.[70–72] Nevertheless, PNI does occur as a consequence of anesthetic techniques. Controversy continues regarding the concept of *intentional* intraneural injection for the purpose of achieving more rapid onset of denser peripheral nerve blockade. Published reports of intentional intraneural injection have noted no nerve injuries, albeit in patient numbers too small to prove safety.[140,141] Similarly, several small clinical studies have also reported no PNI despite *unintentional* intraneural injection.[136,142] Nevertheless, the advisory panel interprets the majority of animal and human PNI studies as supporting the concept that anesthesiologists should not purposefully seek needle-to-nerve contact[143] or intentional intraneural injection.

Surgical Risk Factors

Most surgical injuries are thought to occur from traction, stretch, transection, or compression injuries. These factors were reviewed in the previous section on surgically related neurologic complications.

Patient Risk Factors

Factors that place patients at an increased risk for anesthesia-related PNIs include metabolic, hereditary, toxic, and entrapment neuropathies and other preexisting neurologic injuries/conditions. Diabetic neuropathy is of particular concern because it seems to increase PNI at least 10-fold as compared with the general population.[26] A large general surgical population study identified peripheral vascular disease, smoking, vasculitis, and hypertension as independent risk factors for perioperative nerve injury.[73]

The Role of Nerve Localization and Monitoring Techniques

Paresthesia

A single randomized clinical trial did not support the elicitation of paresthesia as a risk factor for PNI.[80] The absence of a paresthesia does not reliably exclude the possibility of needle-to-nerve contact nor does it prevent PNI. Nevertheless, severe paresthesia that occurs with needle advancement or injection should prompt the cessation of either maneuver, and repositioning of the needle should be considered.

Peripheral Nerve Stimulation

Peripheral nerve stimulation is characterized by low sensitivity, but high specificity, for needle-to-nerve contact. When a motor response occurs at a low current output, such as 0.2 mA or lower, one cannot reliably discern if the needle tip is abutting the nerve or is subepineurial.[10,144] Conversely, current output greater than 0.5 mA is generally associated with extraneural needle placement,[141,145] although reports exist of intraneural needle tip placement at currents approaching 2.0 mA.

Injection Pressure Monitoring

Interest continues in the controversial practice of injection pressure monitoring. The clinical usefulness of this monitoring modality remains poorly defined. Avoidance of high resistance to injection seems to be a reasonable strategy during peripheral nerve blockade because studies consistently show that low opening pressures (<15 psi) are associated with injection into non-neural tissues. However, injection pressure monitoring seems to be most valuable as a negative predictor of PNI, that is, low injection pressure correlates with no PNI, but high injection pressure is not consistently linked to PNI. Unfortunately, anesthesiologists cannot reliably discern injection pressure based on syringe feel alone.[146,147] With regard to direct pressure monitoring systems, studies suggest that the technique cannot reliably detect intraneural intrafascicular injection and that needle-to-nerve contact and intrafascicular injection can be indistinguishable from each other.[148–150]

Ultrasound Guidance

Ultrasound guidance has not been associated with a reduction of PONS or long-term PNI.[21,22,33] The inability of ultrasound to reduce nerve injury may stem from technical and/or training limitations in discerning nerve from surrounding tissues (insufficient resolution to distinguish fascicles from connective tissue) or it may be related to anesthesiologists attempting to place the needle as close to the nerve as possible, thereby potentially increasing the risk for unintended subepineurial injection. Recent studies suggest that injecting local anesthetic adjacent to the brachial plexus, rather than within the fascial sheath, results in equivalent neural blockade.[151]

In summary, PNI is a diverse and complicated entity that may be associated with anesthetic, surgical, patient-related, or a combination of risk factors. In recent years, ultrasound studies have demonstrated that anesthesiologists place block needles within the nerve much more frequently than previously imagined and that most of these occurrences are not associated with PNI. The practice advisory panel interprets the weight of animal and human evidence to support the practice of avoiding needle placement that abuts or enters the nerve. Although there is no evidence that PNS, ultrasound, or pressure monitoring can prevent PNI, the panel believes it reasonable to consider using several of these modalities in combination when appropriate. Our advice is tempered by our limited knowledge of those factors that most influence PNI and recognition that those factors vary with the specific nerve involved, the peripheral block performed, and with unique patient and surgical factors. Recommendations regarding nerve localization techniques are presented in Table 11.

PATIENTS WITH PREEXISTING NEUROLOGIC DISEASE

The "double-crush" theory was first proposed by Upton and McComas[152] in 1973. The theory maintains that patients with preexisting neurologic compromise anywhere along the neural pathway may be at increased susceptibility for subsequent nerve injury from a secondary low-grade insult such as might occur during the perioperative period from surgery or anesthetic causes. Moreover, the resultant nerve damage may exceed the additive effects of 2 low-grade injuries[153] (Fig. 2). Preexisting neurologic conditions, many of them subclinical, might set the stage for subsequent double-crush scenarios, including such broad etiologies as mechanical, ischemic, toxic, metabolic, and autoimmune conditions. Preexisting neurological conditions have historically led to recommendations not to perform regional anesthetics.[154] The intent of our practice advisory was to analyze and summarize current evidence so that clinicians and their patients can make better informed decisions when presented with the conundrum of whether or not to offer regional anesthetic or interventional pain medicine procedures to patients with preexisting neurologic disease.

Although new information on the issue of performing regional anesthetic techniques in patients with preexisting neurologic disease is limited, this evidence reinforces our previous recommendations regarding patients with diabetes mellitus and spinal stenosis. Furthermore, there is a substantial amount of new information on postsurgical inflammatory neuropathies (PSINs). More detailed discussion on the topic of performing blocks in

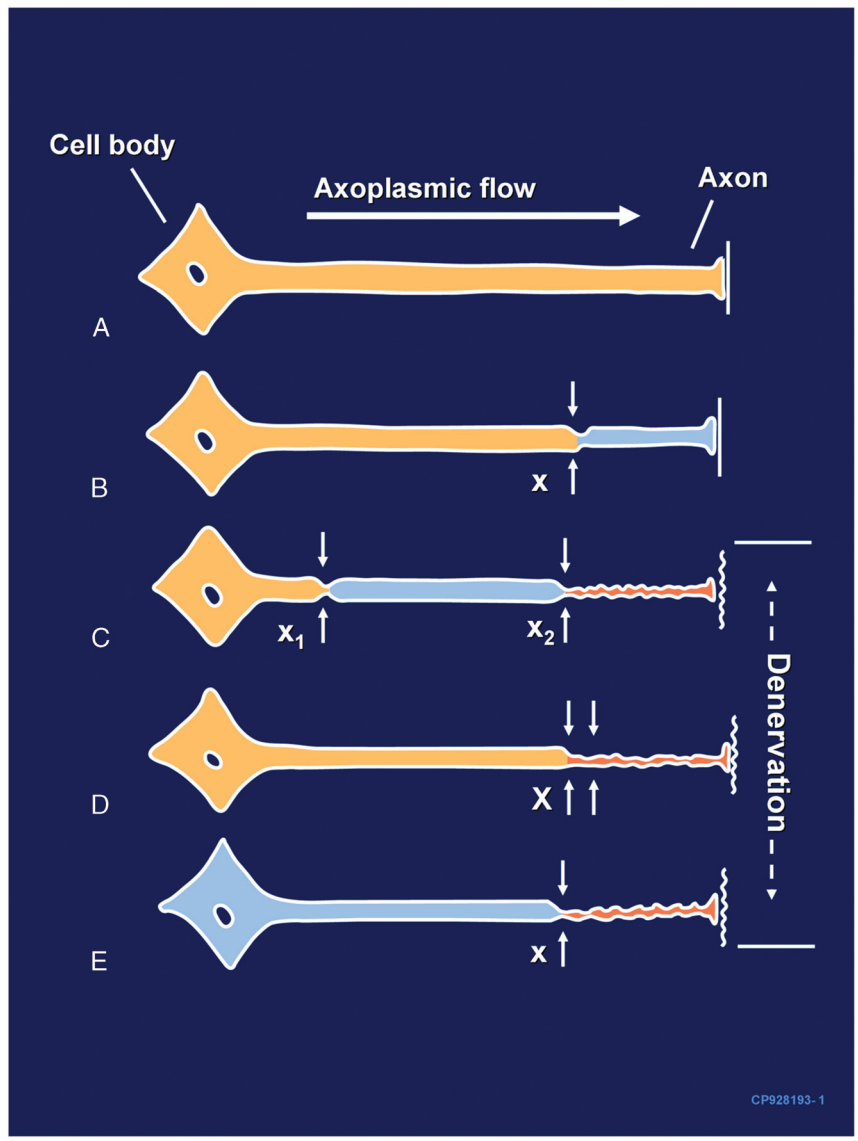

FIGURE 2. Neural lesions resulting in denervation. Axoplasmic flow is indicated by the degree of shading. Complete loss of axoplasmic flow results in denervation (C, D, E). A, Normal neuron. B, Mild neuronal injury at a single site (x) is insufficient to cause denervation distal to the insult. C, Mild neuronal injury at 2 separate sites (x1 and x2) may cause distal denervation (ie, "double crush"). D, Severe neuronal injury at a single site (X) may also cause distal denervation. E, Axon with a diffuse preexisting underlying disease process (toxic, metabolic, ischemic) may have impaired axonal flow throughout the neuron, which may or may not be symptomatic, but predisposes the axon to distal denervation after a single minor neural insult at x (ie, "double crush"). By permission of Mayo Foundation for Medical Education and Research.

patients with preexisting neurologic disease is contained in the supporting article by Kopp et al.[16]

Preexisting Peripheral Nervous System Disorders

Peripheral neuropathies are either hereditary or acquired. The most common inherited disorders are from the collective category of Charcot-Marie-Tooth (CMT) disease, which affects approximately 1 in 2500 humans. A few case reports and small case series describe the use of either peripheral or central regional anesthetic techniques in CMT patients without apparent worsening of their underlying condition. However, clinical evidence is too sparse to allow for definitive recommendations other than if a regional technique is chosen; extra precautions should be taken to minimize other surgical or anesthetic risk factors. Most patients with preexisting peripheral nervous system disease have acquired peripheral neuropathies such as diabetes mellitus or chemotherapy-induced neuropathies.

Diabetic Polyneuropathy

Diabetes mellitus is associated with several types of neuropathies, but distal symmetric sensorimotor polyneuropathy (diabetic polyneuropathy or DPN) is most common and is present in up to 50% of long-standing diabetic patients. Although animal studies[155,156] consistently report that diabetic nerve fibers are more sensitive to the blocking effects of local anesthetics and may have increased susceptibility to local anesthetic neurotoxicity, it is unclear if these findings are clinically relevant in humans. A small number of clinical studies attest to higher peripheral nerve block success rates in diabetic patients,[157] but such increased sensitivity to local anesthetics may not necessarily reflect increased susceptibility to neurotoxicity. However, a single-institution study reported that 0.4% (95% CI, 0.1%–1.3%) of patients with sensorimotor neuropathy or DPN who underwent spinal anesthesia subsequently developed new or progressive postoperative neurologic deficits, which is a higher incidence than that observed in the institution's general surgical population.[49] Although this finding does not absolutely link spinal anesthesia to increased risk in patients with DPN, it does suggest that the anesthetic may have been a contributing factor. Another area of concern in patients with DPN involves nerve localization technique; diabetic nerves are less sensitive to electrical stimulation, which theoretically increases the risk of intraneural needle placement when localizing nerves using a PNS.[158] Although ultrasound guidance has not decreased the rate of PONS in the general population, it is possible that the advantages of ultrasound guidance—facilitating avoidance of intentional needle-nerve contact and reducing local anesthetic volume—may eventually prove beneficial in at-risk populations such as diabetic patients.[21] In summary, patients with DPN may be more susceptible to double-crush injury, but current clinical evidence is suggestive rather than definitive. Nevertheless, we recommend that, in profoundly symptomatic patients, consideration be given to limiting local anesthetic concentration and/or dose, avoidance of adjuvant epinephrine,[159] and ultrasound guidance to maintain needle tip distance from the nerve.

Chemotherapy-Induced Neuropathy

Approximately 30% to 40% of patients who receive neurotoxic chemotherapeutic agents (eg, cisplatin, vincristine, paclitaxel) develop peripheral neuropathy. The risk of nerve injury is increased further in those patients with preexisting neuropathic changes from diabetes mellitus or alcoholism. Many of these chemotherapy-induced neuropathies are subclinical. A note of concern pertinent to these patients was raised by an isolated case report of severe brachial plexopathy after peripheral nerve blockade in a patient with subclinical chemotherapy-induced neuropathy.[160]

Inflammatory Neuropathies

The inflammatory neuropathies include Guillain-Barré syndrome (GBS) and recently highlighted postsurgical inflammatory neuropathies (PSIN). Most case reports of GBS come from (usually successful) use of neuraxial blockade in obstetric patients. However, major concerns include the potential for autonomic instability and consequent exaggerated responses to neuraxial blockade and reactivation of previously dormant GBS symptoms, both of which have been reported.[16] There are too few data to make recommendations on GBS and concurrent regional anesthetic techniques other than to suggest that decisions be made on an individualized basis that accounts for risk and benefit.

Postsurgical Inflammatory Neuropathies

There is growing awareness of inflammatory etiologies for perioperative nerve injuries, including Parsonage-Turner syndrome,[161] lumbosacral radiculoplexus neuropathies,[162] and PSIN.[163,164] Distinguishing features of these neuropathies include their delayed appearance (within 30 days of surgery, although some may be apparent immediately), which is usually followed by a period of normal recovery. Clinical presentation also includes signs and symptoms outside of the expected location of anesthetic blockade or surgery and a period of intense pain out of proportion to what would be expected from the surgery, which then resolves, only to be followed by weakness. Postsurgical inflammatory neuropathy is thought to be an immune-mediated idiopathic response to a physiologic stress, such as infection, vaccination, or surgery.[164] The associated neurologic deficits may be focal, multifocal, or diffuse. The greatest risk of PSIN is surgeons and anesthesiologists not considering its diagnosis and, in so doing, delaying potentially useful therapies. When patients present with this constellation of symptoms, urgent neurological consultation is warranted. Although the natural history without treatment is one of probable slow recovery, once diagnosed, many neurologists recommend suppressing the immune response with prolonged high-dose steroids or immunoglobulin to minimize the immune-mediated nerve injury, although such therapies have not been proven. In contradistinction from much perioperative nerve injury, most patients with PSIN improve with treatment if diagnosed early.

Preexisting Central Nervous System Disorders

As with preexisting peripheral nervous system disease, anesthesiologists historically were reluctant to offer regional anesthetic–based techniques to their patients with preexisting CNS diseases.[154] Although modern data are limited, most studies of the general surgical population[50] and obstetrics[165,166] have not found that regional techniques place most patients with active disease at risk for new or worsening symptoms. Despite these reassuring findings, the decision to perform neuraxial anesthetic or interventional pain medicine procedures in patients with preexisting CNS disease still demands risk-to-benefit consideration.

Multiple Sclerosis

The focal demyelination that characterizes multiple sclerosis (MS) contributes to its classic "waxing and waning" pattern. When coupled with known perioperative stressors that can worsen the disease process, such as hyperpyrexia, infection, and/or emotional stress, it is often difficult to sort out the causes for perioperative progression or new onset of MS-related symptoms. Although classically considered a CNS disease, some portion of patients (from 5% to 47%)[167,168] also have peripheral demyelination. The clinical significance of peripheral MS is unclear because there are very few case reports that link MS to injury after peripheral nerve blockade.[169] Conversely, there are case series that support the

general safety of neuraxial anesthesia in parturients with MS.[165,170] Importantly, the obstetric model may not be ideal because MS patients have diminished frequency of relapse during pregnancy but an increased rate postpartum. To maximize safety in obstetric patients, it is recommended that the dose and concentration of local anesthetic be limited. Epidural anesthesia is considered safer than spinal anesthesia because it does not deposit local anesthetic directly adjacent to the CNS (ie, the spinal cord).

Postpolio Syndrome

Postpolio syndrome (PPS) is the most prevalent motor neuron disease in North America. The largest series (n = 79) of PPS patients to receive neuraxial anesthesia documented no worsening of symptoms.[50] Nevertheless, the paucity of data on these patients suggests that the risk and benefit of a neuraxial technique be balanced against that of general anesthesia.

Amyotrophic Lateral Sclerosis

The greatest perioperative risks of amyotrophic lateral sclerosis (ALS) are respiratory and/or neurologic deterioration. A few case reports attest to the apparent safety of neuraxial or peripheral blockade in ALS patients,[16] but these reports are insufficient for general recommendations. As with other CNS preexisting diseases, the risk and benefit of regional techniques should be balanced against those of general anesthesia.

Spinal Canal Pathology

Emerging concerns regarding patients with spinal stenosis were discussed in the section on neuraxial pathophysiology.[13] With regard to previous spine surgery, a recent publication reported no evidence that these patients were at risk for developing new or progressive neurologic deficits when they underwent spinal anesthesia.[58] Although previous spinal surgery should not be considered a contraindication to neuraxial anesthetic or interventional pain medicine techniques, consideration might be given to preprocedure imaging to better define relevant anatomy, deformity, and/or surgical implants.[58]

Neural Tube Defects

Congenital neural tube defects may present at birth as open spinal dysraphisms (eg, meningocele or meningomyelocele) or closed spinal dysraphisms, which range from isolated defects of posterior vertebral column closure (spina bifida occulta) or more serious malformations such as diastematomyelia (split cord malformations), tethered spinal cord syndrome, or dural ectasia (lumbosacral widening or caudad displacement of the dural sac). A few case reports have described successful spinal or epidural anesthesia in parturients who previously underwent surgical correction of open spinal dysraphisms. These cases were characterized by extensive cranial spread of a dense local anesthetic block, with limited caudad spread below the site of surgical correction. Thus, if the decision is made to provide neuraxial anesthesia in this subset of patients, it is recommended that the block needle is inserted cephalad to the original lesion.

The closed spinal dysraphisms are challenging because the proceduralist or patient may not always be aware of the defect. Failure of a single vertebral arch to fuse (isolated spinal bifida occulta) is common in the general population (10%–24%).[171] It is recommended that needle insertion occur above the level of spinal abnormality, assuming its presence is known. A total of 11 cases of successful epidural anesthetics using normal doses of local anesthetic have been reported in isolated spina bifida patients.[16] In contrast, patients with complex spina bifida should not receive neuraxial anesthesia. This recommendation is based on reports of neurologic complications in patients who underwent a variety of neuraxial techniques; in some of those cases, the defect was unrecognized before the procedure. Patients with complex spina bifida often have associated conditions, such as cutaneous manifestations over the level of abnormality, involvement of more than 1 lamina, or associated bowel, bladder, or neurologic symptoms. If the presence of a neural tube defect is known or suspected, the underlying neuroanatomy should be documented with radiographic imaging before considering a neuraxial technique. We recommend that complex closed spinal dysraphisms be considered a contraindication to neuraxial techniques. In patients with spina bifida occulta, neuraxial techniques may be considered after appropriate risk (technical difficulties, dural puncture, or atypical local anesthetic spread) is balanced against perceived benefit.

Recommendations for performing neuraxial or peripheral anesthesia/analgesia procedures in patients with preexisting neurologic disease are presented in Table 12.

DIAGNOSIS AND TREATMENT

Since our 2008 advisory,[4,5] new information has evolved concerning postoperative inflammatory neuropathies. We have added new information on acute interventions that may possibly improve neurologic outcome, both acutely and in relation to long-term management of the neuropathic pain that occasionally results from these injuries. We have updated our previous algorithm that contains a structured approach to diagnosis and initial management (Fig. 3). Although this advisory focuses on nonhemorrhagic and noninfectious neurologic complications, these entities will be briefly noted throughout this section for both completeness and perspective. Readers are encouraged to refer to the ASRA practice advisories on these topics for details[7,8] and should seek the most up-to-date versions of these works. Summary articles are available on the ASRA Web site (www.asra.com).

Timely Recognition of Perioperative Nerve Injury

Early recognition and appropriate stratification of suspected perioperative nerve injury into those that require emergent imaging and/or neurologic evaluation are of paramount importance to afford patients the best opportunity for full or partial recovery, especially in the case of neuraxial injuries. Nonetheless, our current advisory[15] notes multiple barriers to appropriate recognition of perioperative nerve injury, including such factors as neurologic deficits being masked by sedation, concurrent analgesics, or continuous catheter use; the absence of ambulatory patient follow-up; or delayed recognition of sensorimotor deficits until after hospital discharge, which has been reported to occur in up to 90% of patients undergoing lower extremity arthroplasty.[70,71] Delayed recognition is more likely to be associated with nonoperative causes of nerve injury, such as immobilization, dressing compression, infection, or inflammation. Such delays also confound the patient's perception of onset. In the "blur" that accompanies typical perioperative events, patients can incorrectly report their symptoms as presenting immediately after surgery despite objective documentation of onset at 48 hours, as for example with perioperative ulnar nerve injury.[172] The complexity of perioperative recognition, the absolute imperative in some cases to diagnose and treat emergently, and operators' unique understanding of the expected consequences of their procedure, all speak to the advisability of direct, candid, and timely conversation between the anesthesiologist or pain physician and the neurologic consultant.[15]

Diagnosis and Treatment of Neuraxial Complications

Certain signs and symptoms after neuraxial blockade should raise suspicion for perioperative nerve injury. Weakness that is

TABLE 12. Recommendations: Regional Anesthesia in Patients With Preexisting Neurologic Disease

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

Peripheral Nervous System Disorders

Hereditary Peripheral Neuropathies

- Patients with CMT disease and hereditary neuropathy with liability to pressure palsy may have clinical or subclinical evidence of a preexisting peripheral neuropathy due to neural compromise from the disease state (Class I).
- Anecdotal case reports and small case series suggest that both peripheral and neuraxial regional techniques may be used in patients with stable CMT or hereditary neuropathy with liability to pressure palsy disease states without worsening their neurologic symptoms. However, a careful discussion regarding the potential risks and benefits of performing regional anesthesia in patients with preexisting neural compromise is strongly recommended (Class III).

Acquired Peripheral Neuropathies

- Patients with diabetic peripheral neuropathy or previous exposure to chemotherapy (eg, cisplatin or vincristine) may have clinical or subclinical evidence of a preexisting peripheral neuropathy caused by neural compromise from the disease state (Class I).
- An abundance of animal data and limited clinical data support the concern that diabetic nerves are more sensitive to local anesthetics and perhaps more susceptible to injury. Therefore, peripheral and neuraxial blockade may theoretically increase the risk of new or progressive neurologic deficits in patients with diabetic peripheral neuropathy (Class II).
- When regional anesthesia is thought to be appropriate in patients with acquired peripheral neuropathy (eg, diabetic peripheral neuropathy or chemotherapy-induced neuropathy), consideration should be given to modify the anesthetic technique (ie, decreasing the concentration of local anesthetic, reducing the total dose of local anesthetic, eliminating or reducing the concentration of vasoconstrictors such as epinephrine) to minimize the potential additive risk (Class II).
- The use of ultrasound guidance may facilitate (a) perineural needle placement and (b) a reduction in the total dose (volume) of local anesthetic administered. However, clinical data demonstrating a reduction in neurologic injury with ultrasound guidance are currently lacking (Class II).

Inflammatory Neuropathies

- Patients with inflammatory neuropathies such as GBS and PSIN are at risk of new or worsening neurologic deficits during the postoperative period regardless of anesthetic technique (Class II).
- Neural compromise secondary to acute neuronal inflammation may be a relative contraindication to regional anesthesia. However, the existing literature can neither support nor refute this claim. Therefore, the decision to perform neuraxial or peripheral nerve blockade in patients with inflammatory neuropathies should be made on an individual basis after a thorough discussion of the potential risks and benefits with the patient (Class III).

CNS Disorders

- Patients with CNS disorders (eg, MS, PPS, ALS) may have clinical or subclinical evidence of a preexisting neurologic deficit caused by neural compromise from the disease state. Furthermore, it is not uncommon for patients with CNS disorders to experience worsening of their neurologic symptoms during the postoperative period regardless of the anesthetic technique (Class I).
- Anecdotal case reports and small case series suggest that neuraxial anesthesia and analgesia may be used in patients with stable neurologic symptoms without worsening their neurologic deficits. However, *definitive* evidence supporting this practice is lacking. Therefore, a careful discussion regarding the potential risks and benefits of performing regional anesthesia in patients with preexisting neural compromise is strongly recommended (Class II).

Spinal Canal Pathology

Previous Spine Surgery

- Prior spine surgery is not a contraindication to the performance of neuraxial anesthesia or analgesia. However, before performing a regional technique, a review of the patient's radiologic imaging or the use of fluoroscopy could be useful to identify the optimal approach to the neuraxis (Class I).
- Under most clinical circumstances, spinal anesthesia may be (a) technically easier to perform and (b) more reliable (ie, higher success rates) than epidural techniques in patients who have previously undergone spine surgery. Patients undergoing neuraxial anesthesia or analgesia after previous spine surgery do not seem to be at higher risk of new or progressive neurologic deficits (Class II).

Neural Tube Defects

- Neural tube defects encompass a wide range of spinal cord malformations, including both open (eg, meningocele, meningomyelocele) and closed (eg, spina bifida occulta, tethered spinal cord syndrome, diastematomyelia, dural ectasia) spinal dysraphisms. Patients with neural tube defects may have clinical or subclinical evidence of a preexisting neurologic deficit caused by neural compromise from the disease state (Class I).
- Because of the wide range and severity of possible spinal cord and vertebral column malformations, patients with neural tube defects should undergo radiographic imaging to fully evaluate and define the extent of their disease state before considering neuraxial anesthesia or analgesia (Class II).
- Anecdotal case reports and small case series suggest that the performance of neuraxial anesthesia and analgesia in patients with complex closed spinal dysraphisms (ie, tethered spinal cord syndrome or diastematomyelia) may result in new or progressive neurologic symptoms. However, *definitive* evidence suggesting an increased risk of neurologic complications is lacking (Class II).
- Anecdotal case reports and small case series suggest that neuraxial anesthesia and analgesia may be used in patients with *isolated* spina bifida occulta (without associated tethered spinal cord syndrome or diastematomyelia) without an increased risk of neurologic injury. However, *definitive* evidence supporting this practice is lacking. Therefore, a careful discussion regarding the potential risks (technical difficulties, unpredictable local anesthetic spread, inadvertent dural puncture, and neural injury) and benefits of performing regional anesthesia in patients with *isolated* spina bifida occulta is strongly recommended (Class II).

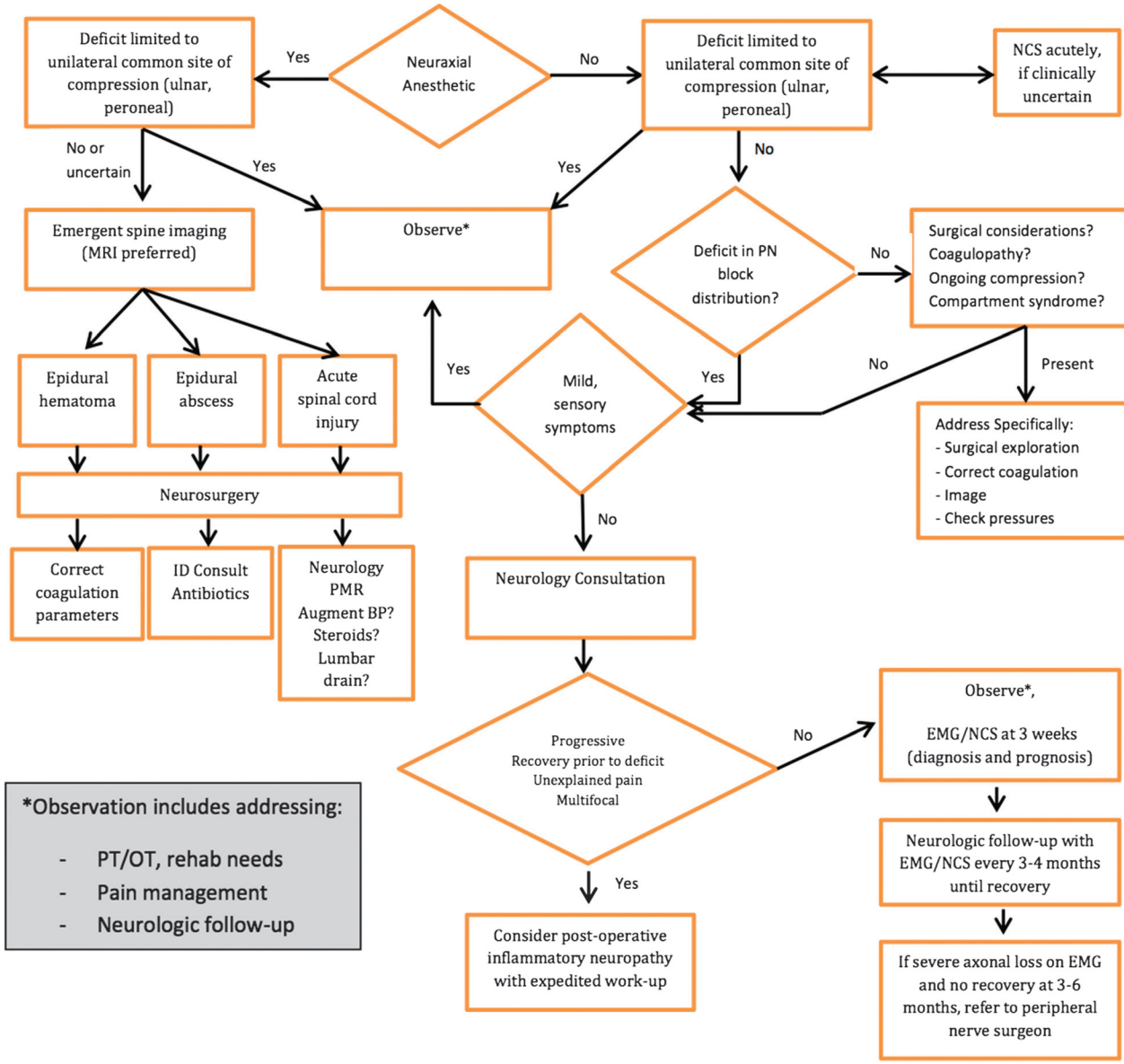

FIGURE 3. Algorithm for the diagnosis and initial therapy of perioperative nerve injuries. PN indicates peripheral nerve; NCS, nerve conduction studies; EMG, electromyography; PMR, physical medicine rehabilitation specialty consultation; BP, blood pressure. From Watson and Huntoon.[15] Used with permission.

more intense than expected, recurrent after initial resolution, progressive, and/or in an area inconsistent with the block (eg, lower leg or foot weakness associated with a thoracic epidural) can be the first presenting symptoms of a significant neuraxial injury.[36,173–175] Back pain is observed less frequently, whereas bowel or bladder symptoms are late. For those mass lesions amendable to emergent surgical decompression, full (40%–66%) or partial recovery is possible if decompression occurs within 8 to 12 hours of symptom onset, although a recent study challenges this assumption.[61] The severity of neurologic deficit at the time of intervention also predicts outcome.[176–178] Frequently noted in medicolegal claims[36] is the failure of anesthesiologists to recognize and begin management of a neuraxial complication in a timely manner—all too often, neurologic deficits are wrongly attributed to the block itself. Inappropriate delays are all the more likely when unenlightened surgical or nursing personnel manage the patient in the absence of anesthesiologist expertise. When injury is suspected, magnetic resonance imaging (MRI) differentiates soft tissues, identifies coexisting spinal canal pathology, and locates an aberrantly placed catheter more effectively than does computerized tomography (CT). However, in the absence of immediately available MRI, an emergent CT scan can identify those space-occupying compressive processes most amenable to emergent surgical decompression (ie, spinal abscess or hematoma).

Table 13 presents the characteristics of neuraxial injury presentation that may aid differential diagnosis. Epidural hematoma is associated temporally with needle/catheter placement or catheter removal and in 75% of cases will have a fulminant presentation within 24 hours.[177] Conversely, spinal epidural abscess or meningitis may have an insidious presentation—a delay of several days

TABLE 13. Differential Diagnosis of Neuraxis Injuries Associated With Anesthetic or Pain Medicine Techniques

	Epidural Abscess	Spinal Hematoma	Anterior Spinal Artery Syndrome	Direct Spinal Cord Trauma
Age of patient	Any age	50% older than 65 y	Any age, but mostly elderly	Any age, but often younger
Previous history	Infection*	Anticoagulants	Arteriosclerosis, abnormal blood pressure	Difficult spinal anatomy
Onset	1–3 d	Sudden	Sudden	Sudden or occult
Generalized symptoms	Fever, malaise, back pain	Sharp, transient back pain and leg pain	None	Paresthesia, especially with injection, or none
Sensory involvement	None or paresthesias	Variable	Minor, patchy–sparing posterior columns (proprioception)	Dermatomal or diffuse paresthesia
Motor involvement	Flaccid paralysis, later spastic	Flaccid paralysis	Flaccid paralysis	Possible weakness or none
Segmental reflexes	Exacerbated*–later obtunded	Abolished	Abolished acutely–later signal change anterior two thirds of cord	Variable
CT scan/MRI	Signs of extradural compression	Signs of extradural compression	Normal acutely	Edema or hemorrhage, needle track
Laboratory data	Rise in inflammatory markers	Clotting abnormality	Normal	Normal

Modified from Wedel and Horlocker.[179] Used with permission.
*Infrequent findings.

after the procedure, followed by indolent fever and back pain, followed by rapid progression to paralysis. Accurate diagnosis and therapy are important because spinal epidural abscess/meningitis have a 15% mortality; earlier diagnosis is also associated with less severe neurologic deficits.[180] Anterior spinal artery syndrome may be heralded by back pain at the level of infarction and bilateral radicular discomfort in 75% of cases, with typically rapid progression to paraplegia or tetraplegia that spares the posterior columns (vibration and proprioception).[181] Complete recovery is extremely rare. Direct spinal cord trauma from needles or catheters may present with unilateral or bilateral symptoms, depending on the anatomical lesion site. If the only symptom after suspected direct trauma is a persistent paresthesia that is nonprogressive and improving, observation alone may be warranted. However, more widespread sensory symptoms (ie, nondermatomal) or motor involvement should prompt MRI and possible neurologic consultation.

In summary, early recognition and appropriate intervention can improve outcome in those patients who have suffered a hemorrhagic, infectious, or inflammatory insult. Unfortunately, the same cannot be said for ischemic, local anesthetic neurotoxic, and/or direct mechanical injury causes. Recommendations for the diagnosis and treatment of neuraxial injuries are presented in Tables 14 and 15.

Diagnosis and Treatment of Peripheral Nerve Complications

Similar to neuraxial injuries, the diagnosis and treatment of PNIs should be approached urgently to rule out potentially correctable lesions, such as from extrinsic or intrinsic compression

TABLE 14. Recommendations: Diagnosis of Perioperative Nerve Injury

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

Neuraxial Injury

- In the setting of neuraxial anesthesia, any concern of spinal cord dysfunction requires emergent neuroimaging (Level I).
- Magnetic resonance imaging is the preferred imaging modality. However, imaging should not be delayed to arrange MRI or to get neurologic consultation. Computerized tomography or CT myelography are acceptable as initial imaging to exclude a compressive lesion (Level I).
- Diagnosis of a compressive lesion (epidural hematoma or spinal epidural abscess) within or near the neuraxis demands emergent neurosurgical consultation for consideration of decompression (Level I).

Peripheral Nerve Injury

- Neurologic consultation is recommended for complete nerve injuries (complete absence of nerve function), incomplete injuries with moderate to severe functional limitations, or progressive neurologic dysfunction (Level I).
- An inflammatory postsurgical neuropathy should be considered if there are multifocal, progressive deficits, unexplained excessive pain despite standard perioperative analgesia and neurologic deficits developing after a period of return to neurologic baseline postoperatively. Neurologic consultation should be considered (Level II).
- Electrodiagnostic studies (EMG and nerve conduction studies) may help confirm neuropraxia with conduction block or define preexisting disease when performed acutely. Axonal loss (prognostic) and the extent of a perioperative neurogenic injury will be better clarified by electrodiagnostic studies performed 3 wk after injury (Level I).

Levels of evidence are based on the 2011 Oxford construct.[18]
EMG indicates electromyography.

TABLE 15. Recommendations: Treatment of Perioperative Nerve Injury

These recommendations are intended to encourage optimal patient care but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- Outcomes for compressive lesions (epidural hematoma or spinal epidural abscess) are dependent on the severity of neurologic impairment and the duration of symptoms at the time of neurosurgical decompression. Most experts agree that neurologic recovery is improved with early decompression (<8–12 h from symptom onset in epidural hematoma and <36 h from symptom onset for spinal epidural abscess) and when the preoperative neurologic deficits are milder in severity (Level I).
- Neuropathic pain is reasonably treated pharmacologically (Level I).
- Functional deficits from neurological injuries should be rehabilitated in concert with rehabilitation specialists (Level II).
- Nerve lesions that fail to resolve 3–5 mo after initial neurologic evaluation should prompt consideration of consultation with a peripheral nerve neurosurgeon (Level II).
- If imaging rules out an operable mass lesion and spinal cord ischemia is suspected, practitioners should ensure at least normal blood pressure or consider inducing high-normal-range blood pressure. The efficacy of CSF pressure modulation via lumbar drains in anesthesia/interventional pain medicine–related spinal cord ischemia is unknown, but the technique is widely used to treat surgical spine ischemia and seems safe in the setting of ischemic spinal cord injury (Class III).
- The role of corticosteroids in anesthesia-related injuries is unknown. Corticosteroids may have a beneficial effect after direct spinal cord trauma and possibly trauma resulting from interventional procedures. However, the potential benefits for these patients should be balanced against the associated risk of corticosteroid-associated hyperglycemia, that is, hyperglycemia worsens brain (and presumably, spinal cord) ischemic injury. We do not recommend the use of corticosteroids for ischemic spinal cord injury. Definitive diagnosis and treatment are best determined in consultation with neurology or neurosurgery colleagues (Class III).

Levels of evidence are based on the 2011 Oxford construct.[18]

(casts, dressings, compartment syndrome, visible hematoma, or occult perineural microhematoma). If a hematoma is suspected, urgent imaging or ultrasonography should be considered. Acute surgical injury should also be ruled out by engaging the surgeon in candid discussion regarding the possibility of nerve transection, excessive traction, or wayward ligatures. Indeed, 1 review reported that more than 90% of surgically explored iatrogenic nerve injuries were linked to intraoperative causes.[182] The goal of timely consultation is to alleviate potentially correctable causes or nonsurgical or anesthesia-related etiologies, such as stroke. Once the need for immediate treatment has been ruled out, the diagnosis of PNI can proceed as directed by initial presenting symptoms (Fig. 3). Pure sensory deficits that occur within the territory of the peripheral block[74] or a classic compression point, for example, common peroneal nerve compression at the fibular head, can be observed and are expected to resolve within days to weeks. However, neurologic consultation should be considered when the deficit involves motor function, is progressive, is characterized by recrudescence of neural blockade, or is difficult to localize and/or reconcile with the expected distribution of the anesthetic block or surgery. Electrophysiologic studies for more severe or unclear cases are typically delayed for 2 to 3 weeks, when signs of Wallerian degeneration first appear. However, early electrophysiologic studies may we worthwhile to define preexisting pathology. Bilateral studies may be indicated if occult conditions are suspected to affect the nonoperative side. Such decisions are best made in consultation with a neurologist. When no or incomplete improvement has taken place by 3 to 5 months, consideration should be given for referral to a peripheral nerve surgeon. Recommendations for the diagnosis and treatment of PNIs can be found in Tables 14 and 15.

Postsurgical Inflammatory Neuropathies

Postsurgical inflammatory neuropathies were discussed previously in the preexisting neurologic disease section. When patients present with this symptom complex in the postsurgical period, urgent neurologic consultation is warranted.

Management of Chronic Pain After Perioperative Nerve Injury

A subset of patients who sustain perioperative nerve injury will develop chronic neuropathic pain. The pain medicine physician is often called on to provide long-term symptomatic management of these patients and to assume coordination of patient education, expectation, and physical therapy. New to this advisory are evidence-based recommendations for the care of these challenging patients, some of whom may have unanswered questions or unrealistic expectations consequent to suboptimal communication with various practitioners during the immediate postoperative episode.

Postsurgical neuropathic pain syndromes may result from surgical injury, such as intercostal neuritis after thoracotomy, or may be consequent to neural blocks administered during the perioperative period. There are several considerations for when it might be appropriate to refer patients with persistent postsurgical pain to a pain medicine specialist—severe pain out of proportion to that expected from a specific surgical procedure; pain that limits patient function; or pain that is progressive, multifocal, and/or difficult to localize. Other signs that should prompt early referral are those consistent with chronic regional pain syndrome, such as neurologic impairment in an area remote from the regional block, surgery, or compression or physical signs such as allodynia, edema, or hyperhidrosis. Readers are referred to the supporting article's[15] detailed recommendations regarding stepwise pharmacologic therapies for these patients, as well as reasonable indications for the use of diagnostic nerve blocks, such as stellate ganglion block. The evidence for neuromodulation therapy is less conclusive; the European Federation of Neurological Societies supports the use of spinal cord stimulation for chronic regional pain syndrome,[183] although there are no supporting studies specific to postsurgical neuropathic pain.

In summary, the diagnosis and treatment of neuraxial injuries demands emergent stratification of those injuries that may be amenable to surgical decompression. Although the management of PNIs is less urgent (particularly when sensory predominant), practitioners are reminded that severe, progressive, or difficult-to-localize deficits demand urgent neurologic consultation to exclude potentially treatable causes such as from compressive etiologies. If

a treatable cause is excluded, there is little that the physician can do to change the course of these injuries. However, pain physicians have a useful role to play in coordinating education, expectation management, and pain modulation in those patients who develop chronic neuropathic pain from their injury.

CONCLUSIONS

The Second ASRA Practice Advisory on Neurologic Complications Associated With Regional Anesthesia and Pain Medicine provides a number of updates to the 2008 advisory. New information has been presented on the incidence of nerve injury inherent to common elective orthopedic surgeries. The advisory contains updated information regarding the pathophysiology of neuraxial and peripheral nerve injury. New or expanded information is presented, particularly with regard to spinal canal pathology, blood pressure control during neuraxial anesthetics, neurotoxicity-related neuraxial injuries, transforaminal pain medicine procedures, and the advisability of performing procedures in anesthetized or deeply sedated patients. The advisory also expands recommendations related to the diagnosis and treatment of these disorders.

Our final conclusion is very similar to that made in 2008: "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."[4]

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APPENDIX 1. Oxford Centre for Evidence-Based Medicine 2011 Levels of Evidence

Levels of Evidence for Treatment Benefits/Does This Intervention Help?	
Level 1	Systematic review of randomized trials or *n*-of-1 trials
Level 2	Randomized trial or observational study with dramatic effect
Level 3	Nonrandomized controlled cohort/follow-up study
Level 4	Case series or case-control studies or historically controlled studies
Level 5	Mechanism-based reasoning

From the Oxford Centre for Evidence-Based Medicine.[18]

APPENDIX 2. Strength of Recommendations

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

This classification system is significantly modified from the American College of Cardiology/American Heart Association construct for classifying strength of evidence.[19]

Neurological Complications Related to Elective Orthopedic Surgery
Part 1: Common Shoulder and Elbow Procedures

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Abstract: Many anesthesiologists are unfamiliar with the rate of surgical neurological complications of the shoulder and elbow procedures for which they provide local anesthetic–based anesthesia and/or analgesia. Part 1 of this narrative review series on neurological complications of elective orthopedic surgery describes the mechanisms and likelihood of peripheral nerve injury associated with some of the most common shoulder and elbow procedures, including open and arthroscopic shoulder procedures, elbow arthroscopy, and total shoulder and elbow replacement. Despite the many articles available, the overall number of studied patients is relatively low. Large prospective trials are required to establish the true incidence of neurological complications following elective shoulder and elbow surgery.

What's New: As the popularity of regional anesthesia increases with the development of ultrasound guidance, anesthesiologists should have a thoughtful understanding of the nerves at risk of surgical injury during elective shoulder and elbow procedures.

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Postoperative neurological deficits can be attributed to patient-, anesthesia-, or surgery-related factors. For elective procedures of the shoulder and elbow, surgical causes of nerve injury include direct trauma, positioning, and retraction.[1–3] It behooves the anesthesiologist performing regional anesthesia to understand the risk that the surgical procedure itself may play in the presentation and evolution of perioperative nerve injury. The individual nerves, mechanisms by which they are injured, and tendency for injury during shoulder and elbow surgery necessarily depend on the type of procedure being performed.

The purpose of this narrative review is to describe the mechanisms and likelihood of neurological injury associated with some of the most common elective shoulder and elbow procedures for which anesthesiologists may administer brachial plexus (BP) blockade. Although anesthetic texts discussing orthopedic procedures are available,[4,5] they do not focus on the mechanism or incidence of postoperative nerve injury. Surgery for fracture fixation has not been included in this review. Relevant information is broadly organized according to type of surgical procedure in order to facilitate reference by anesthesiologists and members of the anesthesia care team.

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METHODS

For the purposes of this narrative review, the authors initially searched MEDLINE (1946 to February 2014) and the Cochrane databases to identify reports of neurological injury after common elective shoulder and elbow surgery, as well as anatomical studies pertaining to the mechanism of nerve injury. The search was performed using the following key words: shoulder, arthroscopy, arthroplasty, replacement, rotator cuff repair, stabilization, Latarjet, nerve injury, neurological injury, and complications. This was repeated for the key words: elbow, arthroscopy, arthroplasty, nerve injury, neurological injury, and complications. The references of all applicable studies and review articles were also manually cross-referenced to ensure completeness.

Inclusion criteria were large cohort studies that reported the incidence of neurological injury after elective shoulder and elbow arthroscopy or joint replacement, open shoulder stabilization, rotator cuff repair, or Latarjet procedures. The authors excluded case reports, pediatric surgery, and nonelective surgery in the setting of trauma or fracture. Orthopedic surgeons with subspecialty interest in shoulder and elbow surgery reviewed each scientific article and their references. The following narrative review does not list all applicable studies; the authors have limited discussion to research articles they felt to be most meaningful and useful to anesthesiologists regularly performing regional anesthesia in the setting of elective shoulder and elbow surgery. We purposefully selected articles that (1) designated nerve injury as a primary outcome; (2) included the largest number of patients, such that isolated nerve injuries in small cohorts would not exaggerate the incidence of nerve injury described herein; and/or (3) specified which nerve was injured anatomically, provided details with regard to the severity of the nerve injury, postulated on the mechanism, and described the incidence of permanent nerve injury and average time to resolution.

Content experts P.D.G.H. and J.S.T. are experienced fellowship-trained shoulder and elbow subspecialty orthopedic surgeons who designated the most common elective shoulder and elbow surgeries to address, selected the most reliable and valid studies to include, and provided their informed, clinically rich perspective to strengthen the unique and practical value of the material presented herein.

SHOULDER SURGERY

Arthroscopic Shoulder Procedures

A variety of shoulder procedures are performed using arthroscopic techniques, most commonly shoulder stabilization (repair of the anterior labrum in the setting of anterior shoulder instability), repairs of the superior labrum and biceps insertion, and

rotator cuff repairs. The reported frequencies of nerve injury related to shoulder arthroscopy is reported to range between less than 0.1% and 10%[6–12] (Table 1). The largest available series involved 14,329 arthroscopic shoulder procedures captured in a self-reported questionnaire completed by orthopedic surgeons. Among these 14,329 procedures, only 4 major postoperative nerve injuries (3 BP and 1 axillary nerve [AXN]) (<0.1%) were reported; however, the limitations of such a study design are self-evident.[11] The mechanisms of nerve injury most frequently implicated during shoulder arthroscopy are stretching secondary to traction and direct trauma due to portal placement. Injury secondary to suture placement and insertion of anchors are thought to be far less common.

Stretch injuries have been associated with the lateral decubitus position because of excessive traction on the BP (Fig. 1A).[13] The arm is typically abducted between 30 and 45 degrees, with traction placed in line with the arm; many surgeons prefer to use this lateral position as it maximizes the amount of working space, especially in the glenohumeral joint when performing labral repairs. Up to a 10% incidence of transient neuropraxia has been reported in patients undergoing arthroscopic shoulder surgery in the lateral position, fortunately with complete resolution within 48 hours[9,12,14,15] (Table 1).

The most commonly injured nerves are the musculocutaneous nerve (MCN), although transient ulnar and radial nerve injuries have been reported secondary to use of excessive traction.[9,10,14] It is postulated that the MCN is especially vulnerable to stretching in the abducted and externally rotated position and potential compression from passage of the MCN through an overstretched coracobrachialis muscle.[9] Transient neurological injury to the dorsal digital nerve of the thumb has also been reported and attributed to inadequate padding at the wrist.[8] Careful attention to arm padding, positioning, and use of less than 12 to 15 lb of traction may be helpful, as both the amount and duration of traction are important factors in the pathogenesis of stretch injury.[9,15,16]

Shoulder arthroscopy performed in the beach-chair position (Fig. 1B) is less commonly associated with stretch injuries of the BP compared with the lateral position.[6] However, the beach-chair position does present its own challenges; improper head positioning is reported to have caused cutaneous neuropraxias (lesser occipital and greater auricular nerve injury secondary to sustained direct compression from the head holder[17]) and even complete midcervical quadriplegia.[13]

While arthroscopic surgery can minimize soft tissue dissection compared with open shoulder surgery, the insertion of portals carries an inherent risk of direct trauma to adjacent nerves (Figs. 2 and 3). Insertion of the lateral portal is associated with injury to sensory branches of the AXN in up to 10% of patients, with the majority of patients improving over time.[7] The greatest traumatic risk to the AXN actually comes from the placement of arthroscopy portals in the anterior-inferior positions: the transsubscapularis portal sometimes used in labral repair can lie as close as 1.5 cm to the AXN.[18] Placement of any anterior portals medial to the coracoid and conjoint tendon risks traumatic injury to the MCN and lateral cord of the BP. Fortunately, permanent injury to these nerves is extremely rare (<0.1%) in the hands of experienced shoulder arthroscopy surgeons.[11,18]

The suprascapular nerve (SSN) can be injured by compression from anchors placed into the superior aspect of the glenoid, such as those used SLAP (superior labrum anterior to posterior) repairs[19,20]; the SSN typically lies 2 cm away from the insertion points of these anchors.[21] Finally and least frequently, the AXN nerve can be injured during insertion of capsulolabral sutures used in shoulder stabilization surgery (Fig. 4); the AXN is just 1 to

TABLE 1. Neurological Complications of Shoulder Surgery

Type of Surgery	Authors	Design	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries, n	Average Time to Resolution	Anesthetic Type	Remarks
Arthroscopy, varied	Berjano et al,[6] 1998	R	141	1.4% (2)	2 UN	0	2–12 wk	GA/RA	Thought to be due to traction around elbow
Arthroscopy	Segmuller et al,[7] 1995	R	304	7% (21)	Sensory disturbance	10	8 mo	GA	Thought to be secondary to lateral portal
Arthroscopy, varied	Pitman et al,[9] 1988	P	20	10% (2)	1 MCN, 1 RN	0	24–48 h	GA	Excessive traction though to be responsible
Arthroscopy, subacromial decompression	Ellman,[8] 1987	NR	50	6% (3)	3 Dorsal digital nerve of thumb	0	NR	NR	Thought to be secondary to insufficient padding
Arthroscopy, varied	Ogilvie-Harris and Wiley,[10] 1986	R	439	0.2% (1)	1 MCN	0	Resolved 6 wk	GA	Likely traction injury
Arthroscopy, varied	Small,[11] 1986	Q	14,329	<0.1% (4)	3 BP, 1 AXN	NR	NR	GA/RA	Questionnaire study
Arthroscopy, varied	Andrews and Carson,[14] 1983	R	120	2.5% (3)	1 MCN, 2 UN	0	NR	GA	—

AXN indicates axillary nerve; BP, brachial plexus; GA, general anesthetic; MCN, musculocutaneous nerve; NR, not reported; P, prospective; Q, questionnaire; R, retrospective; RA, regional anesthetic; RN, radial nerve; UN, ulnar nerve.

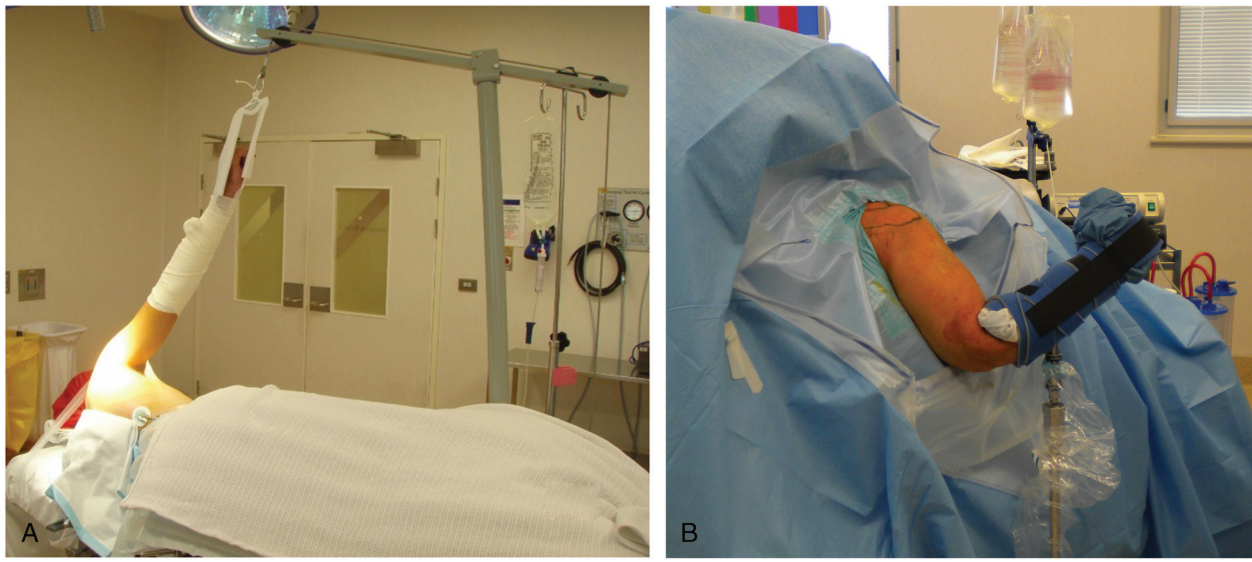

FIGURE 1. A, Right shoulder arthroscopy in lateral decubitus with traction device. B, Right shoulder arthroscopy with patient in beach-chair position, with the use of a mechanical arm holder. Images used with the permission of www.boneschool.com.

1.5 cm below the inferior glenohumeral capsule where capsular sutures are routinely inserted.[22] As such, surgeons are advised to maintain a "safe zone" minimum distance of 1 cm from the glenoid for the placement of capsular sutures.[23]

Open Shoulder Procedures

Open shoulder surgery may include open rotator cuff surgery, open shoulder stabilization, and total shoulder replacement (TSR). The nerves most susceptible to injury during open shoulder surgery are the AXN, MCN, and SSN. Burge and colleagues[24] have demonstrated that the shortest nerves (ie, AXN and MCN) are at highest risk for traction injury during open shoulder surgery.

Open rotator cuff surgery is performed using either the mini–open technique (deltoid split) or open technique (deltoid detached from the acromion). The most commonly injured nerve is the anterior branch of the AXN, which lies just deep to the deltoid muscle; however, the rate of reported injury is very low (2.6%), and symptoms are usually transient.[25] This branch of the AXN is usually found approximately 5 cm distal to the acromion; therefore, surgeons limit their deltoid split to a distance of 5 cm from the acromion. However, the distance from the acromion to the anterior branch of the AXN can be variable, with mean distances reportedly ranging between 31 and 80 mm; abduction of the arm decreases this distance even further.[26–29] Repair of massive rotator cuff tears requires special dissection into the supraspinatus and infraspinatus fossa, risking injury to the SSN as it passes around the suprascapular notch.[30,31] However, SSN injury can be especially difficult to distinguish from either tendon retear or expected postoperative weakness after surgery in the absence of formal nerve conduction studies.[30]

Open shoulder stabilization surgery is performed through a deltopectoral approach, using the interval between the deltoid muscle and the pectoralis major. The reported rate of neurological

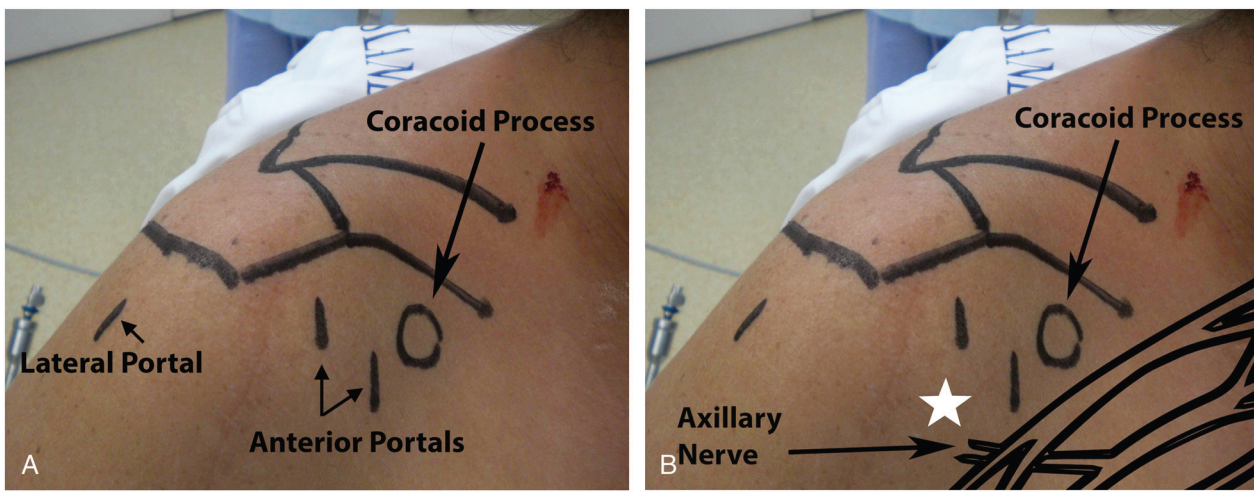

FIGURE 2. A, Anterior glenohumeral portals and lateral portals used in shoulder arthroscopy. The lines on this right shoulder identify the bony anatomy of the clavicle and acromion. B, Identical photograph with BP illustration superimposed. The white star indicates the transsubscapularis portal, demonstrating its proximity to the AXN. All portals must remain lateral to the coracoid process to avoid damage to the BP. Images used with the permission of www.boneschool.com.

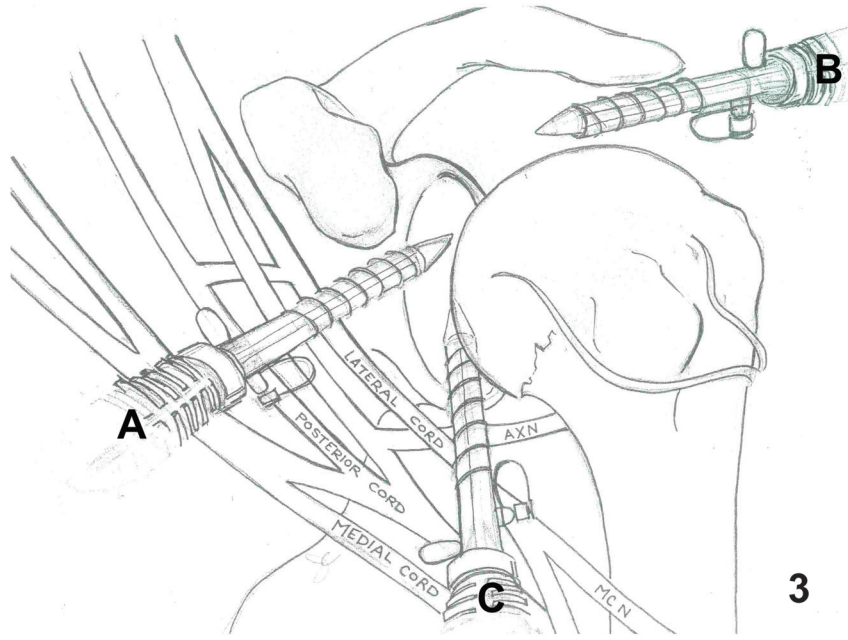

FIGURE 3. Left shoulder illustration depicting the lateral and anterior glenohumeral portals, used in rotator cuff and labral repair surgery, and their relationship to the BP, with patient in a beach-chair position. A, Anterior rotator interval portal. B, Posterior glenohumeral portal. C, Transsubscapularis portal. Image used with the permission of www.boneschool.com.

injury varies between 0.8% and 8.2% (Table 2). The MCN is at particular risk of injury in this approach because of compression by retractors placed under the conjoint tendon to keep the interval open.[32] It is therefore recommended that caution be used in muscle retraction (Fig. 5). Excessive traction in the setting of open shoulder stabilization has also been reported to cause diffuse BP injury.[32] Finally, the AXN may also sustain direct traumatic injury during the deltopectoral approach, as entry to the glenohumeral joint usually requires division of part or all of the subscapularis muscle to expose the capsule. As the AXN passes under subscapularis to exit through the quadrangular space, surgeons will customarily preserve the inferior-most quarter of the subscapularis muscle in order to protect the AXN (Fig. 6).

A Bristow-Latarjet operation is a procedure sometimes used in primary shoulder stabilization, involving a coracoid osteotomy, with transfer of the bone block and attached conjoint tendon to the anterior glenoid.[34,35] A systematic review published in 2013 identified 21 cases of nerve injury among 1904 surgeries (1.2%),

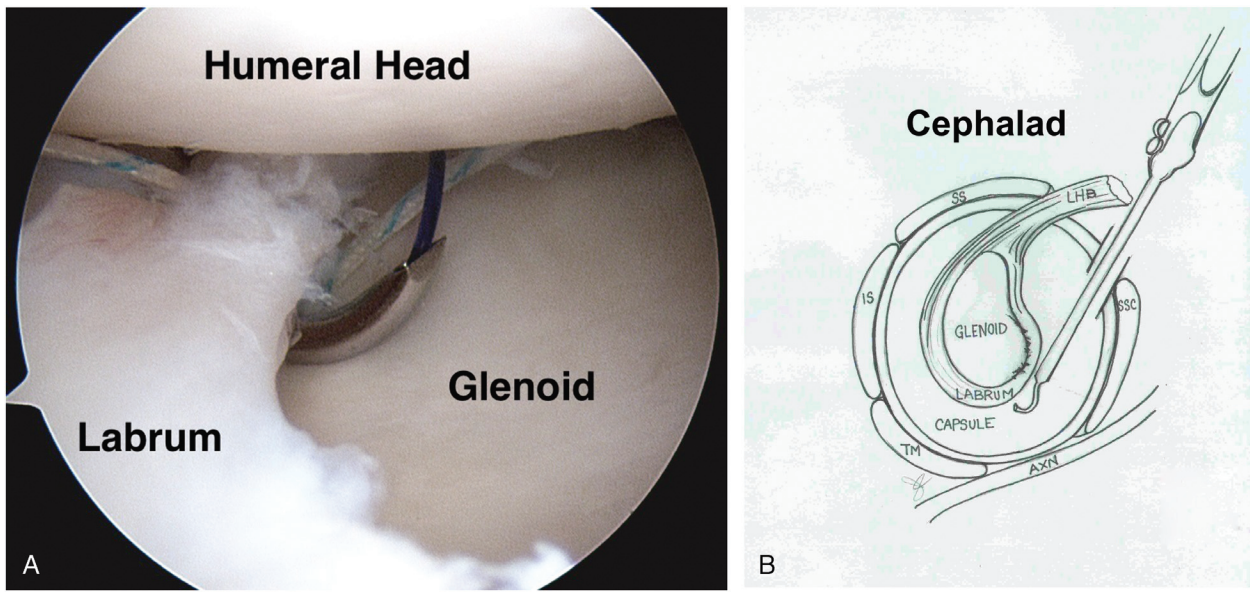

FIGURE 4. A, Arthroscopic right shoulder stabilization, demonstrating use of a suture passer through the anterior capsule and labrum. Taking too deep a bite at the inferior glenoid margin theoretically places the AXN at risk. B, Artist's rendition of the glenohumeral anatomy, depicting arthroscopic repair of an anterior labral lesion. The AXN passes below the shoulder capsule at a distance of 1 to 1.5 cm from the glenoid. LHB indicates long head biceps; SSC, subscapularis; SS, supraspinatus; IS, infraspinatus; TM, teres minor. Images used with the permission of www.boneschool.com.

TABLE 2. Neurological Complications of Open Shoulder Surgery

Type of Surgery	Authors	Design	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries, n	Average Time to Resolution	Anesthetic Type	Remarks
Open rotator cuff repair	Mansat et al,[25] 1997	NR	114	2.6% (3)	1 AXN, 1 UN, 1 RN (secondary to sling)	0	NR	GA	Branches of AXN likely secondary to surgical trauma
Open rotator cuff repair, massive	Zanotti et al,[30] 1997	R	10	10% (1)	1 SSN	NR	NR	NR	—
Open shoulder stabilization	McFarland et al,[33] 2002	P	128	0.8% (1)	1 AXN	0	6 wk	GA	—
Open shoulder stabilization	Ho et al,[32] 1999	P	282	8.2% (23)	8 diffuse BP injuries, 8 lateral cord or MCN, 7 sensory defects only	5	3.5–4 mo	NR	Thought to be secondary to traction from retractors
Latarjet	Shah et al,[36] 2012	P	45	10% (5)	2 MCN, 1 RN, 2 AXN	2	2 mo	NR	Thought to be secondary to traction from retractors

AXN indicates axillary nerve; BP, brachial plexus; GA, general anesthetic; MCN, musculocutaneous nerve; NR, not reported; P, prospective; R, retrospective; RN, radial nerve; SSN, suprascapular nerve; UN, ulnar nerve.

with the MCN most commonly injured, followed by the AXN and diffuse brachial plexopathies.[37] The MCN is especially at risk because of coracoid mobilization, with the entry point of the MCN into the coracobrachialis varying anywhere between 3.1 and 8.2 cm from the tip of the coracoid.[38,39] The AXN and the BP are at risk for the same reasons as in open shoulder stabilization. Case reports of SSN injury exist, likely due to glenoid screws impinging on the SSN as it runs along the posterior glenoid or due to overpenetration when drilling. Anatomical studies therefore recommend avoiding medial deviation of the glenoid screws[38,40] (Fig. 7).

Shoulder Replacement

The incidence of neurological complications associated with anatomic TSR is reported to be between 0.8% and 4.3%,[41–44] although a prospective study identified a transient neuropraxia in 16.7% of patients[45] (Table 3). A review in 1996 identified that diffuse BP injuries were the most commonly encountered nerve injury,[42] with isolated injuries to the AXN, MCN, and ulnar nerve also described.[45–48] Proposed mechanisms of nerve injury during shoulder arthroplasty include direct trauma, compression secondary to retractors, or hematoma and traction.[46] A prospective study

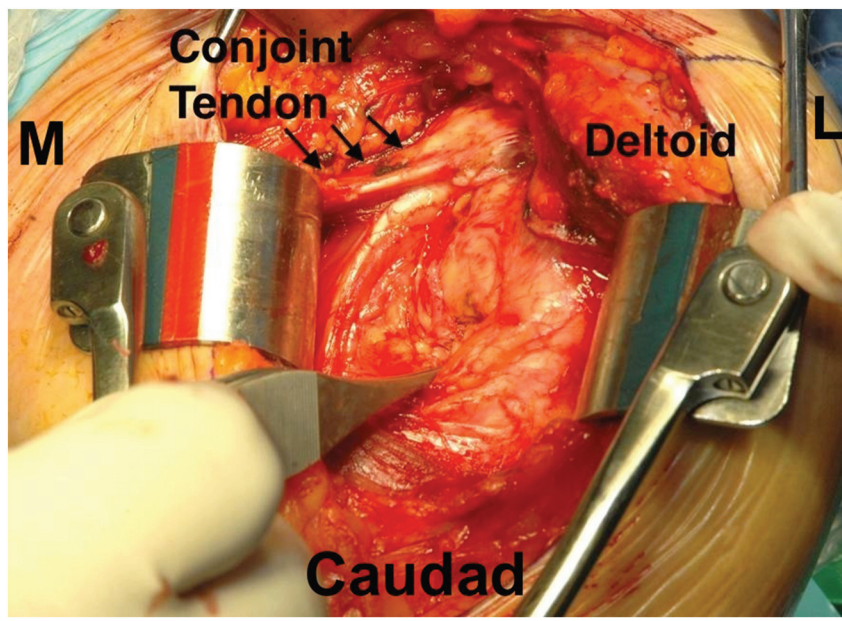

FIGURE 5. Clinical photograph of the deltopectoral approach utilized in open shoulder stabilization or shoulder arthroplasty, with the subscapularis tendon being divided in this left shoulder. Retractor blades have been placed under the deltoid and the conjoint tendon to expose the subscapularis tendon (identified by the forceps); the retractor blade under the conjoint tendon risks compression of the MCN. The AXN also passes under the subscapularis musculotendinous unit, placing it at risk in this approach. M indicates medial; L, lateral. Image used with the permission of www.boneschool.com.

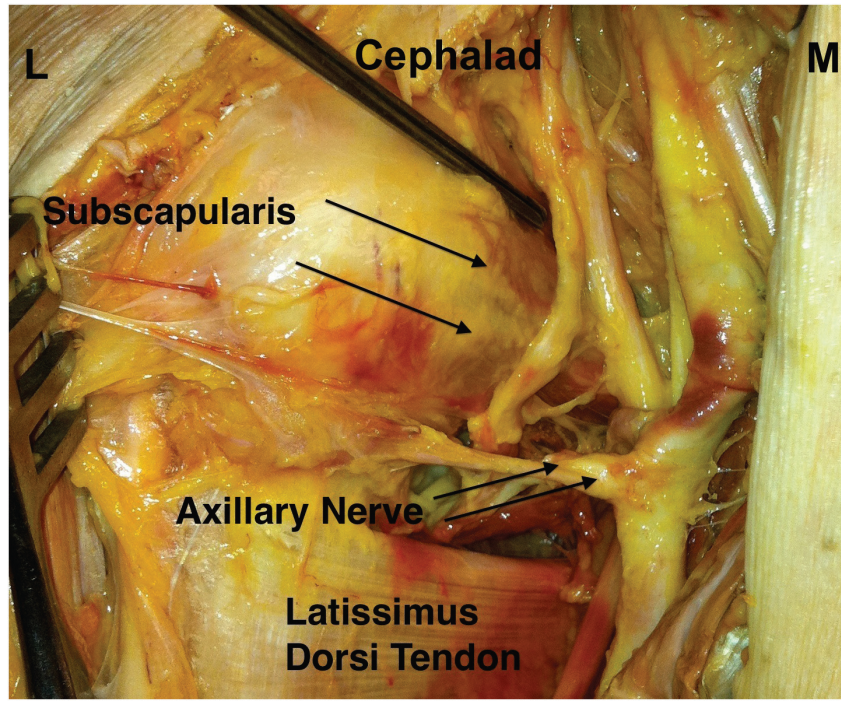

FIGURE 6. Anatomical dissection of the right shoulder demonstrating the AXN passing from anterior to posterior under the inferior border of the subscapularis musculotendinous unit. As the subscapularis tendon is usually divided for access to the shoulder, the nerve is at risk and must be protected. M indicates medial; L, lateral. Image used with the permission of www.boneschool.com.

of 30 patients by Nagda and colleagues,[45] using intraoperative nerve monitoring, found that more than 50% of patients undergoing TSR demonstrated intraoperative nerve dysfunction, seemingly related more to arm position than retractor use. Nerve dysfunction was seen mostly during glenoid preparation, with the arm in extreme external rotation and extension.[45] Among these 30 patients, 4 had clinical evidence of nerve injury (all of which had resolved by 6 months). Patients with very stiff shoulders (external rotation <10 degrees) and a history of prior shoulder surgery were most at risk.[43,45,49,50]

The reverse TSR is a reconstructive option for osteoarthritis in the presence of a massive rotator cuff tear (rotator cuff arthropathy). The incidence of clinical neurological impairment in the setting of reverse TSR is reported to be between 0.6% and

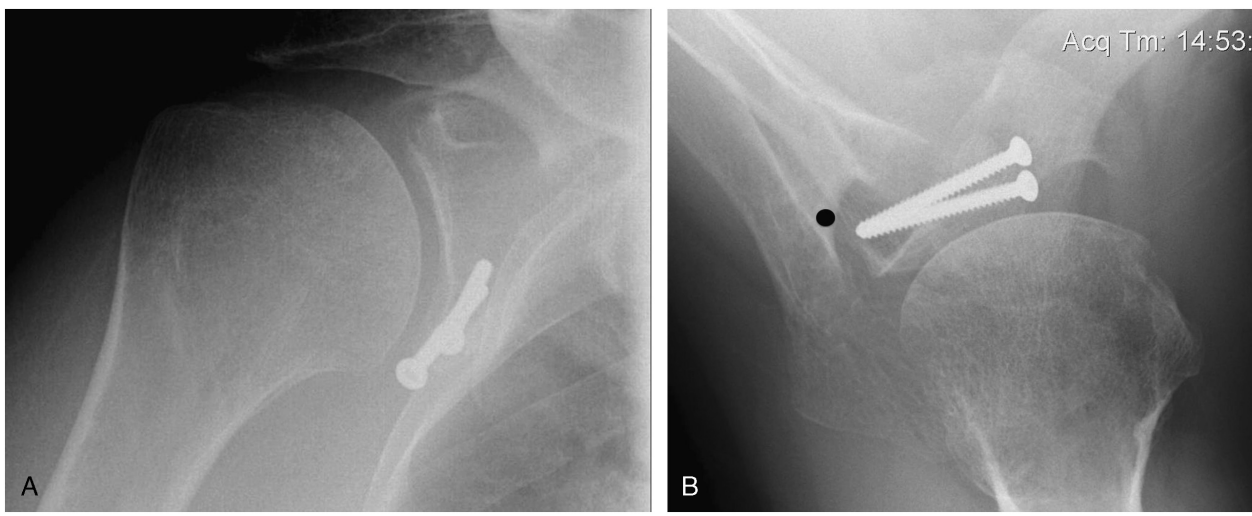

FIGURE 7. A, Postoperative anteroposterior radiograph of the right shoulder after a Latarjet procedure, demonstrating transfer of the coracoid process and conjoint tendon to the anterior glenoid, with screw fixation of the bone block onto the glenoid. B, Axillary lateral radiograph of the same shoulder, demonstrating screws passing through the bone block and from the anterior to the posterior aspect of the glenoid. The black dot demonstrates approximate location of SSN—screws penetrating through the posterior glenoid can potentially cause injury to this nerve. Images used with the permission of www.boneschool.com.

TABLE 3. Neurological Complications of TSR

Type of Surgery	Authors	Design	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries, n	Average Time to Resolution	Anesthetic Type	Remarks
Anatomic TSR	Ladermann et al,[46] 2011	P	23	5.2% (1)	1 BP	1	NR	RA	Postop hematoma thought to be cause
Anatomic TSR	Nagda et al, 2007	P	30	16.7% (5)	3 AXN, 1 BP, NR other	0	6 mo	GA	Thought to be secondary to traction
Anatomic TSR	Lynch et al,[42] 1996	P	417	4.3% (18)	17 BP, 1 MN	5	Majority by 6 mo	GA/RA	Thought to be secondary to traction
Reverse TSR	Walch et al,[47] 2012	P	213	3.6% (8)	2 BP, 1 AXN, 4 UN, 1 MN	5	<1 mo	NR	Thought to be secondary to traction and lengthening
Reverse TSR	Kempton et al,[51] 2011	P	152	0.6% (1)	Not specified	0	Weeks	GA/RA	—
Reverse TSR	Boileau et al,[48] 2006	P	45	2.2% (1)	1 AXN	1	NR	NR	—

AXN indicates axillary nerve; BP, brachial plexus; GA, general anesthetic; MCN, musculocutaneous nerve; MN, median nerve; NR, not reported; P, prospective; RA, regional anesthetic; SSN, suprascapular nerve; TSR, total shoulder replacement; UN, ulnar nerve.

3.6%,[47,48,51] with a variety of discrete nerve and BP injuries reported (Table 3). The risk of nerve injury is thought to be higher with reverse TSR than anatomic TSR because of permanent lengthening of the arm and subsequent stretch and elongation of the BP (Fig. 8).[46] A prospective series comparing anatomic and reverse TSR demonstrated nearly an 11-fold increase in the rate of postoperative changes recorded on electromyography in the reverse TSR cohort.[46] The majority of the electromyography deficits were related to the AXN and associated with a mean arm lengthening of 2.7 cm. Reverse TSR has also been implicated in injury to the SSN, because of the need to secure the glenoid component with multiple screws (Fig. 9).[52] Importantly, SSN nerve injury is notoriously difficult to diagnose clinically because most patients also have massive rotator cuff tears and supraspinatus muscle wasting.[53]

ELBOW SURGERY

Because of the high density of nerves traversing the elbow, surgery in this region is extremely hazardous. The minimal soft tissue envelope afforded by the elbow provides little protection for this rich neural environment. For this reason,

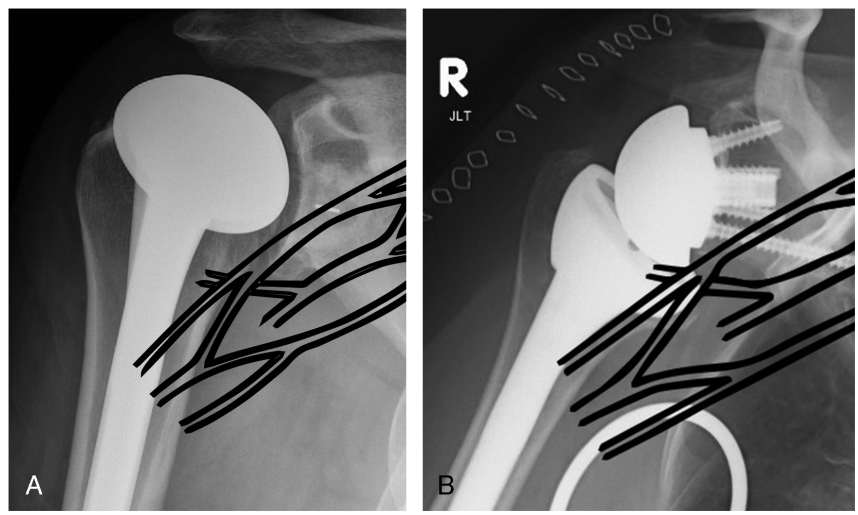

FIGURE 8. A, Postoperative anteroposterior radiograph of the right shoulder, demonstrating an anatomic TSR most commonly performed for primary osteoarthritis. An illustration of the BP has been superimposed. B, Postoperative anteroposterior radiograph of the right shoulder, demonstrating a reverse TSR, required in the setting of arthritis and a massive rotator cuff tear (rotator cuff arthropathy). Reverse TSR is associated with arm lengthening, potentially stretching the BP as depicted. Images used with the permission of www.boneschool.com.

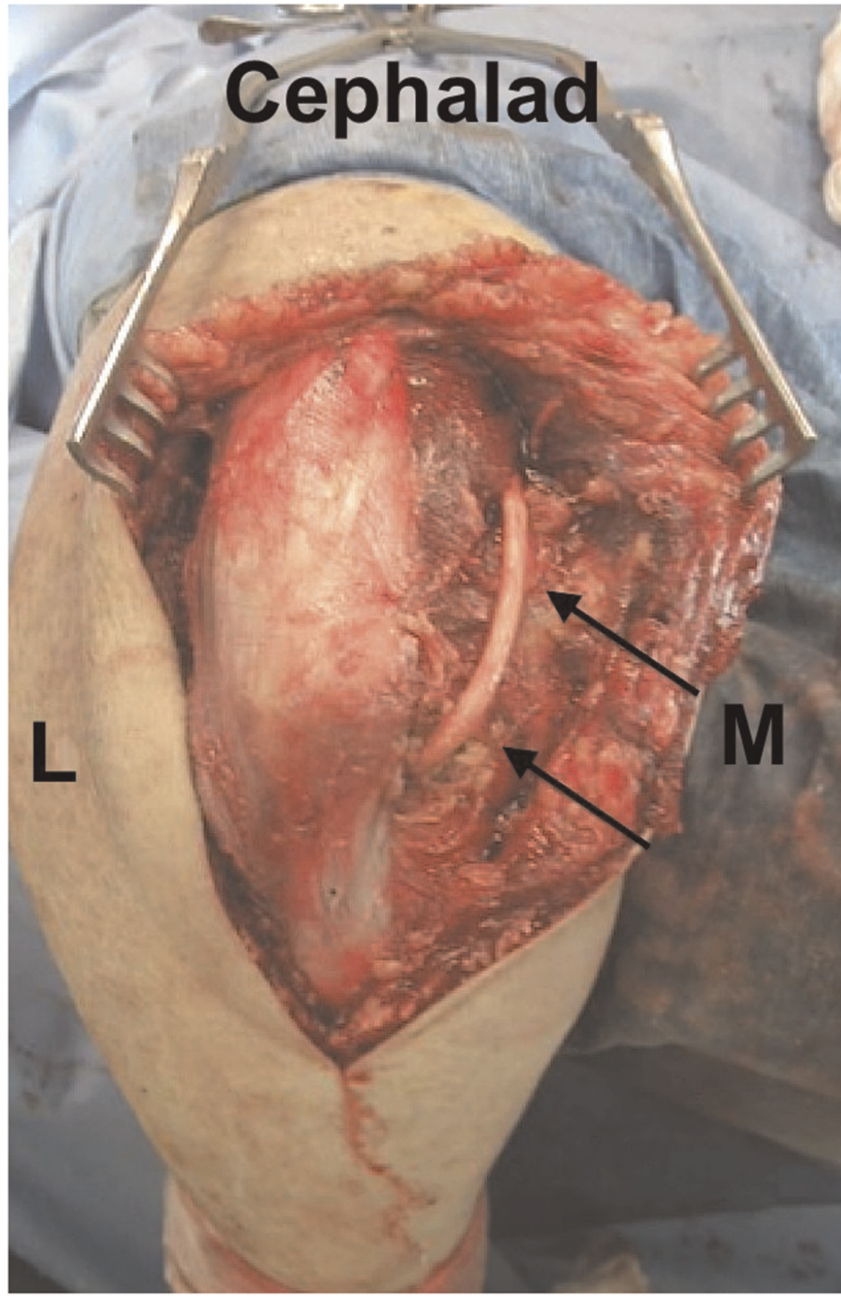

FIGURE 9. Posterior approach to the left elbow for total elbow arthroplasty. The patient is in the lateral decubitus position, left side up, with the left elbow placed over a bolster. The ulna nerve (arrows) has been exposed prior to opening the joint. M indicates medial; L, lateral. Images used with the permission of www.boneschool.com.

iatrogenic neurological injury is unfortunately relatively common about the elbow (Table 4).

Elbow Replacement

The posterior approach is the standard incision for total elbow replacement (TER). Of all the standard surgical approaches to the elbow, the posterior is the safest as the incision violates the fewest cutaneous nerves, and the larger deep nerves are safe if the dissection is maintained in the midline.[54] However, the dissection required in order to perform TER is extensive, requiring exposure of entire elbow joint, endangering particularly the ulnar nerve.[55,56] To minimize nerve damage, the initial steps of a TER procedure are identification, neurolysis, and protection of the ulnar nerve (Fig. 9).

Despite such efforts, transient postoperative ulnar nerve paresthesias occur in up to 21% of patients[57–60] (Table 4). Persistence of any ulnar neuropathic symptoms (either sensory or motor) beyond 6 weeks is less common, but has been described in up to 10% of patients.[62] A systematic review conducted in 2011 identified the rate of ulnar neuropathy to be nearly 3% among 2938 TER procedures.[59] Acute mechanical irritation, exposure to heat from cement, and compression by hematoma are the suspected

TABLE 4. Neurological Complications of Elbow Surgery

Type of Surgery	Authors	Design	Total Surgeries	Rate of Nerve (n)	Nerves Injured	Permanent Nerve Injuries, n	Average Time to Resolution	Anesthetic Type, % (n)	Remarks
TER	Aldridge et al,[58] 2006	R	41	12% (5)	5 UN	0	2 wk	NR	—
TER	van der Lugt et al,[61] 2004	P	204	4.9% (10)	10 UN	2	NR	NR	3 Patients with complete paresthesia underwent a nerve release
TER	Ewald et al,[60] 2003	R	202	21.3% (43)	43 UN	6	Majority within days	NR	33/43 Had sensory changes that resolved in 1–2 d
TER	Morrey and Adams,[57] 1992	R	68	15% (10)	10 UN	1	Majority within days	NR	—
Elbow arthroscopy	Nelson et al,[73] 2014	R	417	1.7% (7)	5 SRN, 1 MN, 1 non specific	0	NR	GA	—
Elbow arthroscopy	Elfeddali et al,[75] 2013	R	200	2% (4)	3 UN, 1 RN	1	6 wk	GA, 53% (106), RA 47% (94)	
Elbow arthroscopy	Kelly et al,[68] 2001	R	449	2.6% (12)	5 UN, 4 SRN, 1 PIN, 1 MABN, 1 AIN	0	6 wk	NR	Majority seen in patients with rheumatoid arthritis or contractures
Elbow arthroscopy	O'Driscoll and Morrey,[63] 1992	R	71	4.2% (3)	3 RN	0	2–3 h	RA	—

AIN indicates anterior interosseous nerve; GA, general anesthetic; MN, median nerve; MABN, medial antebrachial nerve; NR, not reported; P, prospective; PIN, posterior interosseous nerve; SRN, superficial radial nerve; R, retrospective; RA, regional anesthetic; RN, radial nerve; TER, total elbow replacement; UN, ulnar nerve.

causes for most cases of ulnar neuropathy.[59] Although radial nerve injury is exceedingly rare in TER, isolated radial nerve damage has been reported in the setting of revision TER surgery.[55]

Elbow Arthroscopy

Elbow arthroscopy is an evolving technique, used predominantly in the surgical management of degenerative or inflammatory elbow conditions (ie, synovectomy, loose body removal, and debridement).[63–66] Iatrogenic neurological injury is one of the most common complications of elbow arthroscopy.[64] Unlike open surgery of the elbow, the important neural structures are not exposed and therefore cannot be easily protected. This underscores the vital importance of a thorough knowledge of topographic anatomy before attempting elbow arthroscopy.[67] Even in the most experienced hands, the reported risk of transient neuropraxia is 2.5%, especially in the setting of rheumatoid arthritis or contractures.[65] Because many surgeons perform an immediate postoperative neurological assessment, some (but not all) authors have advocated the avoidance of regional anesthesia during elbow arthroscopy.[67,69]

Every nerve within the vicinity of the elbow has been the subject of reported injury from elbow arthroscopy, with injury to the superficial radial and ulnar nerves most common[63,68,70–73] (Table 4). Fortunately, iatrogenic nerve palsy (ranging between 1.7% and 4.2%) in the setting of elbow arthroscopy is almost always transient, with recovery occurring between several hours to fewer than 6 weeks in almost all cases.[63,68,74,75] The most severe injury is complete or partial transection of a nerve, with several case reports describing such injury to the anterior interosseous, radial, ulnar, and median nerves.[75–77] Although rare, permanent hand dysfunction is the consequence.

The insertion of portals used to gain access to the elbow joint is one of the most common causes of iatrogenic nerve injury.[68,69,71,73] In fact, the inherent risk is so great that any previous injury or surgery that distorts elbow anatomy is considered a contraindication to the procedure.[67,74] There are multiple portals described—in most cases, the average distance to the local superficial nerves is up to 2 cm.[65,67] However, Unlu and colleagues[78] demonstrated that with the elbow in the 90 degrees of flexion, the anterolateral portal was only 4.8 mm from the radial nerve, the anteromedial portal was only 12.9 mm from the median nerve, and the superomedial portal was only 16.2 mm from the ulnar nerve.

DISCUSSION

The mechanism, likelihood, and severity of neurological injury associated with shoulder and elbow surgery depend on the type of surgery being performed and may be confounded by the administration of regional anesthesia. Table 5 presents a summary of the most common nerve injuries associated with each procedure and the postulated mechanism of injury. In general, transient nerve injury associated with shoulder and elbow surgery is fairly common, and the likelihood of permanent nerve damage is not insignificant.

The vast majority of the publications addressing nerve injury in the setting of elective shoulder and elbow surgery are retrospective and do not designate neurological injury as a primary outcome. These studies may underestimate the true incidence of neurological complications. Moreover, because of the narrative nature of this review, selection bias cannot be excluded from the material presented herein.

An understanding of the patterns of iatrogenic nerve injury related to common elective shoulder and elbow procedures may assist in the diagnosis and management of these patients. Although it is often not possible to definitively identify the cause of

TABLE 5. The Most Common Nerve Injuries Associated With Common Elective Shoulder and Elbow Procedures and the Postulated Mechanism of Injury

Type of Surgery	Most Common Nerves Injured	Mechanism
Shoulder arthroscopy	Musculocutaneous nerve	Stretch secondary to positioning
	Dorsal digital nerve of the thumb	Compression
Open rotator cuff repair	Branches of the AXN	Trauma from surgical approach
Open shoulder stabilization/Latarjet	AXN	Direct trauma/traction
	Musculocutaneous nerve	Retractors under the conjoint tendon
Total shoulder replacement (anatomic and reverse)	Diffuse brachial plexus injury	Extreme arm positioning to access glenoid
	AXN	Direct trauma/traction
	Musculocutaneous nerve	Retractors under the conjoint tendon
Elbow arthroscopy	Ulnar nerve	Traumatic injury secondary to portal placement
	Superficial radial nerve	
Total elbow replacement	Ulnar nerve	Direct trauma
		Compression from retractors or hematoma
		Thermal damage from cement

nerve injury especially with the associated use of regional anesthesia, we are hopeful that this review will afford anesthesiologists a better understanding of the specific nerves at risk during the most common shoulder and elbow procedures.

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Neurological Complications Related to Elective Orthopedic Surgery
Part 2: Common Hip and Knee Procedures

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Abstract: Many anesthesiologists may not be familiar with the rate of surgical neurological complications of the hip and knee procedures for which they are providing local anesthetic–based anesthesia and/or analgesia. Part 2 of this narrative review series on neurological complications of elective orthopedic surgery describes the mechanisms and likelihood of peripheral nerve injury associated with some of the most common hip and knee procedures, including arthroscopic hip and knee surgery and total hip and knee replacement.

What's New: As the popularity of regional anesthesia continues to increase with the development of ultrasound guidance, anesthesiologists should have a thoughtful understanding of the nerves at risk of surgical injury during elective hip and knee procedures.

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Many anesthesiologists may not be familiar with the rate of surgical neurological complications of the most common elective hip and knee procedures for which they are providing local anesthetic–based regional anesthesia (RA) and/or analgesia. The rate of iatrogenic nerve injury directly attributable to the surgery itself may be similar to or even exceed that traditionally associated with RA techniques.[1,2] It behooves the anesthesiologist performing RA to understand the risk that the surgical procedure itself may play in the presentation and evolution of perioperative nerve injury. The individual nerves, mechanisms by which they are injured, and tendency for injury during elective hip and knee surgery necessarily depend on the type of procedure being performed.

In part 2 of this narrative review series on neurological complications of orthopedic surgery, we describe the mechanisms and likelihood of peripheral nerve injury associated with some of the most common elective hip and knee procedures for which anesthesiologists may administer RA. Surgery for fracture fixation has not been included in this review. Relevant information is broadly organized according to type of surgical procedure in order to facilitate reference by anesthesiologists and members of the anesthesia care team.

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METHODS

For this narrative review, the authors conducted a search of MEDLINE (1946 to February 2014) and the Cochrane database to identify studies that primarily sought to capture the frequency of neurological injury after common elective hip and knee surgery, as well as anatomical studies pertaining to the mechanism of nerve injury. The search was performed using the following key words: hip, arthroscopy, arthroplasty, replacement, revision, nerve injury, neurological injury, and complications. This was repeated for the following key words: knee, arthroscopy, arthroplasty, replacement, anterior cruciate reconstruction (ACLR), meniscal repair (MR), nerve injury, neurological injury, and complications. The references of all applicable studies and review articles were also manually cross-referenced to ensure completeness.

Inclusion criteria were large cohort studies that reported the incidence of neurological injury after elective hip and knee arthroscopy or joint replacement, revision surgery, ACLR, and MR. The authors excluded case reports, pediatric surgery, and surgery in the setting of trauma or fracture.

Orthopedic surgeons with subspecialty interest in hip and knee surgery reviewed each scientific article and its references. This narrative review does not list all applicable studies; the authors limited their discussion to research articles they felt to be most meaningful and useful to anesthetists regularly performing RA in the setting of elective hip and knee surgery. We purposefully selected articles that (*a*) designated nerve injury as a primary outcome; (*b*) included the largest number of patients, such that isolated nerve injuries in small cohorts would not falsely inflate the incidence of nerve injury described herein; and/or (*c*) specified which nerve was injured anatomically, provided details with regard to the severity of the nerve injury, postulated on the mechanism, and described the incidence of permanent nerve injury and average time to resolution.

Content experts M.D. and D.B.W. are experienced fellowship-trained hip and knee subspecialty orthopedic surgeons who designated the most common elective hip and knee surgeries to address, selected the most reliable and valid studies to include, and provided their informed, clinically rich perspective to strengthen the unique and practical value of the material presented herein.

TOTAL HIP REPLACEMENT

Total hip replacement (THR) is one of the most commonly performed orthopedic procedures and is used to relieve pain related to osteoarthritis of the hip. Depending on surgeon preference, THR can be performed through either a posterior, lateral, or anterior approach. The posterior approach involves dividing the external rotators of the hip (including the piriformis tendon) to access the hip joint. The lateral approach to the hip necessitates detachment of the abductor muscles (gluteus medius and minimus) from the greater trochanter, whereas the anterior approach (less commonly used) involves opening the interval between sartorius and tensor fascia lata muscles to access the hip joint. Although

the proximity of the sciatic (posterior approach), lateral femoral cutaneous (anterior approach), and superior gluteal nerves (SGNs) (lateral approach) theoretically renders these nerves more susceptible to iatrogenic injury with each approach, the evidence is mixed as to whether the surgical approach independently affects the rate of nerve injury.[3,4] A recent Cochrane review comparing surgical approaches identified an increased rate of nerve injuries with the lateral approach (10/49, 20%) compared with the posterior approach.[5–7]

The reported rate of neurological complication associated with THR surgery varies between 0.08%[8] and 88.3%,[9] a variation attributable to the different approaches used, indications for surgery, revision surgery, and whether transient neuropraxia was purposefully sought as the primary outcome measure for the study[8,10–14] (Table 1). Most cases of nerve injury are attributed to compression of nerves by retractors,[15] excessive leg lengthening,[4,13] and traction injuries during dislocation and manipulation of the hip. Most of these nerve injuries occur during the surgical procedure; however, delayed nerve injury can develop postoperatively as a result of a hematoma.[10,16] The nerves most commonly injured are the sciatic nerve and its peroneal branch,[4,10,13] the lateral femoral cutaneous nerves (LFCNs),[9,17] and the femoral nerve[4,8,12]; the tibial branch of the sciatic nerve[18,19] and the obturator nerve[10,12] are far less commonly affected (Table 1).

Sciatic Nerve and Its Branches (Common Peroneal and Tibial)

The reported incidence of sciatic nerve palsy associated with THR ranges from 0.08%[3] to 3.7%.[14] The common peroneal nerve (CPN) branch is more commonly injured that than the larger

TABLE 1. Neurological Complications of Hip Replacement Surgery

References	Approach	Design	Total Surgeries, n	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries, n	Average Time to Resolution	Remarks
Bhargava et al[17] (2010)	Anterior	R	81	14.8% (12)	LFCN	2	2 y	Nerve injury resulted in sensory paresthesia only
Goulding et al[9] (2010)	Anterior	P	60	88.3% (53)	LFCN	50	1 y	Higher incidence of nerve injury in those undergoing hip resurfacing as opposed to standard THR
Picado et al[21] (2007)	Lateral	P	40	42.5% (17)	SGN	1	12 mo	All nerve injuries diagnosis by EMG
Farrell et al[4] (2005)	Varied	R	27,004	0.17% (47)	CPN > SN > FN	29	21.1 mo	Results from a large database, with surgery performed using multiple approaches
Pekkarinen et al[19] (1999)	Varied	R	4339	0.6% (27)	CPN, TN	12	NR	Both primary and revision surgery included in this article
Navarro et al[3] (1995)	Varied	P	1000	0.8% (8)	CPN > SN > FN	7	5 mo	—
Nercessian et al[10] (1994)	Varied	R	7133	0.48% (34)	CPN > SN > FN > LFCN, ON	13	3-14 mo	A higher incidence of nerve injury was seen in revision surgery compared with primary THR
Nercessian et al[8] (1994)	NR	R	1298	0.08% (1)	SN	NR	NR	Both primary and revision THR cases included
Schmalzried et al[18] (1991)	Lateral	R	3126	1.7% (53)	CPN > SN > FN > TN	29	2 y	—
Amstutz et al[26] (1982)	NR	R	88	7.5% (5)	CPN	2	NR	This series looks at revision THR only
Weber et al[12] (1976)	NR	R	2012	0.7% (14)	SN > FN > ON	10	1 year	—
Wilson and Scales[14] (1973)	Lateral	R	108	3.7% (4)	SN, CPN	0	NR	—
Buchholz and Noack[11] (1973)	NR	R	3205	1.52% (60)	SN, FN, CPN	16	NR	—

CPN indicates common peroneal nerve; FN, femoral nerve; LFCN, lateral femoral cutaneous nerve; NR, not reported; ON, obturator nerve; P, prospective; R, retrospective; SGN, superior gluteal nerve; THR, total hip replacement; TN, tibial nerve.

sciatic nerve or its tibial branch,[4,18] most likely because of the relatively subcutaneous location of the CPN in comparison to the tibial branch. Indeed, the tibial nerve is rarely injured in isolation.[18] Compression by retractors and traction is widely thought responsible; direct surgical laceration of the sciatic nerve and its branches is rare.[4,10,18] Postoperative hematoma, which most commonly involves the gluteal compartment, has also been implicated in sciatic nerve palsy, sometimes presenting as late as 2 weeks postoperatively.[4,10]

Femoral Nerve

Femoral nerve palsy is rare, reportedly varying between 0.01%,[4,10] and 0.29%.[12] Although the femoral nerve is never normally visualized within the surgical field during THR, the foremost cause of femoral nerve injury is thought to be compression due to improper placement of the anterior acetabular retractors, regardless of the approach, as the tip of the retractor is placed near the expected trajectory of the femoral nerve.[15,20] However, femoral nerve palsy can be seen in association with sciatic nerve palsy, suggesting that the femoral nerve is susceptible to traction injuries as well.[3,12] Femoral nerve palsy has also been caused by compression from hematomas involving the iliacus muscle[16] and by thermal injury from extrusion of cement.[12]

Superior Gluteal Nerve

The SGN is particularly at risk during the lateral approach to the hip, as this approach requires partial detachment of the abductor muscles from the greater trochanter in order to access the hip joint. Clinically, it can be difficult to differentiate SGN injury from expected postoperative weakness of the abductors secondary to surgical detachment.[21] In a prospective study of 40 patients undergoing THR, injury was diagnosed on electromyography (EMG) in 42.5% (17/40) of patients postoperatively, with only 1 patient having a positive Trendelenburg gait at 1 year.[21] Anatomical studies have demonstrated that the SGN travels deep to gluteus medius muscle at a distance of 5 cm from the tip of the greater trochanter.[22] It is therefore recommended that surgeons respect a 3- to 5-cm "safe" zone proximal to the greater trochanter and do not divide the abductor muscles any more proximally than this.[23,24]

Lateral Femoral Cutaneous Nerve

The anterior approach to THR risks injury to the LFCN that runs along the sartorius muscle[9,17] (Table 1). The reported risk to the LFCN when using the anterior approach varies between 14.8%[17] and 88.3%.[9] The reported rate with other THR approaches is 0.01%.[10] The LFCN nerve may either be compressed by retractors or surgically lacerated; however, the majority of the paresthesia suffered as a result of injury resolves over time, and there is no evidence of functional limitation.[9,17]

Obturator Nerve

The obturator nerve is theoretically at risk from direct trauma while drilling screws in the anterior aspect of the acetabulum to secure an uncemented acetabular component,[25] or thermal injury due to cement extrusion (in the case of a cemented acetabulum). However, the reported incidence of obturator nerve injury is rare (0.01%),[10] and the exact cause is unknown.[10,12]

Special Considerations

Developmental Dysplasia of the Hip

Patients with developmental dysplasia of the hip have varying degrees of hip shortening, placing the sciatic and femoral nerve at high risk during the restoration of leg length during THR.[4] The reported incidence of nerve palsy in patients with developmental dysplasia of the hip is 5.2%, compared with 1.3% for all other patients undergoing primary THR.[18] Schmalzried et al[18] suggested that sciatic nerve injury is due to compression by prominent prosthetic or osseous structures. Edwards et al[13] identified the degree of leg lengthening as a cause; CPN palsy was associated with as little as 2.7 cm of leg lengthening, whereas entire sciatic nerve palsy was associated with an average of 4.4 cm of leg lengthening.[13] The CPN may be more vulnerable to stretch injury than the tibial branch of the sciatic nerve likely due to reduced connective tissue.[13]

Revision THR

Revision THR is technically more difficult than primary surgery because scar tissue and contractures obscure normal anatomical planes. Difficult resection and strenuous traction often required for extraction of old hardware and insertion of new hardware predispose the sciatic nerve and its branches to traction injuries.[26] As such, the incidence of nerve palsy after revision THR is up to 3 times higher than primary THR[27]; the incidence of CPN injury approaches 7.5% in the setting of revision THR.[23,26] Femoral nerve injury has been reported in up to 3.8% of patients following revision THR.[18,28]

HIP ARTHROSCOPY

Hip arthroscopy is a technically demanding and difficult procedure that is indicated for the treatment of labral tears, femoroacetabular impingement, removal of loose bodies, and treatment of chondral lesions.[29,30] Access to the hip joint is difficult because of the deep engagement of the femoral head within the acetabulum and the strong capsule and muscular structures that resist joint distraction.[30] Overall, the reported rate of nerve injury after hip arthroscopy ranges from 0.4[31] to 13.3%,[32] with injuries to the pudendal and sciatic nerves most commonly described[32–36] (Table 2).

In order to access the hip joint, longitudinal traction of up to 20 kg may be required, in conjunction with the use of a perineal post. For this reason, up to 10% of patients undergoing hip arthroscopy will suffer transient neuropraxia due to compression pudendal nerve by the perineal post.[29,32,37,38] Injuries to the sciatic (between 0.3%[31] and 6.7%[32]) and femoral nerve (between 0.01%[31] and 0.15%[39]) are also thought to be secondary to excessive amounts and/or durations of hip traction.[35,36,40] Intraoperative nerve monitoring has demonstrated that it is the maximum traction weight, and not the total traction time, that is the greatest risk factor for sciatic nerve dysfunction during hip arthroscopy.[41] Nonetheless, limitation of traction time to 2 hours is recommended.[42]

Nerves can also be directly injured by the placement of the 3 main portals used to access the hip joint (Fig. 1). The anterior portal passes through the lateral aspect of sartorius and rectus femoris muscles, the anterolateral portal pierces the gluteus medius muscle, whereas the posterolateral portal passes just behind gluteus medius muscle.[43] A cadaveric study demonstrated that the mean distance between the anterior portal and the LFCN was only 5 mm (range, 0–28 mm), and 24 mm (range, 5–48 mm) from the femoral nerve, whereas that for the posterolateral portal (passing posterior to the greater trochanter to enter the hip joint) was 40 mm (range 16–70 mm) from the sciatic nerve.[44] Laceration and permanent injury to the LCFN secondary to insertion of the anterior portal has been described.[35,45,46]

TOTAL KNEE REPLACEMENT

The reported incidence of major nerve injury (CPN, tibial nerve) after total knee replacement (TKR) ranges from 0.3%[47] to 9.5%[48] (Table 3). The CPN is most at risk of injury during TKR. The CPN is not normally visualized during surgery, as it lies

TABLE 2. Neurological Complications of Hip Arthroscopy

References	Design	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries	Average Time to Resolution	Anesthetic Type	Remarks
Telleria et al[41] (2012)	P	61	7% (4)	2 CPN, 2 SN	0	3–7 d	GA	In this article, EMG was used intraoperatively, identifying a 58% rate of transient nerve injury
Konan et al[30] (2011)	P	100	4% (4)	4 Pudendal nerve	NR	NR	NR	A study of a single surgeon's first 100 cases, demonstrating that the complication rate decreased over time
Souza et al[38] (2010)	R	194	2.6% (5)	5 Pudendal nerve	0	8.4 wk	GA	—
Sampson[36] (2005)	R	1001	2% (20)	10 CPN, 4 pudendal nerve, 4 SN, 1 FN/SN	0	2–3 d	NR	This study also demonstrated that the complication rate decreased over time
Clarke et al[31] (2003)	P	1054	0.4% (4)	3 SN, 1 FN	0	3–6 h	GA	—
Griffin and Villar[39] (1999)	P	640	0.6% (4)	3 SN, 1 FN	0	3–6 h	GA	—
Glick[32] (1990)	R	60	13.3% (8)	4 SN, 4 pudendal nerve	0	NR	GA	—
Byrd[37] (1994)	P	20	10% (2)	2 Pudendal nerve	0	1 wk	GA	First 20 consecutive cases of hip arthroscopy done by single surgeon—learning curve article

CPN indicates common peroneal nerve; EMG, electromyography; FN, femoral nerve; GA, general anesthetic; NR, not reported; P, prospective; R, retrospective; RA, regional anesthetic; SN, sciatic nerve.

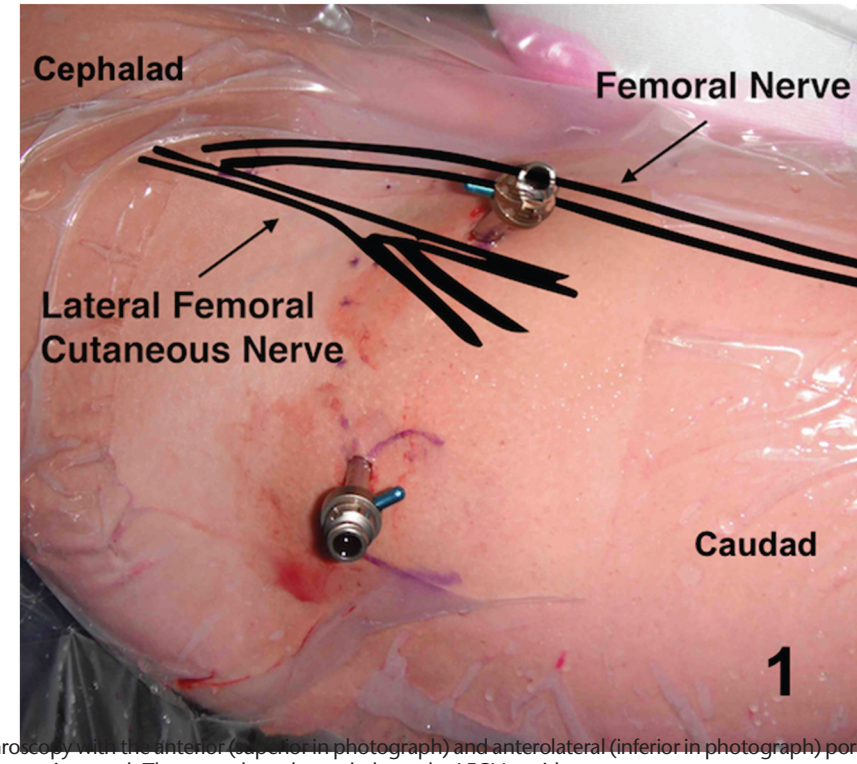

FIGURE 1. Hip arthroscopy with the anterior (superior in photograph) and anterolateral (inferior in photograph) portals. The path of the LFCN and femoral nerves superimposed. The anterolateral portal places the LFCN at risk.

TABLE 3. Neurological Complications of TKR

References	Design	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries	Average Time to Resolution	Anesthetic Type	Remarks
Subramanian et al[60] (2009)	P	32	81% (26)	IPSN	13	2 y	NR	50% Recovery of sensation at 2 y
Hopton et al[59] (2004)	P	113	86% (97)	IPSN	NR	NR	NR	4.5% Of patients had significant hypersensitivity
Schinsky et al[50] (2001)	R	1476	1.3% (19)	15 CPN, 4 CPN/TN	6	18 mo	GA/RA	Rheumatoid arthritis was a significant risk factor for nerve injury
Idusuyi and Morrey[47] (1996)	R	10,361	0.3% (32)	26 CPN, 6 CPN/TN	16	NR	GA/RA	Nerve injury associated with preoperative valgus deformity and use of epidural anesthesia
Borley et al[61] (1995)	P	25	100% (25)	IPSN	NR	NR	NR	7% Of patients had a significant degree of numbness
Horlocker et al[53] (1994)	R	361	2.2% (8)	4 CPN, 4 CPN/TN	4	NR	32% (115) GA, 68% (246) RA	Each case of nerve injury not diagnosed until after cessation of epidural anesthesia
Asp and Rand[56] (1990)	R	8998	0.3% (26)	CPN	12	3.2 y	NR	—
Rose et al[49] (1982)	R	2626	0.87% (23)	CPN	21	NR	NR	Poor rate of recovery identified in patients with CPN injury
Knutson et al[48] (1983)	P	42	9.5% (4)	CPN	NR	NR	NR	In this study, all patients had a diagnosis of rheumatoid arthritis

CPN indicates common peroneal nerve; GA, general anesthetic; IPSN, infrapatellar branch saphenous nerve; NR, not reported; P, prospective; R, retrospective; RA, regional anesthetic; TN, tibial nerve.

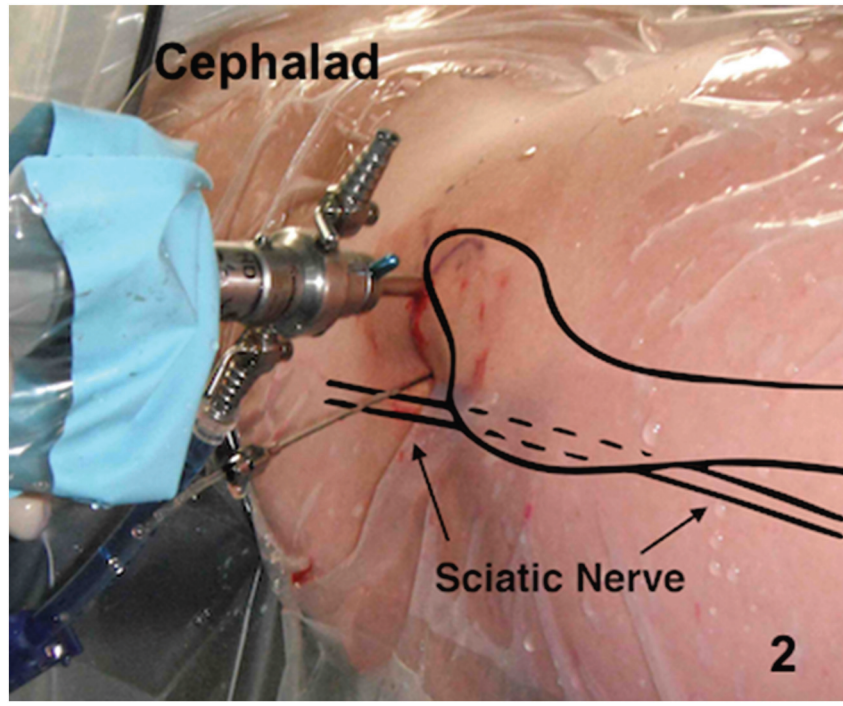

FIGURE 2. Hip arthroscopy with the anterolateral (superior in photograph) and posterolateral (inferior in photograph) portal. The path of the sciatic nerve has been superimposed. The posterolateral cannula (in this case, used for drainage) can place the sciatic nerve at risk. Images used with the permission of www.boneschool.com.

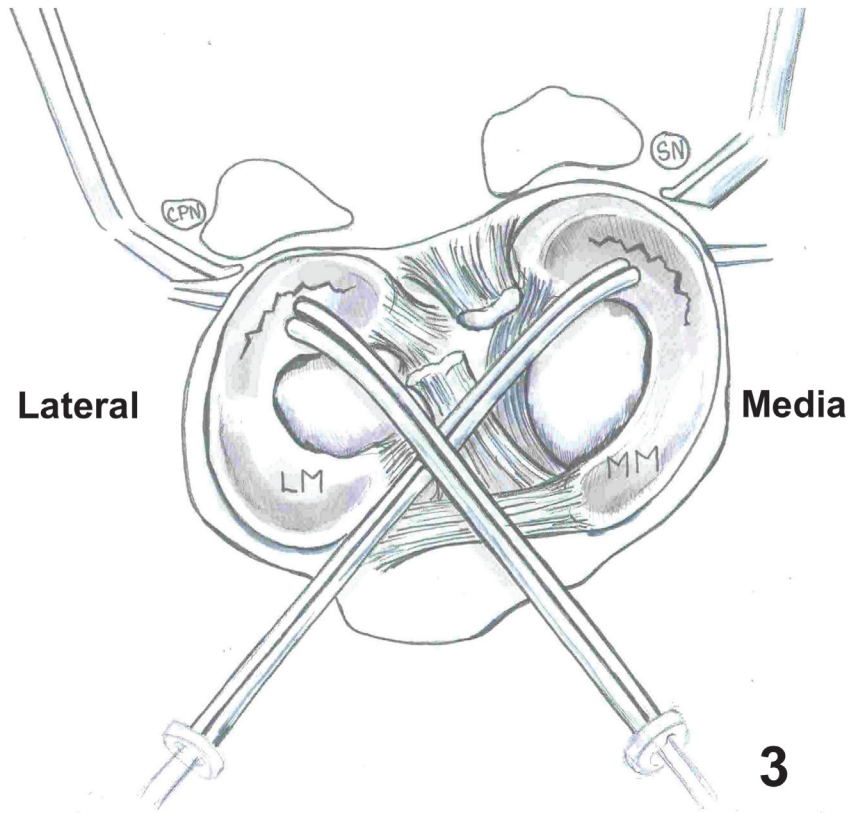

FIGURE 3. A, Inside-out MR technique. The passage of needles places the saphenous nerve (SN) and common peroneal nerve (CPN) at risk during repair of medial (MM) and lateral meniscal (LM) tears, respectively. It is recommended surgeons make an incision and protect the nerves using retractors when using this technique. Images used with the permission of www.boneschool.com.

TABLE 4. Neurological Complications of Arthroscopic Knee Surgery

References	Type of Surgery	Design	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries	Average Time to Resolution	Anesthetic Type	Remarks
Miller[70] (1988)	Arthroscopy, inside-out MR	P	96	2% (2)	1 CPN, 1 saphenous	1	6 mo	NR	73% Of patients had both ACLR and MR, which may contribute to nerve injury
Mochida and Kikuchi[65] (1995)	Arthroscopy	P	81	22.2% (18)	IPSN	NR	NR	NR	—
Austin and Sherman[68] (1993)	Arthroscopy, inside-out MR	P	101	8% (8)	7 Saphenous nerve, 1 CPN	0	4 mo	GA/RA	48.5% Of patients also had ACLR
Barber[69] (1987)	Arthroscopy, inside-out MR	P	24	22% (5)	Saphenous nerve	0	NR	NR	All nerve injuries seen were transient
Small[64] (1986)	Arthroscopy, varied	Q	375,069	0.06% (229)	Saphenous nerve > CPN > FN > SN	NR	NR	GA/RA	—

ACLR indicates ACL reconstruction; CPN, common peroneal nerve; FN, femoral nerve; GA, general anesthetic; IPSN, infrapatellar branch of the saphenous nerve; MR, meniscal repair; NR, not reported; Q, questionnaire; P, prospective; R, retrospective; RA, regional anesthetic; SN, sciatic nerve.

posterior to the fibula head before coursing around the fibula neck (Fig. 2). Traction is the most likely cause of injury, and direct trauma is uncommon. Recovery after injury is guarded with full recovery in only 20% of patients.[47,49] Multiple factors are associated with CPN palsy after TKR, with varying mechanisms of injury postulated.

Common Peroneal Nerve

Valgus Knee Deformity

The foremost risk for CPN injury after TKR is correction of a severe valgus deformity (>12 degrees).[48,49] Mechanical stretching of the nerve itself during acute surgical correction of the valgus deformity to normal alignment is the likely mechanism of injury.[49] Tethering of the CPN at the neck of the fibula renders the CPN more susceptible to traction injury than the tibial nerve. Extensive soft tissue dissection required to correct large deformities may also result in vascular compromise in this area.[49]

Flexion Contractures

Correction of flexion contractures of more than 10 degrees has been associated with an Increased risk of CPN injury, presumably due to acute traction.[48,49] Discovery of a CPN palsy postoperatively in patients with flexion contractures is treated by placing the knee in 20 degrees of flexion; the reported dramatic improvement in some patients lends credence to the traction theory.[49]

Rheumatoid Arthritis

Patients with rheumatoid arthritis have an increased risk of postoperative CPN palsy (up to 9.5%) compared with patients with osteoarthritis.[48,50] This is likely due to the high rate of valgus deformities and flexion contractures in rheumatoid patients. However, patients with rheumatoid arthritis without valgus deformity may also develop CPN palsy, possibly due to an underlying predisposition toward the development of neuropathies in the setting of rheumatoid arthritis.[50,51]

Prolonged Tourniquet Time and Pressure

Tourniquet times greater than 120 minutes are associated with CPN injury.[52,53] Compression injury from the tourniquet may well be responsible for patients with combined CPN and tibial nerve palsies.[47] Increasing the tourniquet pressure is known to slow nerve conduction velocities in animal models.[54,55] However, the exact relationship between tourniquet inflation pressure (ie, between 300 and 350 mm Hg) and nerve function is unknown.

Preexisting Neuropathy

Patients with preexisting neuropathy or nerve root compression including spinal stenosis and lumbar radiculopathy have been shown to be at increased risk of postoperative CPN palsy,[47] potentially as a consequence of "double-crush" phenomenon. It is theorized that a nerve that is already compromised may be more susceptible to a second insult, secondary to decreased reduction in axoplasmic flow.[47]

Postoperative Hematoma

Postoperative bleeding and hematoma formation at the wound site can compress the CPN.[47,48,56] Common peroneal nerve palsy has been described 5 months after TKA in a patient with coagulopathy and late development of a hemarthrosis.[48]

Epidural Anesthesia

Because an insensate limb may mask the pain or discomfort associated with compression of the very superficial CPN at the level of the fibular head and neck,[47] it has been reported that the use of postoperative epidural anesthesia can increase the risk of

CPN palsy compared with spinal or general anaesthesia following TKR.[47] It has also been reported that the use of patient-controlled analgesia may delay the diagnosis of compartment syndrome in trauma.[57] However, a recent systematic review found no evidence that RA techniques or patient-controlled anaesthesia was associated with a delay in diagnosis of acute compartment syndrome.[58] It may be reasonable to avoid a preoperative sciatic nerve block in patients at high risk of CPN palsy (ie, those with severe valgus deformities or advanced fixed flexion contractures), such that an examination can be performed immediately after surgery, and the knee flexed to decompress the CPN.

More common yet more benign than CPN injury is disruption of the sensory nerves (infrapatellar branch of the saphenous nerve or its terminal branches, and the medial and intermediate cutaneous nerves of the thigh) as they cross the midline skin incision.[59] The use of a midline skin incision is associated with skin numbness at the anterior aspect of the knee in 81%[60] to 100%[61] of patients after TKR. While up to 50% of patients report resolution of numbness at 2 years,[60] between 4.5%[59] and 7%[61] of patients report a significant problem at follow-up.

ARTHROSCOPIC KNEE PROCEDURES

A variety of knee surgeries can be performed using arthroscopy; the most common include meniscectomy, MR, and anterior cruciate ligament (ACL) reconstruction. The most common neuropraxia associated with knee arthroscopy is of the infrapatellar branch of the saphenous nerve, secondary to surgical trauma.[62–64] The saphenous nerve travels vertically caudad behind the sartorius muscle and divides into 2 main terminal branches, the infrapatellar and the sartorial branch. The infrapatellar branch of the saphenous nerve travels along the medial aspect of the patella to provide cutaneous sensation from the lower patella to the upper anterior portion of the leg.[65] The sartorial branch supplies sensation to the medial aspect of the leg. Both branches of the saphenous nerve are at risk of direct trauma when establishing the anteromedial portal, as the course of the nerve is highly variable. Almost a quarter of all patients who undergo knee arthroscopy report a postoperative sensory disturbance on the anterior aspect of the knee.[65] Loss of sensation after incision on the anterior aspect of the knee is commonplace; thus, surgeons may neglect to report it as it may not be considered a complication in the formal sense.

Meniscal Repair

The majority of nerve injuries seen after knee arthroscopy occur in association with MR, especially when utilizing inside-out techniques[66,67] (Fig. 3). For the inside-out technique, suture needles are passed from inside the knee, through the meniscus, and tied down over the capsule—nerves may be injured by needle perforation or by sutures.

The incidence of injury to the saphenous nerve during medial MR is reported to be between 2%[70] and 22.2%[65] (Table 4). The saphenous nerve is most at risk during inside-out repair of the medial meniscus, as the blind passage of needles used in this technique can easily injure or capture the nerve.[71] It is recommended that an incision be used in association with blunt dissection to the capsule, before needles are passed.[72] Saphenous nerve injury occurring despite the use of a posterior incision and direct visualization of needle passage is likely caused by retractor traction.[72] All-inside MR devices were designed to avoid the risk of nerve injury and eliminate the need to make incisions, by placing anchors through the meniscus to rest behind the capsule. A recent systematic review identified a higher rate of nerve injury with inside-out repair compared with all-inside MR (9% vs 2%),[67] possibly due to irritation of the saphenous nerve by the all-inside meniscal implants.[73]

TABLE 5. Neurological Complications of ACL Reconstruction (ACLR)

References	Type of Surgery	Design	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries	Average Time to Resolution	Anesthetic Type	Remarks
Figuero et al[81] (2008)	ACLR, HS	P	22	77% (17)	20 IPSN, 2 IPSN/saphenous nerve	NR	NR	NR	No functional impairments seen
Jameson and Emmerson[78] (2007)	ACLR, HS	R	87	60% (52)	29 LSCN, 23 saphenous nerve, 10 IPSN	36	13 mo	NR	LSCN thought to be injured by ACLR femoral fixation method
Sanders et al[79] (2007)	ACLR, HS	R, Q	62	74% (46)	14 Saphenous, 12 IPSN, 20 saphenous/IPSN	NR	NR	NR	Nerves thought to be damaged during HS harvest
Portland et al[82] (2005)	ACLR, BPTB	R	42	59% (20)	IPSN	NR	NR	NR	—
Kartus et al[77] (1999)	ACLR, BPTB	P	604	0.3% (2)	1 Saphenous nerve, 1 CPN	NR	NR	NR	—

BPTB indicates bone patella tendon bone; CPN, common peroneal nerve; FN, femoral nerve; HS, hamstring; IPSN, infrapatellar branch of the saphenous nerve; LSCN, lateral sural cutaneous nerve; NR, not reported; Q, questionnaire; P, prospective; R, retrospective.

In a similar manner to the saphenous nerve, the CPN is at risk of direct trauma during inside-out repair of the lateral meniscus; owing to the close proximity of the CPN, many authors recommend the use of posterior incisions and retraction.[66,74–76] Fortunately, CPN injuries are rarely described.[62,70,75]

ACL Reconstruction

Anterior cruciate reconstruction is most commonly performed using a hamstring or bone-patella tendon-bone (BPTB). The majority of nerve injuries after ACLR are sensory disturbances as a result of transection of the infrapatellar branch of the saphenous nerve during both BPTB[77] and hamstring graft harvest.[78–80] The reported incidence varies between 0.3%[75] and 77%[81] (Table 5). This wide variation is likely related to whether or not new postoperative paresthesias were intentionally sought as a primary outcome measure. Using horizontal rather than vertical incisions can decrease the incidence of injury, as this orientation is less likely to injure both branches of the saphenous nerve.[82,83] The sartorial branch of the saphenous nerve becomes subcutaneous between sartorius and gracilis muscles, placing it at risk during hamstring tendon harvest when the sartorius fascia is divided in order to harvest the semitendinosus and gracilis tendons[81,84,85] (Fig. 4). Recent patient surveys have indicated that paresthesias in the sartorial nerve distribution following ACLR are more common than previously thought.[78,79] It is postulated that the tendon stripper may be the cause of this sensory disturbance, which fortunately has minimal functional implications for the patient.[79] Finally, there are isolated case reports in the literature describing injury to the sciatic nerve by the tendon stripper[86] and CPN by the bicortical tibial screw.[87]

DISCUSSION

Surgical nerve injury in elective hip and knee surgery most often results from compression or stretch secondary to retractor placement or traction and, although not uncommon, tends to recover with time. Fortunately, severe or permanent nerve injury, such as that resulting from laceration of major nerves, is rare.

Although the literature addressing nerve injury related to hip arthroscopy is relatively robust, the quality of evidence relating to nerve injury following the most commonly performed elective hip and knee surgeries is undermined by its largely retrospective nature (THR and TKR) or low numbers of subjects (knee arthroscopy, ACL reconstruction). Furthermore, the majority of the publications that address nerve injury in the setting of elective hip and knee surgery do not designate neurological injury as a primary outcome; these studies may underestimate the true incidence of neurological complications. Last, because of the narrative nature

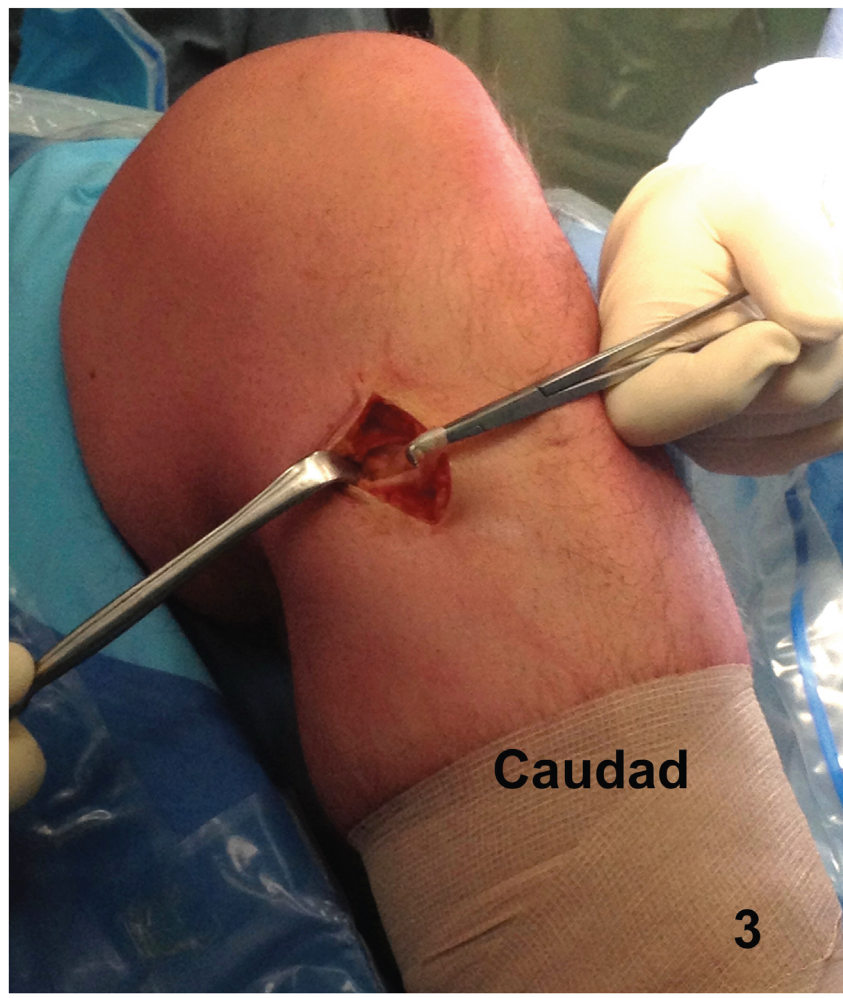

FIGURE 4. Incision for hamstring harvest before ACLR. The incidence of injury to the infrapatellar branch of the saphenous nerve is 53%. Images used with the permission of www.boneschool.com.

of this review, selection bias cannot be excluded from the material presented herein.

Although it is often not possible to definitively identify the cause of nerve injury in the setting of hip and knee surgery, especially with the associated use of RA, we are hopeful that this review will afford anesthesiologists a better understanding of the specific nerves at risk during the most common hip and knee procedures. Understanding the patterns and likelihood of iatrogenic nerve injury may inform and facilitate preoperative risk-benefit discussions with patients considering a regional anesthetic, as well as assist in the diagnosis and management of neurological complications in the postoperative period.

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Neurological Complications Related to Elective Orthopedic Surgery
Part 3: Common Foot and Ankle Procedures

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Abstract: Part III of a review series on neurological complications of orthopedic surgery, this article describes the mechanisms and likelihood of peripheral nerve injury associated with some of the most common elective foot and ankle procedures for which anesthesiologists may administer regional anesthesia. Relevant information is broadly organized according to type of surgical procedure to facilitate reference by anesthesiologists and members of the anesthesia care team.

What's New: As the popularity of regional anesthesia continues to increase with the development of ultrasound guidance, anesthesiologists should have a thoughtful understanding of the nerves at risk of surgical injury during elective foot and ankle procedures.

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Many anesthesiologists may not be familiar with the rate of surgical neurological complications of the most common elective foot and ankle procedures for which they are providing local anesthetic-based regional anesthesia (RA) and/or analgesia.[1,2] The rate of iatrogenic nerve injury directly attributable to the surgery itself may be similar to or even exceed that traditionally associated with RA techniques. It behooves the anesthesiologist performing RA to understand the overall risk that the surgical procedure itself may play in the evolution of perioperative nerve injury, as well as the potential mechanism of injury. The individual nerves, mechanisms by which they are injured, and tendency for injury during foot and ankle surgery necessarily depend on the type of procedure being performed.

In Part III of this review series on neurological complications of orthopedic surgery, we describe the mechanisms and likelihood of peripheral nerve injury associated with some of the most common elective foot and ankle procedures for which anesthesiologists may administer RA. Relevant information is broadly organized according to type of surgical procedure to facilitate reference by anesthesiologists and members of the anesthesia care team.

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METHODS

For the purposes of this narrative review, the authors initially searched MEDLINE (1946 to February 2014) and the Cochrane database to identify reports of neurological injury after common elective foot and ankle surgery, as well as anatomical studies pertaining to the mechanism of nerve injury. This was performed using the following key words: foot, ankle, nerve, nerve injury, neurological injury, ankle arthroplasty, ankle fusion, ankle arthrodesis, fibular osteotomy, hallux valgus surgery, ankle arthroscopy, and complications. The references of all applicable studies and review articles were also manually cross-referenced to ensure completeness.

Inclusion criteria were cohort studies that reported the incidence of neurological injury after elective foot and ankle arthroscopy, joint replacement, fusion, osteotomy, and reconstruction. The authors excluded case reports. Orthopedic surgeons with subspecialty interest in foot and ankle reviewed each scientific article and their references. The following narrative review does not list all applicable studies; rather, the authors have limited their discussion to research articles they felt to be most valuable to anesthesiologists regularly performing RA in the setting of elective foot and ankle surgery. We purposefully selected articles that (1) designated nerve injury as a primary outcome; (2) included the largest number of patients, such that isolated nerve injuries in small cohorts would not falsely inflate the incidence of nerve injury described herein; and/or (3) specified which nerve was injured anatomically, provided details with regard to the severity of the nerve injury, postulated on the mechanism, and described the incidence of permanent nerve injury and average time to resolution.

Content experts A.V. and J.T.L. are experienced fellowship-trained foot and ankle subspecialty orthopedic surgeons who designated the most common elective foot and ankle surgeries to address, selected the most reliable and valid studies to include, and provided their informed, clinically rich perspective to strengthen the unique and practical value of the material presented herein.

ANKLE ARTHROSCOPY

Ankle arthroscopy is a procedure used for the treatment of osteochondral lesions, loose bodies, bony and soft tissue impingement, synovitis, ankle osteoarthritis (OA), septic arthritis, and ankle arthrodesis.[3–7] A procedure performed with the use of a thigh tourniquet, ankle arthroscopy may focus on the anterior aspect of the joint (anterior ankle arthroscopy), the posterior aspect of the joint (posterior ankle arthroscopy), or a combination thereof.

Anterior Ankle Arthroscopy

Anterior ankle arthroscopy is generally performed through 2 anterior arthroscopy portals, 1 anteromedial and 1 anterolateral

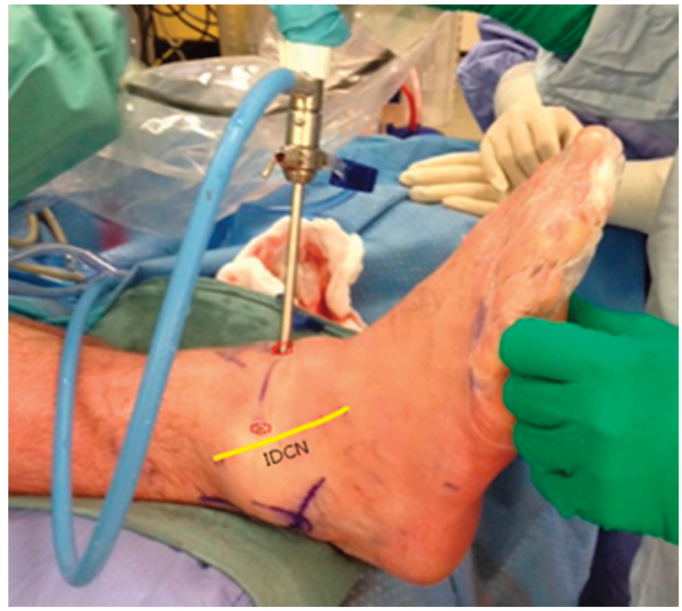

FIGURE 1. Anterior ankle arthroscopy. The location of the intermediate dorsal cutaneous nerve (IDCN) (yellow line) is outlined in relationship to the 2 commonly used anterior portals (red circles). Images used with permission from Andrea Veljkovic, MD.

(Fig. 1). The anteromedial portal is positioned medial to the tibialis anterior tendon, creating potential for transection injury to the branches of the saphenous nerve, which is located just medial to the tibialis anterior tendon. The anterolateral portal is created lateral to the peroneus tertius tendon, which is in the immediate vicinity of the intermediate dorsal cutaneous nerve (IDCN) (Fig. 1). The IDCN is a branch of the superficial peroneal nerve (SPN), and supplies sensation to the dorsum of the foot.[8] The IDCN can be transected with portal placement, or if not transected, it can be encased in scar after closure. Improper portal placement or aggressive debridement of the anterior capsule places the deep peroneal nerve (DPN) at risk of trauma. The DPN is located in the interval between the extensor hallucis longus and the extensor digitorum communis tendons.[9] Last, noninvasive strap traction or invasive pin traction is sometimes used to facilitate access to the joint. Invasive traction had been commonplace upon the advent of ankle arthroscopy but has now been largely replaced by strap traction placed externally around the ankle. Excessive noninvasive traction places all nerves that cross the ankle at risk of traction neuropraxia. Also, all nerves are at risk of irritation due to stretch or local repetitive trauma from alternating portals and using instruments as required.

Cutaneous nerve injury is relatively common after anterior ankle arthroscopy, with a reported rate of 0% to 8.6%[9–16] (Table 1). The SPN is the most commonly injured nerve. Superficial nerve injuries occur in up to 5.7% of patients undergoing anterior ankle arthroscopy.[10–14,17] However, a review of the literature reveals that anterior ankle arthroscopy has been associated with iatrogenic injury to every cutaneous nerve around the ankle, including the DPN (0%–2.5%),[10–14,17] the sural nerve (0%–2.3%),[10–14,17] and the saphenous nerve (0%–0.8%).[12,13,17] Most of these cutaneous nerve injuries are likely the result of traumatic injury sustained during portal placement,[9] with the exception of sural nerve injury, which is thought to be caused by excessive distraction or insertion of pins for invasive traction.[10]

Fortunately, most iatrogenic nerve injuries related to anterior ankle arthroscopy seem transient. In a retrospective cohort of 612 patients undergoing anterior ankle arthroscopy, persistent neurological symptoms were reported in only 0.2% of patients at 10 years postoperatively.[9] Martin et al[15] performed a retrospective study of 58 patients undergoing anterior ankle arthroscopy, noting that 8.6% of patients reported sensory changes, with most resolving over time; 3.4% of patients reported permanent neurological symptoms at a mean follow-up time of 25 months. These higher nerve injury rates reported by Martin and colleagues may well reflect the early part of the learning curve when ankle arthroscopy was popularized in the 1980s, as well as the more common use of invasive pin traction at that time.

Prolonged use of tourniquets for longer than 120 minutes on the lower limb has been associated with common peroneal nerve injury.[18,19] However, this clinical picture presents with diffuse sensorimotor neuropathic findings in contrast to the specific small branch nerve injuries described previously.

Posterior Ankle Arthroscopy

Posterior ankle arthroscopy is a relatively novel technique with an expanding list of indications, including posterior ankle impingement, os trigonum syndrome, and flexor hallucis longus stenosis.[20–22] Posterior ankle arthroscopy is performed through 2 main portals, posteromedial and posterolateral, placed on either side of the Achilles tendon (Fig. 2). Owing to its proximity to the Achilles tendon, the sural nerve is at risk of traumatic transection, stretch, or contusion when inserting and using the posterolateral portal,[23] with a reported frequency as high as 7%.[24–30]

The tibial nerve (TN) is at risk when inserting the posteromedial portal; surgeons must take care to direct instruments laterally to avoid traumatic TN injury. However, the literature is scant regarding the incidence of TN injury. One retrospective study of 15 patients by Marotta and Micheli[28] described transient paresthesia in distribution of the TN in 6.7% patients; there were no cases of permanent injury (Table 1). The mechanism of this sensory neuropraxia is thought to be secondary to irritation from arthroscopic instruments.

TABLE 1. Neurological Complications Associated With Arthroscopic Procedures, in Foot and Ankle Surgeries

Author	Design	Type of Arthroscopy	Portals Used	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries	Average Time to Resolution	Anesthetic Type (n)	Remarks
Zengerink and van Dijk, 2012	R	Anterior	Anterolateral portal	1305	1.9% (25)	0.39% (5) DPN 0.92% (12) SPN 0.23% (3) sural nerve	NR	NR	NR	—
		Posterior	Posterolateral portal			0.23% (3) saphenous nerve 0.15% (2) TN (calcaneal branch)				
Ferkel et al, 1996	R	Anterior	Anterolateral portal	612	4.4% (27)	2.5% (15) SPN injury 0.9% (6) sural nerve injury	NR	NR	NR	All neurological complications were caused by direct injury
		Posterior	Anteromedial portal Posterolateral portal			0.8% (5) saphenous nerve injury 0.2% (1) DPN in jury				
Deng et al, 2012	R	Anterior	Anterolateral portal	260	3.5% (9)	1.9% (5) SPN 0.8% (2) DPN	NR	NR	NR	—
		Subtalar	Anteromedial portal Posterolateral portal (if needed)			0.4% (1) sural nerve 0.4% (1) saphenous nerve				
Amendola et al, 1996	R	Anterior	Anterolateral portal Anteromedial portal	79	3.8% (3)	2.5% (2) DPN injury 1.3% (1) lateral SPN injury	NR	NR	98.7% (78) GA 1.3% (1) RA	None of the patients recovered nerve function at their last follow-up
Ferkel and Hewitt, 2005	R	Anterior	Anterolateral portal Anteromedial portal Posterolateral portal	35	0% (0)	No neurovascular injury was observed	NR	NR	GA/RA	—
Barber et al, 1990	R	Anterior	Anterocentral portal Anterolateral portal Anteromedial portal	53	5.7% (3)	5.7% (3) permanent superficial nerve injury	3	No recovery	NR	The dorsum of the foot was involved in all 3 permanent nerve injury cases
Martin et al, 1989	R	Anterior	Anterolateral portal Anteromedial portal	58	8.6% (5)	5.2% (3) temporary paresthesia 3.4% (2) permanent sensory losses	2	NR	GA	Permanent sensory damage thought to be caused by anterolateral portal
Ferkel et al, 2001	R	Anterior	Anterolateral portal Anteromedial portal Posterolateral portal	612	0.2% (2)	0.1% (1) neuroma 0.1% (1) numbness between second and third toe	2	NR	NR	Only permanent nerve injuries were reported. The total presented here does not include temporary nerve injuries

Continued next page

TABLE 1. *(Continued)*

Author	Design	Type of Arthroscopy	Portals Used	Total Surgeries	Rate of Nerve Injury (n)	Nerves Injured	Permanent Nerve Injuries	Average Time to Resolution	Anesthetic Type (n)	Remarks
Guhl, 1988	R	Anterior	Anterolateral portal	131	3.1% (4)	2.3% (3) sural nerve paresthesia 0.8% (1) Neuroma	NR	NR	GA/RA	The nerve injury was at the portal site for arthroscopy, not the site of pin placement. Complications decreased with the use of distraction
Willits et al, 2008	R	Posterior	Posterolateral portal Posteromedial portal	24	20.8% (5)	20.8% (5) temporary numbness/irritation of the scar	0	NR	NR	—
Nickisch et al, 2012	R	Posterior	Posterolateral portal Posteromedial portal	189	3.7% (7)	1.6% (3) sural nerve paresthesia 2.1% (4) plantar numbness	1 plantar numbness 1 sural nerve paresthesia	NR	23.8% (45) GA 76.2% (144) RA	1 complete and 1 mild surgical resolution seen in 2 patients with plantar numbness. Gabapentin resolved symptoms in 2 patients with sural nerve paresthesia
Galla and Lobenhoffer, 2011	R	Posterior	Posterolateral portal Posteromedial portal	30	6.7% (2)	6.7% (2) sural nerve injuries	NR	NR	NR	—
Marotta and Micheli, 1992	R	Posterior	Posterolateral portal	15	6.7% (1)	6.7% (1) transient TN sensory neurapraxia	0	1 y	NR	—
Hamilton et al, 1996	R	Posterior	Posterolateral portal OR Posteromedial portal; 1 - posteroanterior and posteromedial portals 1 - posterolateral and posteromedial portals	41	2.4% (1)	2.4% (1) dysesthesia around the scar	NR	NR	92.7% (38) GA 6.4% (3) RA	—
Guo et al, 2010	R	Posterior	Posterolateral portal Posteromedial portal	43	4.7% (2)	2.35% (1) sural nerve sensory loss 2.35% (1) medial calcaneal numbness	NR	NR	NR	Open surgery resulted in sural nerve sensory loss, endoscopic technique resulted in medial calcaneal numbness
van Dijk, 2006	R	Posterior	Posterolateral portal	146	1.4% (2)	1.4% (2) diminished sensation over the heel pad of the hindfoot	NR	NR	GA/RA	—
Ogut et al, 2011	R	Posterior	Posterolateral portal OR Posteromedial portal	60	3.3% (2)	1.65% (1) sural neurinoma 1.65% (1) sural nerve injury	NR	NR	GA/RA	The sural neurinoma resolved via surgery

GA indicates General anesthetic; n, Number; NR, not reported; R, retrospective; RA, regional anesthetic.

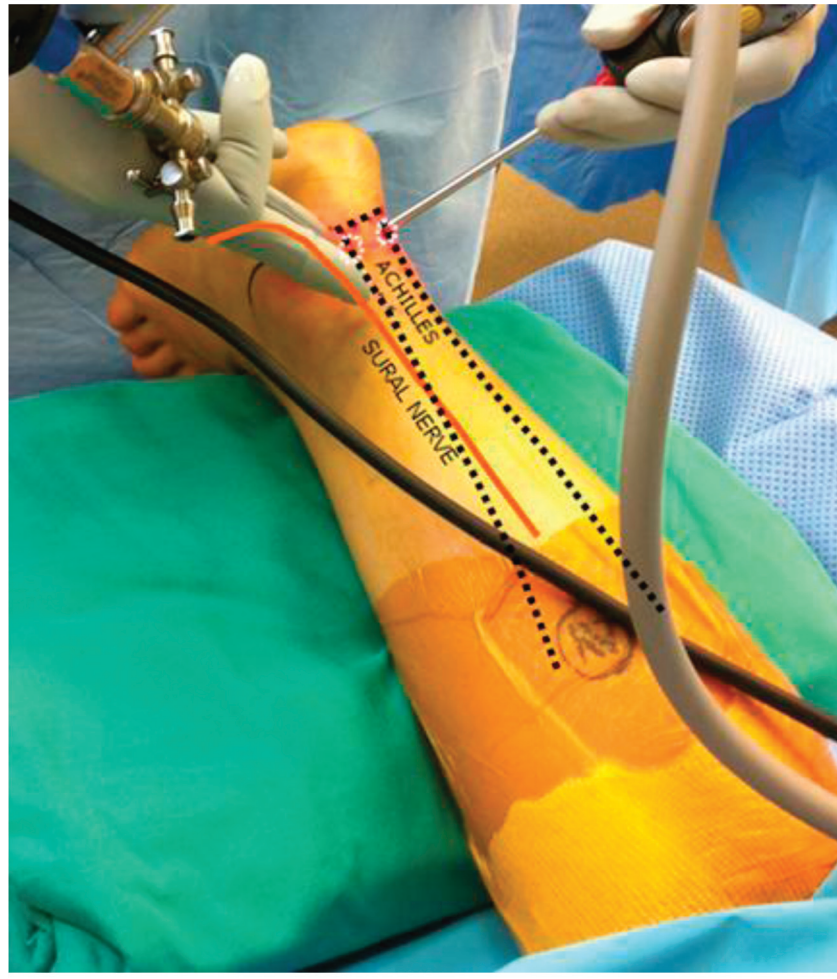

FIGURE 2. Posterior ankle arthroscopy. On average, the sural nerve (red line) is 1.88 cm from the lateral Achilles border (tendon outlined in dashed black line). The midline of the sural nerve is an average distance of 9.8 cm from the calcaneum, as it crosses the lateral border of the Achilles. The 2 commonly used portals are outlined as white circles. Images used with permission from Andrea Veljkovic, MD.

Finally, patients may complain of plantar heel paresthesia after posterior ankle arthroscopy likely resulting from injury to either a branch of the sural nerve (reported rate, 1.6%–6.7%) [25,31] and/or the medial calcaneal nerve (0.7%),[32] which can have an aberrant course in close proximity to the posteromedial portal.

TOTAL ANKLE REPLACEMENT

Total ankle replacement (TAR), indicated for the treatment of pain and dysfunction related to ankle joint OA, is a procedure that is growing in popularity. There are 2 main surgical approaches used when performing TAR, both of which are usually performed using a thigh tourniquet; the anterior approach is the most commonly used, whereas the lateral approach has been advocated recently due to its potential for improved biomechanics and wound healing.

Anterior Approach

The anterior approach to TAR involves division of the superior extensor retinaculum, using the surgical interval between the tibialis anterior and extensor hallucis longus tendons (Fig. 3). The medial dorsal cutaneous nerve, a branch of the SPN, is often identified overlying over the extensor retinaculum, whereas the DPN is found lateral to the extensor hallucis longus tendon (Fig. 3).

A recent meta-analysis investigating outcomes after the anterior approach to TAR described an overall rate of nerve injury of 1.3%,[33] although reported rates range from 0% to 28.6% (Table 2).[34–47] Neurological symptoms after TAR are most commonly reported in the distribution of the peroneal nerve.[35–37,46] Sensory paresthesiae in the distribution of the SPN and DPN reportedly range between 0% and 17.1%[43,45,47] and 0% and 12.9%, respectively.[39,40,43,45,47] However, the true rates of postoperative neurological symptoms in the distributions of the SPN and DPN likely approach the higher end of the previously listed ranges, reflecting the meticulous follow-up by Knecht and colleagues.[43] Patients are generally accepting of persistent dorsal paresthesia in light of the technical demands of TAR surgery because function is not affected and plantar sensation is preserved.

Similar to ankle arthroscopy, most of TAR surgery is performed under thigh tourniquet. It may be possible that some of

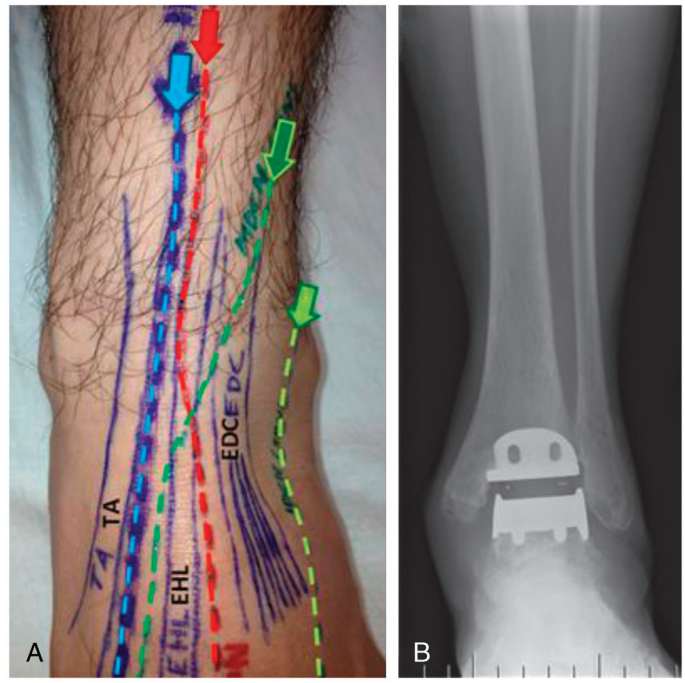

FIGURE 3. A, The anterior approach to total ankle replacement (TAR). The anterior incision (blue dashed line) is shown in relation to the deep peroneal nerve (DPN) (red dashed line), medial dorsal cutaneous nerve (green dashed line), and intermediate dorsal cutaneous nerve (IDCN) (light green dashed line). The 3 tendons illustrated previously are the tibialis anterior tendon (TA), extensor hallucis longus tendon (EHL), and the extensor digitorum longus tendon (EDC). B, AP x-ray of a patient after a TAR. Images used with permission from Andrea Veljkovic, MD.

the combined SPN/DPN nerve injuries described by Knecht and colleagues[43] were secondary to tourniquet use; however, clinical differentiation between direct surgical injury to the SPN and DPN versus tourniquet-induced pressure ischemia of the common peroneal nerve in the postoperative setting after TAR can be very difficult.

The risk of clinically significant TN injury in the setting of TAR is likely less than 5%.[36,37,46] Although Hamel[35] reported a rate of 21.4% for TN injury, only 1 of the 14 patients reported permanent neuropathy. Kofoed[48] prospectively followed 20 patients undergoing TAR and identified neurological symptoms in the distribution of the TN in only 1 (5%) patient; these symptoms were not permanent. Although laceration of the TN with the oscillating saw (blind cut from anterior to posterior) has been reported, most of iatrogenic TN injuries are likely related to either stretching during intraoperative surgical exposure and distraction from placement of the polyethylene spacer, or postoperative tarsal tunnel syndrome.[36,39] Tarsal tunnel syndrome refers to TN compression by the overlying laciniate ligament, a strong fibrous band that extends from the medial malleolus above to the calcaneus below. The development of tarsal tunnel syndrome in this setting is likely due to acute changes in alignment produced by realignment form the TAR. These patients may benefit from a tarsal tunnel release[40] (Fig. 4).

In the clinical setting, patients tolerate SPN, DPN, and sural nerve paresthesia reasonably well with minimal effect on their daily function. In contrast, TN paresthesia is often tolerated poorly as it affects the plantar sensation of the foot. Hyperesthesia of the SPN, sural, and TN may require prolonged physical therapy for desensitization, as well as medications for neuropathic pain.

Lateral Approach

The lateral approach to TAR involves an incision over the lateral fibula, which risks laceration to the SPN, and a separate medial incision, risking injury to the branches of the saphenous nerve. Due to the recent advent of the lateral approach for TAR, no studies have been published which specifically investigate the incidence of nerve injury related to this approach. Nonetheless, it seems reasonable to assume that potential postoperative neurological symptoms in the distribution of the SPN would be relatively common, as seen using the same incision for fibular fracture fixation.[49] In a cross-sectional retrospective study of 120 patients at follow-up, Redfern et al[49] reported that 21% of the patients experienced postoperative neuropathic SPN symptoms after operative lateral malleolar fracture fixation compared to 9% of the patients managed nonoperatively in a cast.

ANKLE ARTHRODESIS/FUSION

Open fusion of the ankle joint is performed in the setting of end-stage ankle OA, osteonecrosis of the talus, and in the salvage of failed TAR (Fig. 5). Similar to the approaches used for TAR, ankle fusion may be performed through either an anterior or a lateral approach (Figs. 3 and 5). For this reason, the risk to cutaneous nerves is similar to TAR, with reported rates of nerve injury during ankle arthrodesis up to 2.6%, with the peroneal nerve most commonly affected (0%–2.3%) (Table 3).[50,51] However, the literature describing peroneal nerve injury after ankle fusion fails to differentiate injury rates between the SPN and the DPN.[50–52] Nonetheless, it is thought that injuries to the SPN or DPN in the setting of ankle fusion result from either traction from retractors or direct laceration.

TRIPLE ARTHRODESIS/FUSION

The fusion of the subtalar, talonavicular, and calcaneocuboid joints (triple arthrodesis) is indicated for posttraumatic deformity,

TABLE 2. Neurological Complications Associated With TARs

Author	Design	Approach	Total Surgeries	Rate of nerve injury (n)	Nerves Injured	Permanent Nerve Injuries	Average Time to Resolution	Anesthetic Type	Remarks
Kofoed, 1995	P	Anterior incision	20	5% (1)	5% (1) TN	NR	NR	RA	Complication caused by retraction lesion of the TN
Mroczek, 2003	R	Anterior incision	50	4% (2)	2% (1) DPN 2% (1) SPN	NR	NR	NR	—
Haskell and Mann, 2004	R	Anterior incision	187	3.7% (7)	1.0% (2) neuroma 2.7% (5) nerve injury	NR	NR	NR	—
Hamel, 2012	R	Anterior incision	14	28.6% (4)	7.2% (1) polyneuropathy 21.4% (3) TN	1 TN	NR	NR	Neuropathy of the TN was due to entrapment of overtensioning; 1 patient recovered after surgical intervention
Pinar et al, 2012	R	Anterior incision	183	5.5% (10)	2.7% (5) TTS 1.1% (2) TN 1.1% (2) neuralgia of SFN 0.55% (1) lumbar sciatica	NR	NR	NR	9 neurological complications were seen from high volume centers, and 1 from low volume centers
Clement et al, 2013	R	Anterior incision	26	0% (0)	No neurovascular injury was observed	NR	NR	NR	—
Hintermann et al, 2004	R	Anterior incision	122	5% (6)	3.3% (4) necrosis 1.6% (2) paresthesia	NR	NR	NR	Minor skin necrosis healed completely in all 4 patients
Bai et al, 2010	R	Anterior incision	67	4.5% (3)	4.5% (3) DPN	NR	NR	NR	1 DPN patient had posttraumatic arthritis, 2 had osteoarthritis
Schenk et al, 2011	R	Anterior incision	218	0.9% (2)	0.45% (1) nerve injury 0.45% (1) sural nerve dysesthesia	NR	NR	NR	Sural nerve dysesthesia was seen in patient undergoing Achilles lengthening
Ali et al, 2007	R	Anterior incision	35	0% (0)	No neurovascular injury was observed	NR	NR	NR	—
Knecht et al, 2004	R	Anterior incision	70	21.4% (15)	8.55% (6) only SPN 4.3% (3) only DPN 8.55% (6) both SPN and DPN	NR	NR	NR	—
Rippstein et al, 2011	R	Anterior incision	233	0.9% (2)	0.45% (1) TN laceration 0.45% (1) SPN and DPN dysesthesia	NR	NR	RA	Treatment was observation for both cases

n indicates Number; NR, not reported; P, prospective; R, retrospective; RA, regional anesthetic; TTS, Tarsal tunnel syndrome.

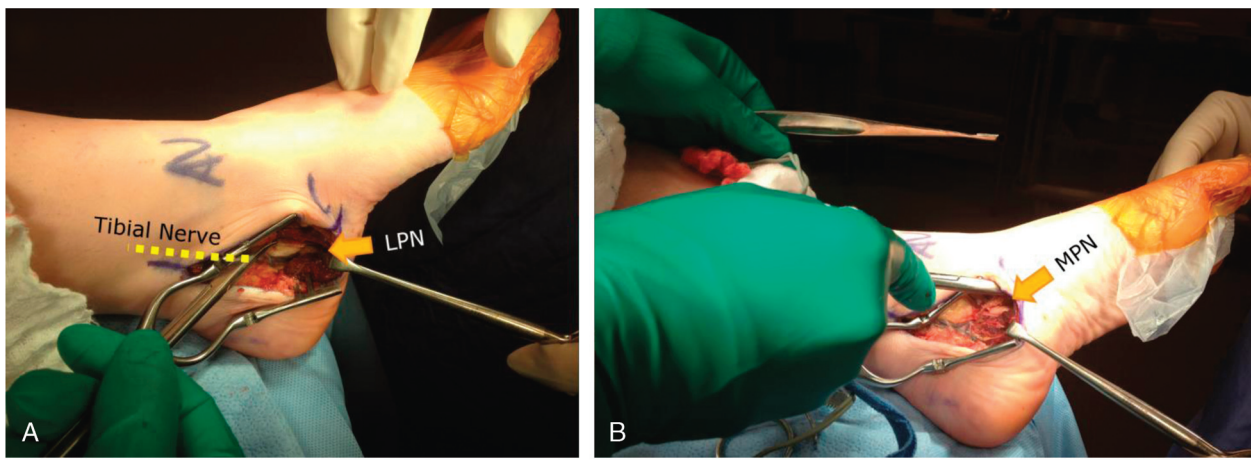

FIGURE 4. Tarsal tunnel syndrome. A, The tibial nerve is depicted by the yellow dotted line. Illustrated previously is also the lateral plantar nerve (LPN) (arrow). B, Clinical photograph demonstrating the medial plantar nerve (MPN) (arrow). Images used with permission from Andrea Veljkovic, MD.

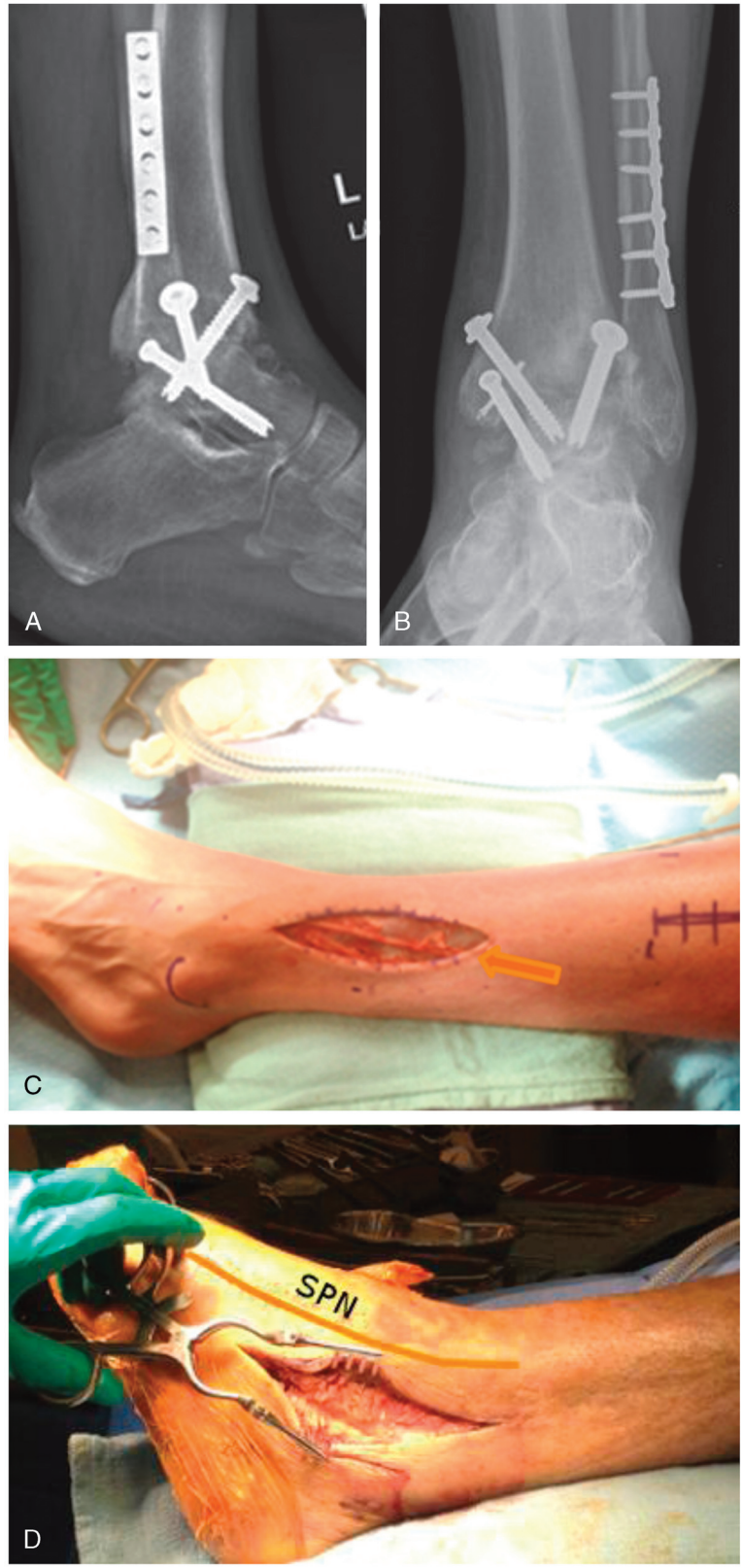

FIGURE 5. Ankle arthrodesis. A, Lateral x-ray post ankle arthrodesis. B, AP x-ray post ankle arthrodesis. C, Lateral incision demonstrating the proximal course of superficial peroneal nerve (SPN) (orange arrow). D, Incision for lateral approach to ankle arthrodesis, demonstrating its proximity the SPN. The SPN can be found exiting the posterior compartment and becoming superficial as it enters the anterior compartment of the leg 3 to 18 cm proximal to the ankle joint. Images used with permission from Andrea Veljkovic, MD.

TABLE 3. Neurological Complications Associated With Arthrodesis, in Foot and Ankle Surgeries

Author	Design	Ankle, Triple, TMT Joint	Approach	Total Surgeries	Rate of nerve injury (n)	Nerves Injured	Permanent Nerve Injuries	Average time to Resolution	Anesthetic Type	Remarks
Frey et al, 1994	R	Ankle	—	78	2.6% (2)	2.6% (2) nerve injury	NR	NR	NR	—
Takakura et al, 1999	R	Ankle	Anterior approach	43	2.3% (1)	2.3% (1) peroneal nerve injury	NR	NR	NR	—
Pell et al, 2000	R	Triple	Lateral incision	132	0.008% (1)	0.008% (1) superficial peroneal neuritis	NR	NR	NR	—
Graves et al, 1993	R	Triple	Medial and lateral incisions	18	0% (0)	No neurovascular injury was observed	NR	NR	GA	—
Weinraub et al, 2010	R	Triple	Medial incision	45	0% (0)	No neurovascular injury was observed	NR	NR	GA or RA	—
Jung et al, 2007	R	TMT	Single dorsal technique OR Dorsal and medial technique	67	6% (4)	4.5% (3) SPN 1.5% (1) sural Nerve	NR	NR	NR	SPN injury was associated with stretching or transection during surgery. Sural nerve neuralgia was the result of a postoperative scar

GA indicates General anesthetic; n, Number; NR, not reported; R, retrospective.

osteoarthritis, chronic instability, rheumatoid arthritis, adult flatfoot, and neuromuscular imbalances.[53] This procedure is most commonly performed through incisions on both the medial and the lateral borders of the proximal foot. The lateral incision is extensive, placing both the dorsal branch of the SPN and the plantar aspect of the sural nerve at risk of either transection or stretch injury due to retraction.[54] However, the reported rate of SPN injury is curiously low (0%–0.08%[53–55]) (Table 3), suggesting that the true rate of nerve injury is underreported.

TARSOMETATARSAL JOINT ARTHRODESIS/FUSION

The main indications for tarsometatarsal (TMT) joint arthrodesis are OA or deformity secondary to Lisfranc injury, which is a fracture and/or dislocation at the TMT joint.[50,56] In situ TMT fusion requires 1 or 2 dorsal incisions between the respective metatarsals, placing the branches of the SPN and the DPN at risk of laceration or stretch injury (Fig. 6). In the setting of any deformity at the TMT joint level, realignment is also required via additional medial foot incisions; these incisions are made in the immediate vicinity of the dorsal medial hallucal nerve (DMHN), a terminal branch of the SPN[57–59] (Fig. 6). The reported rate of

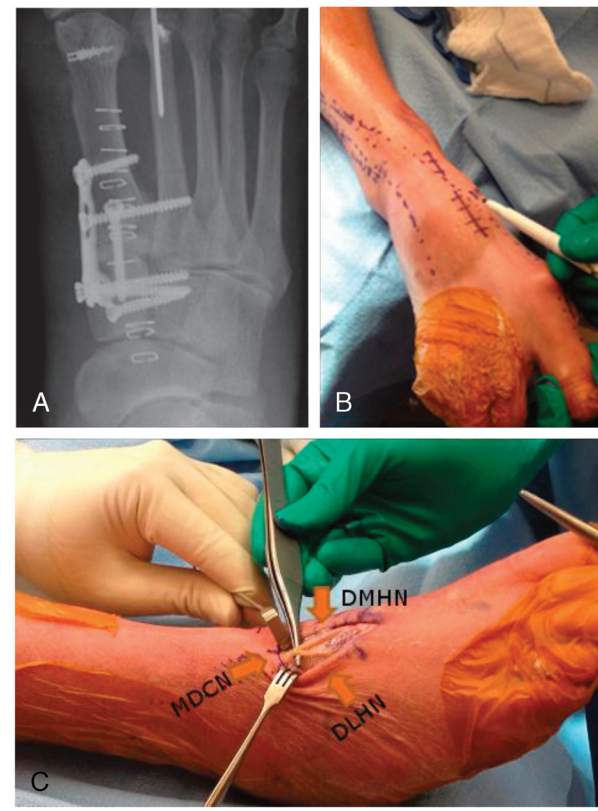

FIGURE 6. TMT joint arthrodesis. A, AP x-ray showing postoperative fusion of the TMT. B, Clinical photograph demonstrating the dorsal incision used for this approach, with the path of the dorsal hallucal nerve (dotted) crossing the incision. C, Clinical photograph of the medial dorsal cutaneous nerve (MDCN) dividing into the dorsal medial hallucal nerve (DMHN) and the dorsal lateral hallucal nerve (DLHN). Images used with permission from Andrea Veljkovic, MD.

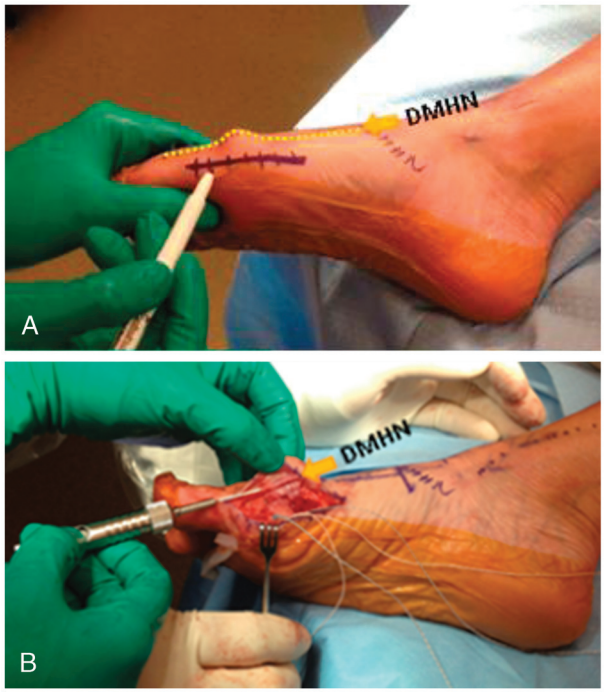

FIGURE 7. Bunionectomy/treatment of hallux valgus deformity. A, The dorsomedial incision used for correction of hallux valgus deformities (bunions) is outlined with the blue pen mark. The dorsal medial hallucal nerve (DMHN) is outlined by the yellow dotted line. B, The DMHN, see arrow, is visible after incision. Images used with permission from Andrea Veljkovic, MD.

DMHN can go up to 6% (Table 3)[56,60]; these patients present with numbness over the medial aspect of the great toe. The mechanism is thought to be due to stretching or transection of the nerve during the surgical approach.[56]

HALLUX VALGUS/BUNIONS

The hallux valgus deformity is a common affliction, reportedly affecting up to 65% of people older than 65 years.[61,62] Most of hallux valgus deformities are corrected using a dorsomedial incision placed over the distal first metatarsal, placing the DMHN at risk of stretch injury or transection[63] (Fig. 7). A secondary dorsal incision placed in the first web space, between the first and second metatarsal head, places the dorsal lateral hallucal nerve (DLHN) at risk when undergoing a lateral release. Although the incidence of nerve injury after hallux valgus surgery is poorly documented, one study reported a rate of postoperative sensory disturbance of 30.5% in a cohort of 59 patients[64]; however, patients with preoperative neurological symptoms[65] were not excluded (Table 4). In contrast, another observational study reported an incidence of 0.5% for iatrogenic DLHN (also known as lateral dorsal cutaneous nerve) injury among a cohort of 185 patients after surgical correction of hallux valgus.[66]

DISCUSSION

Elective foot and ankle surgery is a relatively new field with accumulating literature. As such, the overall number of patients included in this review is relatively low. Further, most of the publications that address nerve injury in the setting of elective foot and ankle are retrospective and do not designate neurological injury as a primary outcome; these studies may underestimate the

TABLE 4. Neurological Complications Associated With Hallux Valgus Surgeries

Author	Design	Approach	Total Surgeries	Rate of nerve injury (n)	Nerves Injured	Permanent Nerve Injuries	Average Time to Resolution	Anesthetic Type	Remarks
Meier and Kenzora, 1985	R	Dorsomedial incision	59	30.5% (18)	30.5% (18) sensory loss or a positive Tinel sign at the site of the incision	NR	NR	NR	—
Ahn et al, 2013	R	Dorsal incision	185	0.5% (1)	0.5% (1) lateral dorsal cutaneous nerve* injury	0	NR	NR	Neuralgia recovered after a weak steroid injection and a topical lidocaine jelly application

*Lateral dorsal cutaneous nerve is also known as the DLHN.
n indicates Number; NR, not reported; R, retrospective.

true incidence of neurological complications. Moreover, due to the narrative nature of this review, selection bias cannot be excluded from the material presented herein. Nonetheless, elective foot and ankle surgery is associated with relatively high rates of iatrogenic neurologic injury due to robust innervation and multiple terminal nerve branches covering a relatively small surface area. Although it is often not possible to definitively identify the cause of nerve injury in the setting of foot and ankle surgery, especially with the associated use of RA, we are hopeful that this review will afford anesthesiologists a better understanding of the specific nerves at risk during the most common foot and ankle procedures. Understanding the patterns and likelihood of iatrogenic nerve injury may inform and facilitate preoperative risk/benefit discussions with patients considering a regional anesthetic, as well as assist in the diagnosis and management of neurological complications in the postoperative period.

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Pathophysiology and Etiology of Nerve Injury Following Peripheral Nerve Blockade

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Abstract: This review synthesizes anatomical, anesthetic, surgical, and patient factors that may contribute to neurologic complications associated with peripheral nerve blockade. Peripheral nerves have anatomical features unique to a given location that may influence risk of injury. Peripheral nerve blockade–related peripheral nerve injury (PNI) is most severe with intrafascicular injection. Surgery and its associated requirements such as positioning and tourniquet have specific risks. Patients with preexisting neuropathy may be at an increased risk of postoperative neurologic dysfunction. Distinguishing potential causes of PNI require clinical assessment and investigation; a definitive diagnosis, however, is not always possible. Fortunately, most postoperative neurologic dysfunction appears to resolve with time, and the incidence of serious long-term nerve injury directly attributable to peripheral nerve blockade is relatively uncommon. Nonetheless, despite the use of ultrasound guidance, the risk of block-related PNI remains unchanged.

What's New: Since the 2008 Practice Advisory, new information has been published, furthering our understanding of the microanatomy of peripheral nerves, mechanisms of peripheral nerve injection injury, toxicity of local anesthetics, the etiology of and monitoring methods, and technologies that may decrease the risk of nerve block–related peripheral nerve injury.

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Knowledge of potential causes, mechanisms, etiology, and risks for nerve injury and a focus on communicating their potential significance to patients and health care professionals are important for prevention and/or perioperative management of a patient with a potential neurologic complication. The objective of this narrative review was to summarize new information on the microanatomy of peripheral nerves, mechanisms of peripheral nerve injection injury, and direct toxic effects of local anesthetics. In addition, we discuss the etiology and existing strategies and methods of monitoring that may decrease the risk of perioperative peripheral nerve injury (PNI) associated with peripheral nerve blockade (PNB).

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METHODS

For the purposes of this narrative review, the authors used an initial MEDLINE search strategy for 1 or more of the following terms: animals; humans; brachial plexus/injuries/pathology/ultrasonography; femoral nerve/injuries/pathology/ultrasonography; peripheral nerves/injuries/ultrasonography; electric stimulation/methods, needles; nerve block/instrumentation/methods; nerve block/adverse effects/methods; anesthesia/conduction/methods, electric impedance, electric stimulation; ultrasonography/interventional; nerve block/methods; anesthetics, local/administration and dosage/adverse effects/pharmacology; peripheral nerve injuries/etiology; tourniquets/adverse effects; peripheral nervous system diseases/epidemiology/etiology; orthopedic procedures/adverse effects; postoperative complications/epidemiology/etiology; inflammation/etiology/pathology; peripheral nerves/drug effects/pathology/ultrastructure; and peripheral nervous system diseases/chemically induced/pathology. The relevant publications were also manually reviewed for additional material. The authors included studies they deemed relevant to contemporary regional anesthesia practice with emphasis on literature published since the 2008 American Society of Regional Anesthesia and Pain Medicine Practice Advisory on Neurological Complications of Regional Anesthesia and Pain Medicine.[1]

DISCUSSION

Anatomical Considerations

A nerve can be considered a distinct organ composed of neural tissue, a connective tissue stroma, and blood supply. Nerve cells, or neurons, are composed of a cell body, dendrites, and an axon. The axon is a cytoplasmic extension of the neuron that transmits electrical signals along its length from the cell body proximally to any distance from a few millimeters to nearly 1 m distally. Most peripheral nerves transmit both afferent motor and efferent sensory signals. In the peripheral nervous system, the majority of axons have a sheath of Schwann cells that encase the axon in a layer of myelin (Fig. 1). The Schwann cells are interrupted at interposed spaces, the nodes of Ranvier, where the process of depolarization and repolarization occurs during the saltatory propagation of the action potential. The endoneurium, perineurium, and epineurium are distinct structures on electron microscopy.[2] Each axon is bound by endoneurium, a thin layer of connective tissue composed mainly of thin collagen fibers. Nerve fibers are organized into groups called fascicles. Within each fascicle, the nerve fibers form an intraneural plexus, in which some axons take positions in different fascicles along their path. Thus, the topographic map of the fascicles varies continually along its path, which at least partially helps to explain why episodes of PNI are unique and unpredictable. In the vicinity of joints, the fascicles are thinner and more numerous, surrounded by a greater amount of connective tissue, which reduces the vulnerability of the fascicles to insults such as pressure and stretching.[3]

Each fascicle is surrounded by a perineurium consisting of continuous and concentric layers of 8 to 18 cells (Fig. 2). The thickness of the perineurium is typically 7 to 20 μm.[2] The layers

of perineurial cells, their tight junctions, and the nonfenestrated capillaries within the endoneurium provide a barrier for diffusion of substances into and out of the fascicles.[2] This important diffusion barrier protects exposure of the axons to chemical injury. There are collagen fibers aligned predominantly along the longitudinal axis of the fascicle. The perineurium allows for some movement of axons within a fascicle and maintains intrafascicular pressure while serving as a physical barrier against mechanical injury.

In contrast to the perineurium, the epineurium is permeable and does not form a barrier (Fig. 3). The epineurium is the dense collagenous tissue that forms the external boundary of peripheral nerve trunks. The epineurial collagen fibers are similar to the collagen fibers of the dura mater and nerve root cuff. There is also interfascicular tissue often referred to as interfascicular or inner epineurium. This inner layer of connective tissue that envelopes the fascicles contains adipose tissue, fibroblasts, mastocytes, blood vessels (and small nerve fibers innervating these vessels), and lymphatics.[2] This interfascicular tissue is loose connective tissue and is in contrast to the dense collagenous tissue that forms the epineurium.

There are other connective tissue layers immediately adjacent to nerves. For example, there is a common extraneural layer of connective tissue that surrounds both components of the sciatic nerve (Fig. 3). This has been described as being analogous to the extraneural connective tissue of the brachial plexus, the prevertebral fascia.[4] In addition, there is a nonspecialized loose network of areolar connective tissue that fills the space between specialized structures such as nerves, muscles, and vessels. This is referred to as deep fascial or paraneural connective tissue, and this contributes to the relative mobility of nerve.[3] However, at specific anatomical locations, nerves are relatively tethered including when nerves are in close proximity to bony landmarks.

Peripheral nerves have 2 independent interconnected blood supplies. The extrinsic blood supply consists of arteries, arterioles, and veins that lie within the epineurium, whereas the intrinsic supply comprises a group of longitudinal capillaries that run within the fascicles and endoneurium. Within the fascicles, the capillaries are nonfenestrated and contribute to the barrier effect. As these capillaries reach the outer border of the perineurium, the capillaries become fenestrated.[2] Vessels that originate in the epineurium and traverse the perineurium form anastomosis between the 2 vascular systems.

Pathophysiology of PNI

Severity of PNI

The clinical importance of block-related PNI depends on its severity. Because the primary determinant of prognosis is the residual integrity of the axons, PNI severity is typically classified according to the relative degree of axonal disruption. Proximal axonal lesions (ie, close to the cell body) are traditionally believed to be more severe than distal axonal lesions (ie, closer to the innervation target) as the likelihood for reinnervation and recovery appears to vary inversely with the distance between the location of the axonal lesion and the target tissue. Two commonly used anatomical classifications are the Seddon[5] and Sunderland[6] scales (Table 1). The Seddon classification includes (from mild to severe) neuropraxia, axonotmesis, and neurotmesis. Briefly, neuropraxia refers to damage to the myelin sheath typically associated with nerve stretching or compression. The axons and supporting elements (endoneurium, perineurium, and epineurium) remain intact. The prognosis for a neuropraxic injury is good, with recovery within weeks to months. Fortunately, most postoperative neurologic symptoms associated with regional anesthesia tend to follow a neuropraxic pattern of injury and recovery.[7] Axonotmesis refers to axonal injury associated with fascicular impalement, nerve crush, or toxic injury, with loss of axonal continuity and an intact endoneurium. Recovery following axonal loss is prolonged and may be incomplete, depending on the extent of disruption and on the distance from the injury site to the corresponding muscle. Neurotmesis refers to complete transection of the nerve, including the axons, endoneurium, perineurium, and epineurial connective

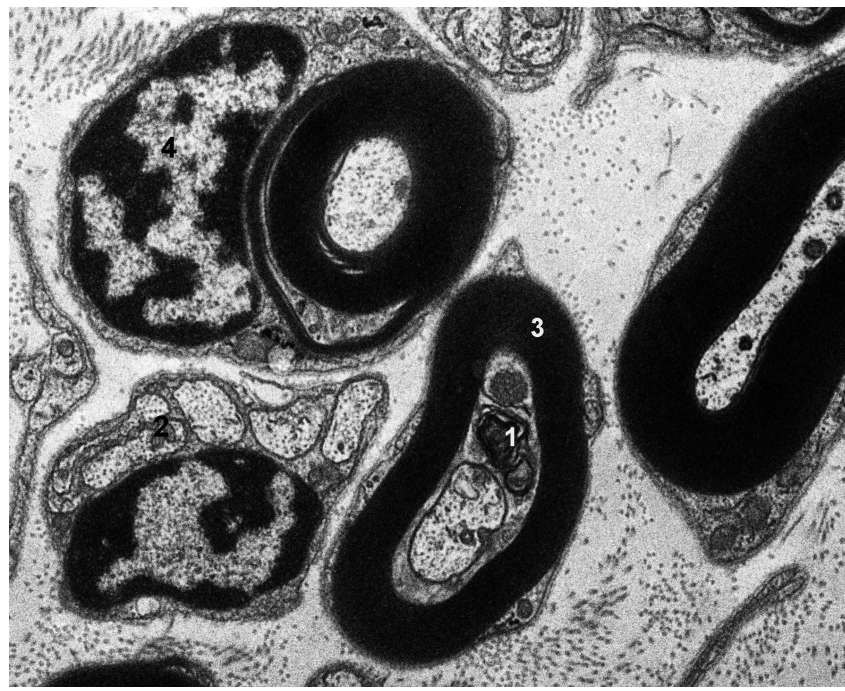

FIGURE 1. Electron microscopic image of the human peripheral nerve. 1: Myelinated axon. 2: Unmyelinated axon. 3: Myelin. 4: Nucleus of Schwann cell.

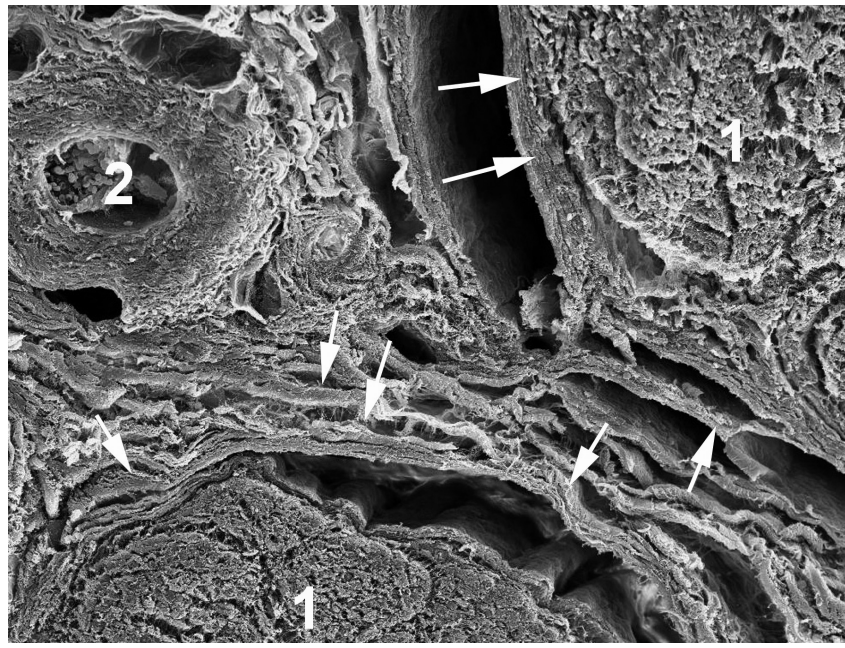

FIGURE 2. Magnified section of the fascicles and perineurium of the human peripheral nerve. 1: Fascicles. 2: Intraneural blood vessel. White arrows: perineurium (perineurial layers).

tissue. Its treatment typically requires surgical intervention, with a guarded prognosis.

Mechanism of Injury

The mechanism of PNI related to the use of PNB traditionally falls into 1 of 3 broad categories: mechanical and injection injury (traumatic), vascular (ischemic), and chemical (neurotoxic). It must be noted that most of our insights from peripheral nerve injection injury are obtained from animal experiments. Because such research is not possible in humans, all mechanisms of PNI are not fully understood.[8] Animal studies significantly vary in species and methodologies, making it difficult to readily extrapolate such data to actual clinical practice.

Mechanical and injection injury

Mechanical compression injury can result from forceful needle-nerve contact from an approaching needle[9] or injection inside the nerve itself. Nerve compression or entrapment may produce a conduction block and, if prolonged, a focal demyelination of some axons along with an increase in neuropeptide production and dorsal horn activity.[8,10] Intraneural injection may lead to sustained high intraneural pressure,[11] which when exceeding capillary occlusion pressure may lead to nerve ischemia. In animals, inadvertent injection of antibiotics, steroids, bovine collagen, botulinum toxin, and local anesthetics into peripheral nerves has been associated with marked histological and in some instances permanent functional neurologic deficits.[12–17]

Although some degree of axonal injury may potentially occur despite there being no injury to the perineurium, site of injection is thought to be critical.[12,15] The main source of block-related PNI is injection of local anesthetic into a fascicle causing direct needle and injection trauma, rupture of perineurium, and loss of the protective environment within the fascicle with consequent myelin and axonal degeneration.[8,12,15,18–20] Of note, even intrafascicular injection of saline can result in axonal degeneration, indicating a baseline level of injury associated with injecting any agent into a nerve.[21] Therefore, while the clinical importance of neurotoxicity remains controversial,[22] the location of the needle tip during injection of the local anesthetic appears to play a crucial role in determining the likelihood and severity of nerve injury.

Vascular injury

Damage to the nerve vasculature during nerve blocks can result in local or diffuse ischemia related to direct injury or acute occlusion of the arteries from which the vasa nervorum is derived, or from a hemorrhage within a nerve sheath. The epineurial circulation is a critical component of the overall neural circulation, and its removal reduces nerve blood supply by 50%.[23] Nerves with an abundance of connective tissue may be less susceptible to compression because external forces are not transmitted directly to epineurial

TABLE 1. Classification of Nerve Injury

Seddon[5]	Sunderland[6]	Processes	Prognosis
Neuropraxia	1	Myelin damage, conduction slowing and blocking	Good
Axonotmesis	2	Loss of axonal continuity, endoneurium intact, no conduction	Fair
Neurotmesis	3	Loss of axonal continuity and endoneurial continuity, perineurium intact, no conduction	Poor
	4	Loss of axonal continuity, endoneurial and perineurial continuity, epineurium intact, no conduction	Poor
	5	Complete nerve transection, no conduction	Poor

vessels. In most circumstances, no single vessel dominates the pattern over an entire length of nerve; however, the sciatic nerve is an exception to this rule, receiving its major arterial supply in the gluteal region from the companion artery to the sciatic nerve (1 of 3 embryological remnants of the axis artery to the lower limb).[24,25]

Local anesthetics and adjuncts reduce neural blood flow in an agent- and concentration-dependent manner.[23,26] Epinephrine reduces neural blood flow to a greater extent than local anesthetics alone and has the potential to cause local vasoconstriction, but its role in causing nerve ischemia and injury is controversial.[26] Neural ischemia may also occur following high-pressure injection and disruption of the intrafascicular microvasculature. Inadvertent vessel puncture, resulting in the formation of an internal or external hematoma that can mechanically compress the fascicles from within or outside the nerve sheath, has been implicated in cases of neurologic injury.[27,28]

Chemical injury

Chemical nerve injury results from tissue toxicity of injected solutions (eg, local anesthetics, alcohol, or phenol) or its additives. The toxic solution may be injected directly into the nerve or into adjacent tissues, causing an acute inflammatory reaction or chronic fibrosis involving the nerve. Much of the research on neurotoxicity of local anesthetics has been done in in vitro models, particularly with intrathecal application. There is evidence that nearly all local anesthetics can have myotoxic, neurotoxic, and cytotoxic effects in various tissues under certain conditions,[17,22,29–37] however local anesthetics do vary in their neurotoxic potential.[16,38,39] Several studies have demonstrated that local anesthetics can lead to fragmentation of DNA and disrupt the membrane potential in mitochondria, resulting in the uncoupling of oxidative phosphorylation, which may result in apoptosis.[40] There appears to be a direct correlation between concentration of the local anesthetic and duration of exposure to the nerve with death of Schwann cells, infiltration with macrophages, and myelin damage.[38,41] Local anesthetics can also directly constrict vasculature and decrease the blood flow to the nerves, potentially resulting in ischemic injury.[42] However, the inherent difficulty in extrapolating these laboratory studies to the clinical practice of modern peripheral nerve blocks is that there is a substantial decrease in the concentration of local anesthetics by the time it reaches the axons.

The site of local anesthetic application (extraneural, intraneural, interfascicular, intrafascicular) may be the primary determinant of whether neurotoxicity will occur and if the concentration is high and duration of exposure prolonged.[15] Most chemical substances, including all local anesthetics, injected intrafascicularly lead to severe fascicular injury, whereas the same substances injected intraneurally but interfascicularly cause less injury.[43] Indeed, needle penetration of a nerve may result in minimal damage if it is not combined with local anesthetic injection within the nerve fascicle.[8,12] In a rodent model, Whitlock et al[15] demonstrated that intrafascicular injection of 0.75% ropivacaine resulted in severe histological abnormalities including demyelination, axonal degeneration, and Wallerian degeneration. However, extrafascicular injection of 0.75% ropivacaine also resulted in axonal injury, although reduced in severity. Farber and colleagues[16] recently reported that all commonly used local anesthetics (bupivacaine, lidocaine, and ropivacaine) produced nerve injury when injected intrafascicularly. In their study, the degree of injury decreased with increasing distance from site of injection.

Inflammatory injury

Inflammatory mechanisms of PNI are being increasingly recognized.[44,45] Nonspecific inflammatory responses targeting peripheral nerves can occur either remote or near the site of surgery, where it becomes difficult to distinguish from other causes of PNI. Inflammatory mechanisms have recently been proposed as the cause for persistent phrenic nerve injury following interscalene block for shoulder surgery. Kaufman and colleagues[46] reported a series of 14 patients with chronic diaphragmatic paralysis following interscalene block. During surgical exploration, adhesions, fascial thickening, vascular changes, and scar tissue (present in 10 of 14 patients) involving the phrenic nerve suggested chronic inflammation and were consistent with a compression neuropathy. Animal data suggest that ultrasound gel can lead to inflammation in the subarachnoidal space[47] and peripheral nerves.[48]

Etiology of Nerve Injury Following PNB

Anesthetic Factors

Several studies have reported that the type of anesthesia (regional vs general) does not appear to influence the incidence of PNI. The University of Michigan performed a retrospective analysis of PNI and did not identify PNB as an independent risk factor for PNI.[49] Three studies from the Mayo Clinic have determined that the choice of regional anesthesia does not increase the risk of PNI following total knee arthoplasty,[50] total hip arthroplasty,[51] and total shoulder arthroplasty.[52] However, surgical literature warns that the risk of block-related PNI may be higher than that reported in anesthesia literature.[46,53–55] In the following section, we discuss several technical, equipment, and anatomical factors that may influence the risk of nerve injury.

Intraneural injection

Avoidance of deliberate trauma to nerves including intraneural injection is a key safety principle of regional anesthesia. The traditional teaching that "nerves should be handled with care" has been recently documented in animal models. Forceful needle-nerve contact and application of needle pressure displacing a peripheral nerve may lead to significant inflammatory changes.[9] Intraneural injection of local anesthetic has long been implicated in the development of PNI.[15,16,18,21,56] However, intraneural injection may occur in clinical practice without resulting in overt signs of nerve injury.[57–59] In fact, unintentional intraneural (but probably extrafascicular) epineurial injection may be more common than previously recognized.[60] In a study by Liu and colleagues,[57] unintentional intraneural injection occurred in 17% of 257 patients having ultrasound-guided brachial plexus block for shoulder surgery, and none of these patients developed signs or symptoms of PNI. The presumed risk of intraneural injection has been challenged by Bigeleisen and colleagues,[58] who reported that nerve puncture and apparent intraneural injection (2–4 mL per nerve) during axillary brachial plexus block in healthy patients did not lead to neurologic injury. Nonetheless, despite various reports of inadvertent or even intentional intraneural injection without neurologic sequelae, the preponderance of available laboratory evidence suggests that intraneural injection must be avoided during PNB.[15,16,18,21,43]

Nerve structure

The structural organization, or internal architecture, of a peripheral nerve provides insight into the relative risk for mechanical injury among different nerves or different locations within the same nerve. Because the epineurium is typically a tougher layer than the surrounding tissues, nerves tend to be "pushed away" by an advancing needle, rather than penetrated. Similarly, when the epineurium is penetrated by a needle, the needle tip and injection are much more likely to enter the interfascicular epineurial or adipose

tissue than the fascicles themselves. Intraneural injection into the interfascicular epineurium may not result in nerve injury. The adipose tissue within the epineurium allows the fascicles to escape the advancing needle; however, this protection may be undermined by abrupt needle advancement needle or forceful needle-nerve contact.[9]

It has been suggested that because of differences in neural architecture, namely, the amount of nonneural connective tissue, proximal sites of PNB may be at higher risk of nerve injury compared with distal sites. Peripheral nerves characterized by tightly packed fascicles and high fascicular-to-connective tissue content, such as the proximal brachial plexus, may be at greater risk of mechanical nerve injury compared with nerves characterized by lower fascicular-to-connective tissue content.[61,62] The common peroneal nerve is an example of a nerve with few fascicles and little epineurial connective tissue. It is well recognized that the common peroneal nerve is at greater risk of nerve injury than the tibial nerve, which is characterized by a multifascicular pattern and an abundance of epineurium.[63] However, there is no clinical evidence that the proximal sites of upper- or lower-limb PNBs place patients at increased or decreased risk of PNB-related neurologic complications compared with distal sites.

Needle type

It seems intuitive that short-beveled needle types are less likely than long-beveled needles to penetrate the protective connective tissue layers (epineurium, perineurium) of peripheral nerves. Selander and colleagues[64–66] documented that a 45-degree-bevel needle is much less likely to penetrate perineurium and inflict fascicular injury than a 15-degree-bevel needle. However, should a nerve fascicle become accidentally impaled during nerve block procedure, the lesions induced by short-beveled needles may be more severe and take longer to repair than those induced by long-beveled needles.[29] Needle-tip characteristics can influence the likelihood of fascicular penetration and nerve injury.[64] Long-beveled needles are more likely to puncture and enter the fascicle compared with short-beveled needles; however, short-beveled needles appear to cause more damage in case of fascicular penetration.[64] Nerve puncture with pencil-point or Tuohy needles causes a similar high degree of posttraumatic regional inflammation, myelin damage, and intraneural hematoma.[67] Increased needle diameter worsens the severity of nerve injury after needle-nerve perforation.[68] In the setting of neuraxial anesthesia, the dural lesions produced by different needle types vary in morphology and characteristics; a Whitacre needle produces a more traumatic opening with tearing and severe disruption of the collagen fibers compared with a Quincke needle that resulted in a clean-cut opening.[69]

PNB in heavily sedated or anesthetized patients

The administration of procedural sedation, a common practice during regional anesthesia, is an inherent aspect of care that impacts patient satisfaction and acceptance of regional anesthesia.[70] The safety of performing regional anesthesia in anesthetized or heavily sedated patients is controversial[71]; however this topic has been addressed in detail in another section of this current practice advisory.

Surgical Factors

Surgical positioning requirements

Neurologic complications occur as a result of patient positioning for surgical requirements.[72] During surgery, patients are placed in positions they would otherwise not tolerate. The physical forces required for surgery (eg, placement of prostheses) can be excessive, potentially stressing anatomical structures remote from the surgical site. Mechanisms of nerve injury related to surgery include traction, transection, compression, contusion, ischemia, and stretch. Regardless of the exact mechanism, a continuum of severity of nerve injury has been described including physical disruption of intraneural blood vessels causing patchy ischemia or hemorrhage, elevated intraneural venous pressures, endoneurial edema, impairment of axoplasmic flow, Schwann cell damage, myelin displacement, axonal degeneration, and Wallerian degeneration.[73] Nerve roots are particularly susceptible to traction and compression, at least in part because the roots lack both epineurial and perineurial tissue.[3] The upper trunk of the brachial plexus is attached medially to transverse processes and laterally by the entry of these nerves into muscles. Loss of muscle tone, as occurs during anesthesia, theoretically exposes the neural elements to traction forces. However, there are also anatomical factors protecting against lateral traction or stretch injury; for example, the fourth, fifth, and sixth spinal nerves are lodged into the gutter of the transverse processes, and therefore, these forces are not transmitted directly to the spinal nerve roots. Furthermore, the dorsal and ventral roots of spinal nerves are protected from lateral traction by wedging of a cone of dura surrounding the nerve root–spinal nerve complex into the intervertebral foramen. More distally (eg, spinal nerves and plexus trunks/divisions), fascicles have their own protective perineurium[74] and a plexiform arrangement that contribute to the tensile strength. In a closed-claims analysis, 9 of 53 anesthetic-related brachial plexus injuries were related to intraoperative positioning (shoulder braces in the head-down position [3 claims], patient's arm suspended on a bar [2 claims], and other malpositions [4 claims]); 2 claims were related to regional anesthesia technique.[75]

Effects of the pneumatic tourniquet

Tourniquet inflation causes nerve damage by mechanical compression and/or ischemic injury.[10,76,77] The main findings of tourniquet neuropathy are motor loss, diminished touch, vibration and position sense, and preserved senses of heat, cold, and pain.[78] Wider tourniquets, using lower cuff pressures and limiting the duration of inflation, are risk reduction strategies.[79] In an experimental model, tourniquet compression resulted in increased vascular permeability, intraneural edema, and sciatic nerve degeneration.[80] In the context of meniscectomy surgery, tourniquet compression can result in femoral denervation, limiting functional recovery.[81,82]

Postsurgical inflammatory neuropathy

Patients with postsurgical inflammatory neuropathy can present with symptoms/signs that are delayed and remote from the surgery. The neuropathies tend to be focal and multifocal with pain and weakness. In the setting of a postsurgical inflammatory neuropathy, the inflammatory-immune response inappropriately targets the nerves of the peripheral nervous system. Biopsy of affected nerves demonstrates a lymphocytic-mediated inflammation and sometimes a frank microvasculitis. This causes neurologic dysfunction and axonal degeneration.[45]

Patient Factors

Preoperative neural compromise

A preoperative neurologic deficit or neural compromise theoretically places a patient at increased risk of PNI. Preoperative neural compromise may result from several mechanisms: entrapment, metabolic, ischemic, toxic, hereditary, and demyelination. Entrapment neuropathies can involve ulnar, median, radial, lateral femoral cutaneous, femoral, and peroneal nerves.[83] Cervical spondylosis results in the intervertebral foramen becoming rough and irregular. The spinal nerve–nerve root complex becomes subject

to repeated trauma, resulting in fibrosis, reducing its mobility, increasing the risk of traction injury during upper-extremity movement. The ulnar nerve may become entrapped in the cubital tunnel at the elbow or at the wrist. Risk factors for ulnar neuropathy include male sex, extremes of body habitus, and prolonged admission.[84] However, in many situations, this "injury" may be an extension of a preoperative morbidity, because in a substantial proportion of patients with a diagnosis of ulnar neuropathies, there were preexisting contralateral electromyographic abnormalities.[85] Carpal tunnel syndrome is the most common upper-extremity neuropathy and may be unmasked postoperatively. Diabetic neuropathies represent a wide range of clinical entities. Chronic ischemia may compromise diabetic nerve fibers and render them susceptible to perioperative insults including local anesthetic toxicity (potentially worsened because the reduced blood flow results in nerves being exposed to larger concentrations of local anesthetics).[86] The occurrence of PNI following neuraxial blockade in patients with diabetic neuropathy has been reported as being (0.4%; 95% confidence interval, 0.1%–1.3%),[87] which is higher than estimates (0.03%[88]–0.008%[89]) reported for the general population.

Medical conditions that have an adverse impact on the microvasculature of the peripheral nerves potentially increase the risk for PNI. These include severe peripheral vascular disease, vasculitis, cigarette smoking, and hypertension.[1,49] Patients with these conditions may be vulnerable to further ischemic insults during the perioperative period. Toxic etiologies include alcohol[90] and cisplatin chemotherapy.[91] Patients with multiple sclerosis may have subclinical preoperative neural compromise within the peripheral nervous system.[92] Patients with hereditary neuropathy with liability to pressure palsies may require only a mild insult resulting in the development of severe PNI.

Lumbar spinal canal stenosis

Lumbar spinal canal stenosis may exaggerate a PNI adversely affecting physical recovery.[93] Spinal canal stenosis is a risk factor for common peroneal palsy following total hip arthroplasty[93] and may be significant in cases of paraplegia or cauda equina syndrome following epidural anesthesia.[89,94] Spinal canal pathology may be asymmetric, and therefore, a unilateral deficit may present following neuraxial anesthesia and potentially falsely implicate a deficit related to PNB. Hebl et al[95] documented new or progressive neurologic deficits following neuraxial anesthesia in patients with preexisting spinal canal stenosis or lumbar disc disease. Overall, 10 patients (1.1%; 95% confidence interval, 0.5%–2.0%) developed new deficits or worsening of preexisting symptoms, which is higher than previous estimates (ranging between 0.03[88] and 0.008[89]).

Nerve Localization Techniques and Monitors and the Risk of PNI

Monitors and nerve localization techniques can potentially reduce the risk of PNI; however, this is a matter of longstanding debate. Newer technologies (eg, ultrasound guidance, injection pressure monitoring, measurement of electrical impedance) have resulted in a resurgence of interest in PNI prevention. The extent to which nerve localization techniques and monitors can prevent PNI is based on the reliability of each device to predict dangerous needle-nerve proximity. The absolute danger of intimate needle-nerve proximity, including intraneural needle tip placement and even intraneural injection, has recently been challenged in several clinical studies.[57–60] However, Farber and colleagues[16] have recently warned against intentional intraneural injection based on their results of neurotoxicity following intrafascicular injections of local anesthetics. Albeit relatively low, the incidence of block-related nerve injury remains one of the most common disabling complications related to administration of anesthesia.[34] More importantly, its severity and impact on the patient's quality of life mandate a systematic and prudent approach toward decreasing the risk for injury through standardization of injection techniques. The effects of nerve localization techniques and monitors on PNI are briefly summarized below according to our current state of knowledge. Evidence-based recommendations regarding measures to reduce the risk of PNI associated with PNB are presented in Tables 2 and 3.

Mechanical Paresthesia

The association between the mechanical elicitation of paresthesia and consequent PNI is controversial.[19,96] Opponents to the intentional elicitation of paresthesia cite increased likelihood of PNI due to traumatic and inflammatory changes that may occur after presumed needle-nerve contact.[19,59] Whereas some studies[19,97] have implicated paresthesia as a risk factor for PNI, this association has not been supported by others,[98] or by the single relevant, prospective, randomized clinical trial published to date.[99] In fact, a recent imaging study revealed that only 38% of patients experienced paresthesia during real-time visualization of needle-nerve contact.[100] Therefore, the absence of paresthesia during the performance of a nerve block does not reliably exclude needle-nerve contact and/or the development of block-related PNI, and PNI has been described both in patients who have experienced paresthesia and in those experiencing no paresthesia during block placement. Regardless, a severe paresthesia, or pain upon needle advancement or injection, may indicate intraneural needle placement and when present should prompt cessation of injection. Premedication with sedative medication may influence how patients perceive and interpret paresthesia. Likewise, ultrasound-guided PNB often involves multiple injections of aliquots of local anesthetic in several different anatomical areas, and the spread of the local anesthetic during multiple injection techniques may impact the potential value of paresthesia as a safety monitor.

Peripheral Nerve Stimulation

Motor response to peripheral nerve stimulation is governed by Coulomb law, which implies that the threshold current required to elicit a response (the minimum stimulating current [MSC]) exponentially decreases as the insulated needle tip advances toward the target nerve.[101] Voelckel and colleagues[102] were the first to elucidate the association between a very low MSC and subsequent PNI. Performing sciatic nerve blocks in pigs, these authors detected histological nerve injury in 50% of the pigs when an MSC of less than 0.2 mA was used, compared with no histological changes at an MSC between 0.3 and 0.5 mA. An MSC of less than 0.2 mA is a specific, but not sensitive, indicator of intraneural needle placement in both animals[103–105] and humans.[59,106] Overall, as a nerve localization technique, peripheral nerve stimulation is characterized by low sensitivity but high specificity for predicting relative needle-nerve proximity. For example, an evoked motor response may not be reliably elicited when the needle is placed in the immediate vicinity of the nerve or even intraneurally.[104,106,107] Furthermore, when a motor response is elicited at low current intensity, needle-nerve contact and intraneural injection cannot be reliably discerned.[108]

Injection Pressure Monitoring

The association between high injection pressures and intrafascicular injection was first described by Selander and Sjostrand[20] in 1978 and subsequently studied in several animal models. In a dog model, an intentional intrafascicular injection was associated with high opening injection pressure (≥25 psi) and corresponding clinical and histological nerve injury.[18] In contrast, extrafascicular

TABLE 2. Evidence Statements Regarding Patient, Anesthetic, and Surgical Factors Contributing to Perioperative Peripheral Nerve Injury

Anesthetic Factors
• Peripheral nerve injection injury with local anesthetic is greatest when the injection is intrafascicular in location. This is likely related to (1) exposure of axons to vastly higher concentrations of local anesthetics compared with extraneural application of anesthetics and (2) mechanical damage to the perineurium and associated loss of the protective environment contained within the perineurium. (Evidence level IIa or class I)[8,12,15,16,21]
• Intrafascicular injections are associated with higher opening injection pressures and risk of PNI compared with perineural injections. (Evidence level IIa or class I)[18,109]
• Local anesthetic toxicity is time and concentration dependent. (Evidence level IIa or class I)[41]
• Epidural anesthesia and general anesthesia, but not PNB, have been associated with PNI.[49] PNB is not associated with PNI following TKA,[50] THA,[51] or TSA.[52]
Patient Factors
• The presence of a preoperative neurologic deficit or neural compromise theoretically places a patient at increased risk of perioperative PNI. (Evidence level III or class II)[87,89,91,95]
• Postoperative neurologic features appear more likely to be related to patient and surgical factors than to be related to PNB (evidence level IIa or class I).[50,51,127] The ulnar nerve at the elbow[73,85,131] and the common peroneal nerve are at increased risk of PNI. (Evidence level III or class II)[63,79,132]
Surgical Factors
• Tourniquet neuropathy can be associated with marked clinical deficits[78] and pathological changes on electromyography.[82,133,134] The duration of inflation and pressure are important factors contributing to its severity. (Evidence level III or class II)[79,135]
• Surgical procedures have unique risk profile. (Evidence level III or class I)[50–52,93]
• Inflammatory mechanisms for PNI are recognized and exhibit features that are physically and temporally remote from PNB. (Evidence level III or class I)[44,45]

TKA indicates total knee arthroplasty; THA, total hip arthroplasty; TSA, total shoulder arthroplasty.

Levels of evidence: Ia, evidence obtained from a meta-analysis of randomized controlled trials; Ib, evidence obtained from at least 1 randomized controlled trial; IIa, evidence obtained from at least 1 well-designed controlled study without randomization; IIb, evidence obtained from at least 1 other type of well-designed quasi-experimental study; III, evidence obtained from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies, and case reports; IV, evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities.

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

injections were not associated with high injection pressures or with nerve injury. In another dog model study,[109] there was clinical and histological nerve injury with intraneural injection when injection pressures were high (≥20 psi), but not when injection pressures were low (<10 psi). During intraneural injection into the median nerves of pigs, Lupu and colleagues[110] were unable to detect a significant correlation between the maximum pressure generated and clinical or histological nerve injury. In this study, peak injection pressures were well below 25 psi, yet 7 of 10 nerve specimens had evidence of axonal damage upon histological examination. In 1 case, axonal damage ensued following a maximum injection pressure of only 2.2 psi. Importantly, functional deficits measured up to 7 days after insult were absent in all 10 pigs studied. More recently, the first such study in human tissue, Orebaugh and colleagues[111] reported that 100% of injections directly into the roots of the brachial plexus of fresh human cadavers resulted in high injection pressures (>30 psi) with 1 occurrence of spread of the injectate into the epidural space.

Several studies have used injection pressure as a monitoring tool during sciatic nerve block without complications.[106,112,113] Robards and colleagues[106] studied 24 patients who each received an injection inside their sciatic nerve at the level of the popliteal fossa. Injection pressures of less than 20 psi were recorded in 20 patients, whereas injection pressures of greater than 20 psi were observed in the remaining 4 patients, prompting cessation of the injection. None of the patients suffered any neurologic dysfunction.[106] In a study of intraneural stimulation thresholds during ultrasound-guided supraclavicular brachial plexus blocks, Bigeleisen and colleagues[59] reported coexistence of high resistance to injection, low current stimulation, and pain on injection with intraneural needle placement. These simultaneous findings necessitated needle repositioning before completing the injection without complication.[59] Finally, Gadsden and colleagues[114] reported that high injection pressure during lumbar plexus block carries a risk for epidural spread.

Assessment of injection pressure (resistance) during PNB is of increasing interest to clinicians and researchers.[115,116] This is not surprising, given that injection into densely packed nerve fascicles requires more force to initiate an injection (opening pressure) than intraneural interfascicular injections into the loose connective tissue. In an attempt to standardize monitoring and documentation of nerve block procedures, a group of North American experts has suggested documenting the resistance to injection as one of the elements of the standard clinical note.[117] However, 2 independent groups found that the clinician's accuracy in gauging injection pressure or the tissue being injected is limited when using a subjective, syringe-feel technique, thus questioning the reliability of subjective assessments.[118,119] In the meantime, several means of monitoring injection pressures have been recommended.[116,120]

Taken together, the data to date suggest that high opening injection pressure can detect needle-nerve contact and intrafascicular injection but not an intraneural interfascicular injection.[109,111] In the first study in patients, Gadsden and colleagues[121] demonstrated that opening injection pressure with the needle tip at 1 mm away from the nerve was consistently lower than 15 psi (mean peak pressure, 8.2 ± 2.4 psi). In contrast, opening injection pressure during needle-nerve contact was 15 psi or greater (mean peak pressure, 20.9 ± 3.7 psi) in 35 of 36 injections. In this study, aborting the injection when opening injection pressure reached 15 psi reliably prevented commencement of injection in 97% cases of needle-nerve contacts.[121] In addition, high opening injection may correlate well with other indices of needle-nerve contact, such as low current stimulation and paresthesia on injection.[59,106] More research is required to determine the clinical benefits of routine injection pressure monitoring and "safe" injection pressure values for various nerve block procedures. Injection pressure monitoring may prove to be most useful for its negative predictive value for functional nerve injury, as no cases of clinically significant neuropathy have been reported in the literature with low injection pressures. Based

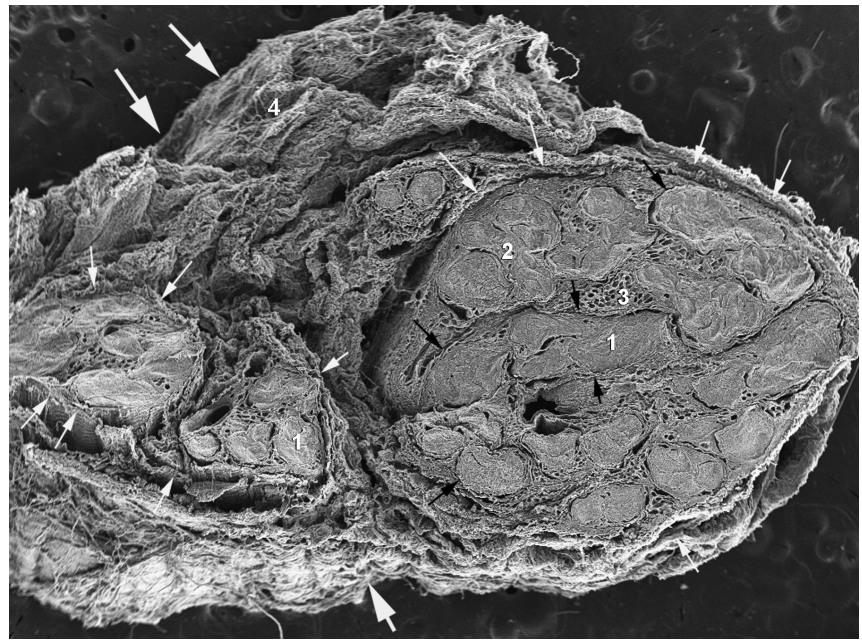

FIGURE 3. Electron microscopic image of the human sciatic nerve. Shown are tibial nerve (right) and common peroneal nerve (left). 1: Example of fascicles. 2: Example of fascicular bundles (≥2 fascicles bound together). 3: Example of interfascicular tissue. 4: Extraneural connective tissue layer surrounding both the tibial and peroneal nerves. Large white arrows: extraneural layer of connective tissue surrounding the sciatic nerve. Small white arrows: epineurium of tibial nerve (right) and common peroneal nerve (left). Black arrows: examples of perineurium.

on the available data, however, avoidance of high resistance (pressure) to injection appears to be a prudent strategy during nerve block injection because a typical injection into perineural tissue requires low opening pressure (<15 psi).

Electrical Impedance

Electrical impedance monitoring is featured in newer nerve stimulators and measures the resistance to flow of an alternating current in an electrical circuit. It is extremely sensitive to changes in tissue composition, particularly water content. In a pig sciatic nerve model, Tsui and colleagues[122] demonstrated that nerves have greater electrical impedance than the surrounding muscle and interstitial fluid because of their low water and high lipid content. They found that the electrical impedance increased abruptly upon entrance into the intraneural compartment relative to the extraneural compartment. The absolute value at which intraneural needle placement occurs could not be determined because of substantial variance within the data. While electrical impedance monitoring appears promising to detect intraneural needle tip placement, it necessarily implies that nerve puncture must occur before a change in impedance is detected. There is also reasonably strong evidence that measurement of electrical impedance can differentiate intravascular from perineural placement of a needle when 5% dextrose is injected before local anesthetic.[123] Based on the available data, impedance monitoring can differentiate between certain tissues, such as muscle and adipose/connective tissue. However, the variability of impedance measurements indicates that further research is required regarding the potential clinical applicability of this modality.[124]

Ultrasound

The use of ultrasound guidance has substantially facilitated the teaching and popularized the utilization of PNBs while decreasing the incidence of systemic toxicity of local anesthetics.[125,126] However, to date, ultrasound has not been shown to decrease the incidence of PNI.[125,127] One of the unique features of ultrasound is its ability to detect intraneural injection, yet whether this technology will ultimately affect the rate of PNI remains to be proven. In animals, ultrasound is sensitive enough to detect as little as 1 mL of injectate[103,105]; however, a much smaller amount of injectate is sufficient to injure the fascicles.[16] Regardless, no animal or human study to date has definitively demonstrated an association between real-time sonographic visualization of intraneural injection of local anesthetic and consequent functional (or otherwise clinically important) nerve injury.[58–60] One reason may be that the resolution of ultrasound machines is not high enough to differentiate intrafascicular injection from the potentially more forgiving extrafascicular compartment. In addition, the ability to interpret such images is highly user-dependent, and also the ability to obtain high-definition, quality images varies among patients.[128] Distinguishing the outer border of a nerve and surrounding nonneural structures is challenging in many patients and anatomical locations. Furthermore, ultrasound guidance may encourage practitioners to place a block needle as close to a nerve or plexus as possible. Albrecht and colleagues[129] determined the maximum distance between needle tip and interscalene brachial plexus while preserving block effectiveness. Their results indicated that a needle tip-to-nerve distance of 8 mm resulted in effective long-lasting analgesia in 50% of patients (however, the 95% confidence interval indicates that potentially the success rate could be higher).[129] This finding is consistent with the results of Spence and colleagues'[130] study, which suggested that local anesthetic injection adjacent to the plexus was as effective as an injection within the sheath.

SUMMARY

Neurologic complications associated with PNB often have a diverse and complex etiology associated with a range of perioperative processes and patient, anesthetic, and surgical factors (Table 3). Peripheral nerves are variable in location, structure, and susceptibility to injury. Mechanisms of PNB-mediated injury

TABLE 3. Evidence Statements Regarding Needle Tip Location, Choice of Local Anesthetic, and Nerve Localization Techniques

Needle-tip location, choice of local anesthetic, and paresthesia

- Intraneural needle insertion does not invariably lead to functional nerve injury.[57–60,113] (Class I)
- Intrafascicular needle insertion and injection should be avoided because it can cause histological and/or functional nerve injury.[12,13,15,16,18,21,43,110] (Class I)
- Paresthesia during needle advancement or upon injection of local anesthetic is not entirely predictive of PNI.[99,136] (Class I)

Nerve localization techniques

- There are no human data to support the superiority of one nerve localization technique over another with regard to reducing the likelihood of PNI.[99,127,137] (Class I)
- Presence of an evoked motor response at a current of <0.5 (0.1 ms) indicates intimate needle-nerve relationship, needle-nerve contact, or an intraneural needle placement.[59,60,104,113] (Class I)
- Absence of a motor response at current of up to 1.8 mA does not exclude needle-nerve contact or intraneural needle placement.[103,104] (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 PNI.[18,109] (Class II)
- Injection pressure monitoring can detect needle-nerve contact for interscalene brachial plexus block.[121] (Class I)
- The common practice of subjectively assessing injection pressure by "hand feel" is inaccurate.[118] (Class I)
- Ultrasound can detect intraneural injection.[105,110] (Class I)
- Current ultrasound technology does not have adequate resolution to discern between an interfascicular and intrafascicular injection.[104,110,138] (Class I)
- Adequate images of needle-nerve interface are not consistently obtained by all operators and in all patients.[57,128] (Class I)

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

include mechanical trauma from needle and injectate, ischemia, direct local anesthetic toxicity, and inflammation. The main source of PNB-mediated neurologic complications is likely mechanical fascicular injury and/or injection of local anesthetic into a fascicle, causing myelin and axonal degeneration. Avoidance of deliberate trauma to nerves including intraneural injection is a key safety principle of regional anesthesia. Fortunately, most postoperative neurologic deficits resolve with time, and the incidence of serious long-term neurologic complications attributable to PNB is relatively uncommon. There is no evidence that ultrasound guidance or any other nerve localization technique reduces the incidence of PNI. The authors consider it reasonable to support an integrated approach to reducing the risk of PNI that likely will vary with PNB type and involve thoughtful patient selection and more than 1 nerve localization technique or monitor. Although several large studies indicate that PNB does not independently increase the risk of PNI following major surgery, nerve injuries occur with ultrasound guidance, and future epidemiologic studies and research on safety monitoring procedures are indicated.

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Neurologic Evaluation and Management of Perioperative Nerve Injury

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Abstract: Neurologic injury after regional anesthesia or pain medicine procedures is rare. Postprocedural neurologic deficits may create high levels of anxiety for the patient and practitioner, although most deficits are limited in severity and can be expected to fully resolve with time. Postoperative anesthesia–related neuraxial and peripheral nerve injuries are reviewed to define an efficient, structured approach to these complications. Emphasis is placed on acutely stratifying the urgency and scope of diagnostic testing or consultation necessity, initiating appropriate definitive treatments, and defining appropriate out-of-hospital follow-up and symptom management.

What's New: Studies pertinent to the recognition, evaluation, and treatment of neurologic assessment of perioperative nerve injury and published since the last advisory on the topic[1] are reviewed and a new structured algorithmic approach is proposed. The evolving literature on postoperative inflammatory neuropathies is reviewed to help define the clinical criteria and to identify patients who would benefit from early neurological evaluation. New sections review potential acute interventions to improve neurologic outcome and long-term management of neuropathic pain resulting from perioperative nerve injury.

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Neurologic injury after regional anesthesia or pain medicine procedures is rare.[2–4] Postprocedural neurologic deficits may create high levels of anxiety for the patient and practitioner, although most deficits are limited in severity and will likely fully resolve with time.[3] Most important to the proceduralist is recognizing injury and stratifying those that require emergent imaging, neurologic or neurosurgical evaluation, and/or treatment from those that can be managed with observation, close clinical follow-up, and symptomatic pain management and rehabilitation. Given the significant medicolegal issues associated with procedurally related neurologic injuries, an efficient structured approach is warranted.

METHODS

The American Society of Regional Anesthesia and Pain Medicine (ASRA) Practice Advisory on Neurologic Complications in Regional Anesthesia and Pain Medicine was convened on March 16, 2012, at the ASRA Annual Meeting in San Diego, California. In preparation for the presentations on the neurologic assessment and management of neuraxial complication and peripheral nerve injuries (PNIs) and on the management of neuropathic pain after nerve injury, an extensive literature search was performed using PubMed. During manuscript preparation, pertinent articles through July 2013 were added. Searches were performed on neuraxial complications, epidural hematoma, spinal epidural abscess (SEA), anterior spinal artery syndrome, spinal cord needle trauma, corticosteroids for spinal cord injury (SCI), lumbar drain for SCI, PNI, postoperative inflammatory neuropathy, Parsonage-Turner syndrome, radiculoplexus neuropathy, electrophysiology and nerve injury, forms of nerve injury, neuropathic pain pharmacologic treatments including meta-analysis and consensus recommendations, complex regional pain syndrome (CRPS) treatments, neuromodulation for neuropathic pain, and derivations of these terms. The literature date was not limited, but special emphasis in preparing the manuscript and recommendations has been placed, when possible, on literature available since the last neurologic assessment and ASRA practice advisory on neurologic complications.[1,5] The level of recommendations are based on those used for the last and current ASRA practice advisory as modified from the American College of Cardiology/American Heart Association construct for classifying strength of evidence.[5]

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DISCUSSION

Temporal Cues and Barriers to Perioperative Nerve Injury Recognition

Postanesthetic or surgical complications should be evident immediately in the postoperative period. However, significant barriers exist in recognizing perioperative nerve injury (Table 1), including patients' tendency to interpret lasting paresthesia or weakness as part of normal recovery, which may delay diagnosis for more than 48 hours postprocedure.[6] This is especially true in PNIs, which are more limited in distribution and severity than neuraxial anesthesia or pain procedure–related catastrophes. This delayed recognition may be more likely with continuous infusion catheters. Reviews of nerve injury after total hip and total knee arthroplasties note that only 77% to 90% of sensorimotor and 20% of sensory complications were recorded during the procedural hospitalization.[7,8] Studies that only include early neurologic injury (<48 hours postoperatively) likely underestimate risk.[6] Studies following patients prospectively for potential neurologic complications of anesthesia should evaluate patients at least up to a point where they are no longer limited by the effects of regional anesthesia, sedation, and parenteral analgesia and include a follow-up inquiry once patients' activity restrictions have been removed.

Injuries recognized late often have (or perhaps more likely have) nonanesthetic/operative-related causes including infection, postoperative inflammation, and consequences of immobilization or compression in the recovery period. The frequency of ulnar neuropathy in surgical cohorts more than 2 days postoperatively, for example, is similar to the frequency in medical patients hospitalized for the same duration.[9] These nonanesthetic/operative complications are often obvious as they occur in a distribution distinct from the surgical or anesthetic site, but when they do coincide with the surgical/anesthetic region, this can further confuse

TABLE 1. Barriers to Perioperative Nerve Injury Recognition

- Sedation
- Postoperative pain or analgesics
- Regional anesthesia
  - —Expect some symptoms in distribution of block/epidural
  - —Failures:
    - To report: Patients presume all symptoms from block
    - To pursue: Caregivers presume symptoms from block
- Patient perioperative naivety/uncertainty
  - —Patient presumes postoperative neurologic symptoms are normal
- Postoperative activity restrictions
- Dressings, drains, castings

the clinical picture.[7,8,10] Confounding the clinical picture further, patients often see the postoperative period as a single time epoch (the "perioperative blur") instead of individual days. As such, retrospectively trying to construct the temporal profile of symptom onset to define a differential diagnosis is imprecise. In a prospective study of postoperative ulnar neuropathy, some patients in follow-up reported that their symptoms were noted "immediately" after surgery, although the prospective evaluations had clearly documented an onset of signs and symptoms more than 48 hours after surgery.[11]

Adding to the challenge of recognizing perioperative neurologic complications is the increasing number of procedures performed in ambulatory surgical centers, where postprocedure anesthesia involvement is limited and there is little time to recognize all but the most serious of complications before the patient is dismissed home. Further, the ambulatory surgical center has limited resources for evaluating a postanesthetic complication. Patients with serious complications will be managed by stabilizing the patient and transferring to a higher acuity level of services for further testing, consultation, treatment, or observation. Patients who are recognized to have milder signs and symptoms before dismissal require coordinated follow-up arranged to address neurologic, rehabilitative, and pain needs; and the ambulatory care center should have a pathway to facilitate these timely outpatient referrals. However, many patients will be dismissed before neurologic symptoms are recognized. Assuring that patients have written information on potential anesthesia complications pertinent to their care and anesthesia contact information may facilitate the patient directly contacting the anesthesia care team, but most patients will contact their surgeon once symptoms are recognized, leaving the anesthesiologist unaware of a problem.

Notably, some barriers to timely recognition of perioperative nerve injury also limit the neurologic or neurosurgical clinical evaluation of a recognized injury. Postoperative activity restrictions, dressings, drains, and casting limit the ability to complete a comprehensive neurologic examination, making deficit localization challenging. Finally, many neurologists are unfamiliar with surgical or regional anesthetic techniques and may not, therefore, know which structures were most immediately at risk procedurally. Useful neurologic consultation will be facilitated by direct and candid communication between the proceduralist and neurologic specialists.

Mechanisms of Injury

The potential mechanisms of anesthesia-related neurologic injury have been previously articulated[12]; however, the mechanism of injury is pertinent to workup and prognosis. Documentation and recognition of preexisting neurologic disease is important, as it may explain falsely localizing neurologic signs evident during the assessment of an apparent postoperative nerve injury. For example, hyperreflexia and a Babinski sign from preexisting cervical spinal stenosis may falsely suggest a central nervous system etiology in a patient with a PNI. Preexisting neurologic disease or nerve injury, although sometimes insufficient alone to cause clinical symptoms, limits the neurologic reserve of a nerve, meaning that it is more susceptible to develop clinical deficits from a second injury (the double crush syndrome). The double crush principle was initially proposed to indicate that a patient with a mechanical nerve root compression (cervical radiculopathy) is more susceptible to developing signs and symptoms from a second site of compression (classically carpal tunnel syndrome).[13,14] Animal models of acute[15,16] and chronic[17] nerve compression have demonstrated that nerves affected by 2 sites of compression function more poorly, as assessed electrophysiologically, than nerves with a single site of compression or than would be anticipated by simple additive damage caused by each isolated compression.[14,18] The principle has evolved to recognize that systemic metabolic processes, such as diabetes, impair nerve function diffusely long before patients develop clinical symptoms (peripheral neuropathy) and that patients with these systemic metabolic processes are more prone to become symptomatic from additional insults to the nerve such as compression of the median nerve at the wrist (carpal tunnel syndrome). This has been shown in an animal model.[19] It has also been long-recognized that patients with diabetes have a higher incidence of carpal tunnel syndrome than nondiabetic patients[20] and diabetes is noted to be a risk factor for postanesthetic PNI.[5] The double crush syndrome has been proposed to contribute to the risk of PNI in a patient receiving cisplatin chemotherapy[21] and may explain an increased risk of neurologic complications with neuraxial anesthesia in patients with preexisting peripheral neuropathy.[22] Preexisting systemic diseases associated with neurogenic impairment (eg, diabetes with neuropathy) likely also impair the potential for recovery after a PNI.

Vascular injuries that cause ischemia or bleeding sufficient to cause cord or nerve compression can be one of the most catastrophic of postanesthesia neurologic complications. Ischemic vascular injuries may be related to an embolic phenomenon, direct trauma, or vasoconstriction of the artery of Adamkiewicz, causing an anterior spinal cord artery syndrome (ASAS) or from watershed ischemia related to hypotension or vasoconstriction.[12] Hematoma formation is critical to recognize, as it is treatable, but devastating if unrecognized. Anticoagulation or bleeding diatheses predispose to hematoma risk and consensus recommendations exist for antiplatelet and anticoagulation use in the setting of regional anesthesia.[2]

Infectious processes can cause neurologic impairment from diffuse involvement (meningitis or a polyradiculopathy) or from abscess formation and compression (epidural abscess).

Mechanical injury (spinal cord or peripheral nerve) from needle or catheter trauma, direct local anesthetic toxicity, or surgical trauma is variable in its severity and prognosis. Although early recognition and intervention can improve the outcome for perioperative nerve injuries from some vascular, infectious, and inflammatory etiologies, there is little that can be done to intervene on or improve on the likelihood of recovery after mechanical injury or direct local anesthetic toxicity.

Some PNIs are unrelated to the anesthetic or surgical intervention, although the anesthesiologist and/or surgeon are often erroneously blamed. For example, there would be appropriate concern for a neuraxial complication in a patient with an epidural catheter who awoke with a foot drop, but careful evaluation may show a simple peroneal compressive neuropathy at the fibular head unrelated to the epidural catheter. Additionally, although compressive neuropathies can occur in the operative theater, they

commonly occur during the postoperative hospitalization.[11] Similarly, there has been increasing recognition that some postsurgical neuropathies are related to an inappropriate inflammatory response directed at the peripheral nervous system.[23] These are important to recognize as they are unrelated to a specific anesthetic or surgical intervention and are potentially treatable.

Neuraxial Complications

Neuraxial complications from anesthetic techniques or pain procedures are rare, but potentially catastrophic. Acute SCI may be heralded by pain at the level of injury and a sensory level. Strength and reflexes are more variable acutely. Lower extremity weakness is often initially diffuse, reflexes absent, and tone flaccid (spinal shock). After neuraxial injury, over time, lower extremity extensor muscles develop increased tone and spasticity (to a much greater degree than the flexor muscles) as a compensatory part of recovery causing the characteristic upper motor neuron pattern of weakness (hip flexor, knee flexor, and foot dorsiflexor weakness, sparing other muscles in the lower extremity), hyperreflexia, Babinski sign (upgoing great toe with stimulation of the sole of the foot), and spasticity classically seen with central nervous system injury. The longer it takes to diagnose and treat a neuraxial complication, the worse the prognosis.[24–27] As such, regardless of pattern, any neurologic complication at or below the level of a recently performed neuraxial anesthetic or pain intervention should be evaluated emergently with imaging (Fig. 1).

Magnetic resonance imaging (MRI) is the preferred imaging modality, as it provides excellent soft tissue differentiation, localizes the catheter and the extent of the pathology within the neuraxis, and will also pick up any pertinent preexisting comorbidities (such as spinal stenosis).[28–31] If an MRI is not immediately available or is contraindicated, then a computed tomographic (CT) scan is acceptable and should be performed urgently. Although CT lacks the sensitivity and discriminatory ability of MRI, it should be sufficient to pick up processes amenable to intervention, such as a space-occupying lesion (hematoma or abscess).[32] Computed tomography may miss intrinsic cord processes (edema from direct cord trauma, syrinx from intramedullary injection, cord ischemia, or unrelated intrinsic cord processes). As such, if an emergent initial CT is negative in the setting of significant neurologic deficits thought potentially related to neuraxial anesthesia or pain intervention, MRI should be arranged for as soon as possible, even if it requires transfer to a facility with more immediate access to spine MRI.

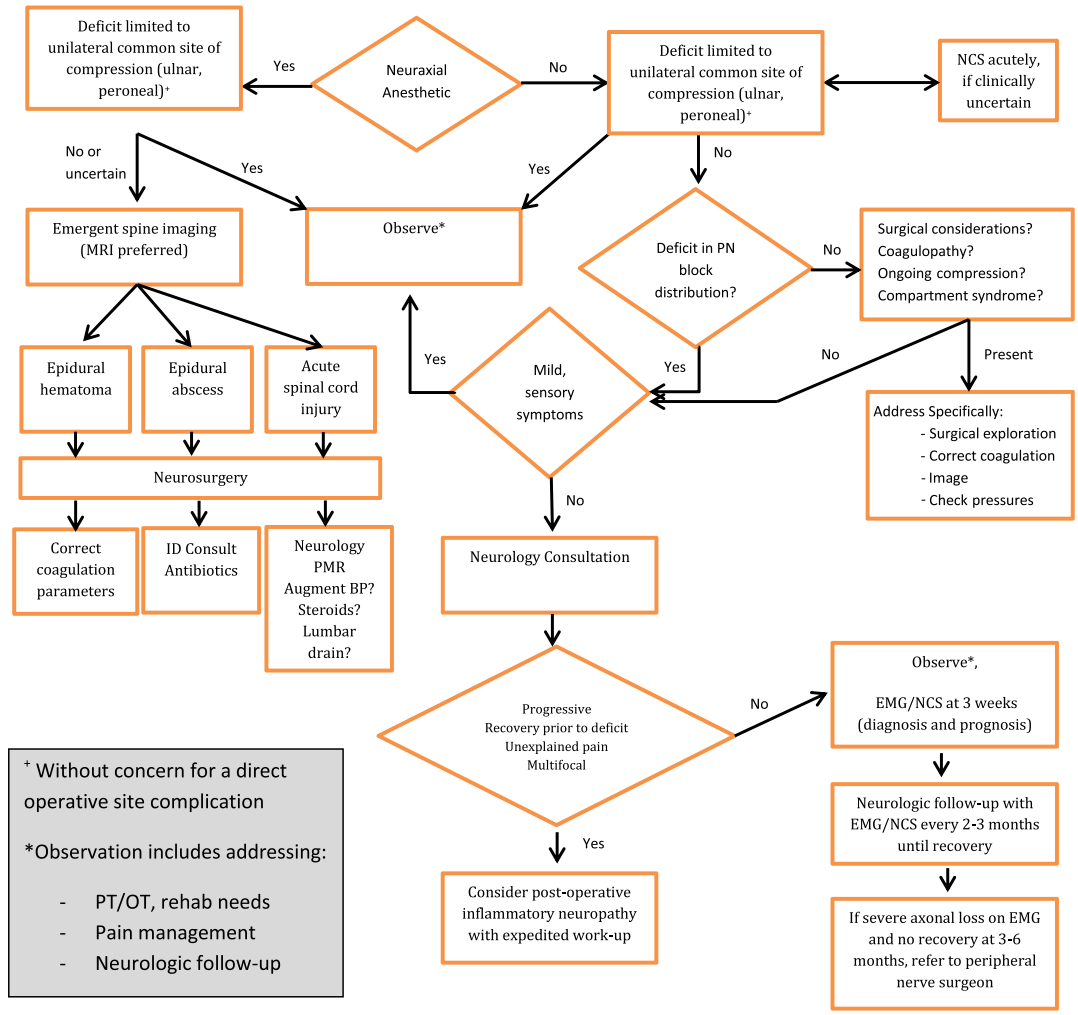

FIGURE 1. Approach to perioperative nerve injury. BP, blood pressure; EMG, electromyography; NCS, nerve conduction studies; PMR, physical medicine rehabilitation specialty consultation; PN, peripheral nerve.

Specific Syndromes

Epidural Hematoma

Epidural hematoma after epidural or spinal anesthesia is rare; however, it can be neurologically devastating.[33–35] Risk factors include anticoagulation (most common), antiplatelet usage, bleeding diathesis, technically challenging epidural or spinal anesthesia, an emergency operation, orthopedic surgery, lumbar stenosis, failure to follow established guidelines, female sex, and older age.[25,33,36,37] Bleeding risk is highest at the time of neuraxial insertion and epidural catheter removal. The risk of epidural hematoma is significantly lower in obstetric compared to perioperative epidurals.[37] For epidural hematoma from any cause, neuraxial anesthesia with anticoagulation or antiplatelets is the fifth most common cause and neuraxial anesthesia without anticoagulation is the tenth most common cause.[25] Epidural hematoma is more commonly idiopathic, anticoagulation-related, or a local complication from spine surgery than from neuraxial anesthesia.[25] Most epidural hematomas occur in the dorsal epidural space at the thoracolumbar junction when associated with anesthesia.

Clinically, patients present with a severe, sharp pain at the level of the bleed, which may be missed in the setting of anesthesia or postoperative analgesia. The pain is usually localized to the neuraxis, but if the hematoma is large enough to compress the exiting spinal roots, radicular irritation may be seen. Axial pain in the postoperative setting must be differentiated from chronic preoperative back pain issues. There may be an intervening pain-free interval (minutes to days), followed by progressive sensory dysfunction and flaccid paralysis below the injury. Bowel and bladder dysfunction is a late complication and occurs in two thirds of patients with epidural hematoma. Those patients with epidural hematoma related to neuraxial anesthesia complications usually present more fulminantly (75% present with deficits maximizing over 24 hours) than nonanesthesia-related cases.[25] Subarachnoid blood may accompany epidural hematoma causing postoperative headache, intractable nausea and vomiting, decreased levels of consciousness, confusion, or seizure.

Magnetic resonance imaging shows T1 imaging isointensity and T2 imaging hyperintensity changes of the epidural hematoma acutely and T1- andT2-weighted imaging hyperintensity in the subacute phase.[38,39] The treatment is immediate reversal of anticoagulation, correction of coagulation parameters, and neurosurgical evaluation. Most patients will require surgical evacuation. Epidural hematoma is a neurosurgical emergency. In a meta-analysis of 613 patients with epidural hematoma from any cause, 5.5% died due to the consequences of the spinal hematoma.[25] Of those evacuated within 8 to 12 hours, 40% to 66% make a complete recovery; whereas when evacuation occurs longer than 12 hours after presentation, more than half of patients are left with no improvement or severe residual neurologic deficits.[24,25,36] The severity of the neurologic deficit at the time of evacuation also affects prognosis with more severe deficits at evacuation having a lower likelihood of a good recovery.[24,33]

Spinal Epidural Abscess/Meningitis

Infectious complication rates of neuraxial anesthesia have generally been from 1 in 40,000 to 1 in 100,000 neuraxial anesthetics.[3,4,40–42] One study suggested a much higher incidence of SEA with a rate of 1 in 1930 epidural catheters, although the median time of catheterization (6 days) was long. Risk factors include diabetes, immunosuppression, systemic cancer, preexisting infection, intravenous drug abuse, alcoholism, or trauma.[43,44] In a series of all patients with SEA (n = 915), 22% had a spinal intervention preceding and 5.5% had a neuraxial anesthetic preceding.[27] The infectious risk with in situ neuraxial catheters increases with time.[43]

Relative to epidural hematoma, which tends to present more fulminantly, SEA presents later (usually days after the neuraxis was accessed) and often more insidiously. Clinically, two thirds of patients with SEA present with localized spinal pain and fever. As with epidural hematoma, if the SEA compresses adjacent spinal roots, radicular pain may be described. Serologic inflammatory markers may be increased, but not universally so, especially in those who are immunosuppressed. This is followed by radicular irritation, then progressive neurologic deficits below the SEA, progressing to paralysis in approximately one third of patients. Patients may alternatively present with a meningitis picture, with fever, headache, confusion, sedation, nuchal rigidity, and seizure, but without localizing features.

Magnetic resonance imaging is the diagnostic test of choice for SEA.[43] Lumbar puncture for cerebrospinal fluid (CSF) evaluation is not necessary for the diagnosis of SEA and risks causing spread to the leptomeninges and meningitis. If meningitis is suspected without SEA, CSF is necessary for diagnosis but should occur only after excluding a local abscess at the catheter site. Most SEAs are in the thoracic or lumbar spine. Treatment is emergent, and requires neurosurgical and infectious disease consultation along with the initiation of antibiotics. The surgical evacuation decision is based on the nature of the neurologic deficit, the duration neurologic deficits have been present, abscess size and location, and patient comorbidities. There are reports of percutaneous drainage,[45,46] but surgical evacuation is generally preferred, particularly in any case with neurologic deficits or cord compression. Mortality is 15% with SEA (whether spontaneous or iatrogenic). Functional recovery is significantly improved in those treated definitively before paralysis or in those with paralysis less than 36 hours. Patients with paralysis greater than 48 hours at the time of evacuation are unlikely to recover.[27,44] It has been said that the primary issue with SEA is not treatment, but early diagnosis before the development of severe neurologic deficits.[26,27] Of all patients with anesthesia-related SEA, 38% recover completely neurologically and 27% remain paralyzed (compared with 43% and 15% of those with spontaneous SEA, respectively).[27]

Anterior Spinal Artery Syndrome

Anterior spinal artery syndrome can occur from spinal cord ischemia in the anterior spinal artery distribution from embolization of atherosclerotic plaque, particulate steroid, or vertebroplasty cement; mechanical or drug-induced vasospasm; dissection; or direct trauma to the artery of Adamkiewicz in the thoracolumbar spine or to the ascending or deep cervical arteries in the cervical spine.[12,47–51] These vascular supplies are particularly at risk with transforaminal epidural steroid injections,[52–55] although they could be conceivably damaged with paraspinal procedures (paravertebral or celiac plexus blocks) or unintentional lateral needle placement during an interlaminar neuraxial procedure.[12]

Clinically, three quarters of patients present acutely with pain at the level of the cord infarct with bilateral radicular pattern radiation, progressing rapidly to flaccid paraplegia or tetraplegia.[56] Because the anterior spinal artery supplies the anterior two thirds of the spinal cord, the most obvious clinic deficits are the paraplegia or tetraplegia. On examination, sensory deficits are limited to pain and temperature modalities (spinothalamic tracts) as the posterior columns are relatively spared. Reflexes will eventually increase, but may be reduced in the hyperacute phase (spinal shock).

Magnetic resonance imaging demonstrates a well-demarcated lesion within the anterior two thirds of the spinal cord bilaterally, with increased T2 signal intensity and abnormalities on diffusion-weighted imaging indicating acute ischemia.[56–58] Importantly, there are older reports of early MRI missing acute cord ischemia.[59,60] As such, an MRI may need to be repeated in 24 to 48 hours if the initial

scan was unrevealing and was performed hyperacutely or without diffusion-weighted imaging.

There is no proven treatment for ASAS and the prognosis is dire. For those who survive, quality of life is often adversely affected by neurogenic bowel and bladder and mobility issues requiring gait aides or a wheelchair.[56,61] Sixty percent of those affected do not improve, minimally improve, or die (23% mortality during hospitalization).[59,61] In a broader spinal cord stroke cohort, in the ASAS subgroup, no patient made a complete recovery.[56]

Direct Cord Trauma

Risk factors for direct cord trauma include anatomic variance (low-lying conus), inaccurate determination of vertebral interspace, incomplete midline fusion of the ligamentum flavum (ie, no loss-of-resistance), or more cephalad blocks (decreasing anterior to posterior diameter of the epidural space).[12] Patients present with pain or paresthesias with injection into the cord due to increased intramedullary pressure and potentially may have pain from needle trauma to the cord without injection. However, needle insertion into the cord without injection may not be painful and paresthesias are not uncommon with properly performed epidural anesthetics, so direct cord trauma may be challenging to recognize during the procedure.[62] The injury type (and prognosis) is variable depending on the site of injury and whether an injection was performed (which will affect the extent of the injury). Clinical signs and symptoms may be unilateral or bilateral depending on where the cord was damaged. Depending on the extent of the damage, it may cause radicular symptoms at the level of the injury, or in more severe cases, cause signs and symptoms of a myelopathy (sensory level, lower limb weakness, or bowel and bladder dysfunction). If a patient has persistent paresthesias only, observation is reasonable, especially if they are unilateral, dermatomal, mild, and/or improving. More serious or widespread sensory and any motor deficit deserves imaging and neurologic evaluation. Magnetic resonance imaging is useful to confirm a SCI and define its extent. Spinal cord edema may be evident at the site of the injury. Recent ASA closed-claims data suggest that these types of direct cord injuries are most prevalent in the cervical spine, often occur in younger patients, and possibly result in major morbidity or mortality.[63]

Role of Other Interventions in the Setting of Neuraxial Injury

Corticosteroids are frequently used in the setting of acute traumatic SCI. A Cochrane review concluded that methylprednisolone given at a dosage of 30 mg/kg over 15 minutes within 8 hours of the injury, with a maintenance infusion of 5.4 mg/kg/h for an additional 23 hours (or a total of 48 hours if the bolus was greater than 3 hours after the injury) improved motor outcomes up to 1 year postinjury.[64–66] Although this is commonly practiced, others question the validity of the results or that it has a benign adverse effect profile and thus conclude that the evidence is insufficient to recommend as a standard guideline.[67–70] Neuraxial anesthetic complications are too rare to study the role of corticosteroids systematically. Steroids are commonly given intraoperatively empirically in the setting of presumed neurologic injury with variable dosing, but the role in neuraxial anesthetic complications is unknown. The reported role of steroids in traumatic SCI has been shown to be effective only in the acute phase (within 8 hours of the injury), but when related to an anesthetic complication, the diagnosis of a cord injury is sometimes delayed postoperatively. Finally, the risk profile of steroids in the postoperative period is unknown and is likely higher than in the posttraumatic setting in terms of infection risk and a potential adverse effect on wound healing. Although the role of corticosteroids in postsurgical neuraxial complications is unknown, it is widely used in other causes of SCI and could be considered if the associated risks are acceptable.

Lumbar drains may increase the perfusion pressure to the spinal cord via CSF drainage and hence decrease the risk of spinal cord ischemia. Lumbar drains are routinely used for open and endovascular surgery on the thoracic aorta (accompanied by blood pressure augmentation in the setting of neurologic deficits). A Cochrane review concluded that the data, albeit limited, support their role.[71–73] There is a case report of neurologic improvement with a lumbar drain in a spinal ischemic syndrome after aortic dissection[74] and a small prospective trial in acute SCI found it to be safe, but the study was inadequately powered to assess efficacy.[75] Although there may be a rationale to consider in the setting of postinterventional ASAS, there are no known reported cases of postinterventional ASAS treated with a lumbar drain.

Peripheral Nerve Injury

Significant barriers to identification of PNIs exist (Table 1). There are also multiple risk factors for PNI in the setting of regional anesthesia (Table 2).

In a patient with a suspected PNI, the first question is whether there is ongoing process causing the neurologic impairment (Fig. 1). Similar to neuraxial procedures, anticoagulation or bleeding tendencies can be associated with PNI, including retroperitoneal hematoma causing a lumbosacral plexopathy or a perineural hematoma affecting an individual nerve. When bleeding complications are considered, they require urgent imaging (CT or ultrasound), reversal of anticoagulation, and possibly evacuation if severe. Likewise, compartment syndrome may be appropriately considered.

It is also important to consider whether a PNI could be surgically related. Candid discussion with the surgical staff regarding the possibilities of nerve transection, whether excessive traction was required during the surgery; if there were any concerns regarding suspicious sutures, clips, or instrumentation placed intraoperatively; or whether there were concerns from vascular, hemodynamic, or electrophysiologic monitoring during the case. If so, a severe postoperative PNI may require surgical exploration. Of peripheral nerve explorations, 17.4% are for iatrogenically induced neuropathies, and 94% of iatrogenic nerve injuries that are operated on were originally injured intraoperatively.[76] In a study of 1614 axillary blocks, surgical variables were thought to be responsible for 89% of the identified neurologic complications, with most being from direct trauma or stretch.[77]

The next priority is to localize the deficit from the PNI and determine if they are in a distribution concordant or distinct from the site of surgery or anesthesia. If the deficits are consistent with a mononeuropathy at a common site of compression (eg, ulnar

TABLE 2. Risk Factors Associated With Perioperative PNI

Patient Characteristics	Perioperative Characteristics
• Preexisting neurologic disease*	• Paresthesia with needle placement
• Diabetes*	• Pain with injection
• Smoker	• Prolonged tourniquet time
• Body mass index extremes	• Positioning—compression or stretch
• Male	• Sedated patient during regional block
• Elderly	• Hypothermia
	• Prolonged hospitalization

*Double crush syndrome.

nerve at the elbow, peroneal nerve at the fibular head), observation is usually appropriate. If this is suspected, but uncertain, nerve conduction studies can be useful acutely to confirm conduction block at the site of compression. Localization is also important as PNIs are frequently in a distinct distribution from where the peripheral nerve block was performed.[7,8,10] This may exonerate the anesthesiologist, but still requires appropriate evaluation and follow-up. If the deficits (persisting beyond the duration of the local anesthetic) are within the distribution of the peripheral nerve (s) blockade and the symptoms are purely sensory (two thirds of PNIs), observation is appropriate because most of these will resolve over days to weeks.[5,78–80] If symptoms persist beyond this, neurologic consultation is appropriate at the time of outpatient follow-up.

In the rare situation in which patients are recognized to have functionally limiting deficits, severe weakness or sensory loss, progressive deficits, or difficult-to-localize neurologic impairment (Table 3), neurologic consultation is appropriate early (in hospital or as an urgent outpatient evaluation if recognized in an ambulatory surgical center and the patient is felt safe to go home). The goal of early neurologic assessment is to identify treatable etiologies (hematoma, inflammatory) or alternative, nonsurgical or anesthesia-related processes that may have a distinct treatment algorithm (such as stroke or conversion disorder).

Postsurgical Inflammatory Neuropathies

There is a growing recognition of the importance of inflammatory causes of postsurgical neuropathies that are unrelated to the anesthetic or surgical technique.[23,81] The classic features for acute inflammatory neuropathies such as Parsonage-Turner syndrome (idiopathic brachial plexopathy),[82] diabetic or nondiabetic lumbosacral radiculoplexus neuropathies,[83] or postsurgical inflammatory neuropathies[23] include severe pain hours to weeks (up to 30 days) after a stressor (anesthesia or surgery for this discussion) that is distinct from that expected perioperatively. Perioperative sedation and analgesia may make early onset cases challenging to recognize. A return to neurologic baseline after surgery, before onset makes this process more readily recognizable, but cannot be defined in many postoperative cases. As the pain spontaneously improves, weakness becomes apparent (electrodiagnostically involvement includes regions beyond those with clinical symptoms). Most commonly, weakness is multifocal or diffuse; however, focal postoperative neuropathies have been reported as well. Most of the reported inflammatory postoperative neuropathies are in distributions distinct from the surgery or regional anesthetic; however, although it is more challenging to define, an inflammatory etiology remains possible within these territories especially if the temporal onset cues, pain history, and ancillary testing (electrodiagnostics, MRI of the plexus, or peripheral nerve) are suggestive. Although systemic inflammation is expected after surgery, the reasons why nonoperated nerves are susceptible to developing localized inflammation and ischemia is unknown. Biopsy of postoperative cases demonstrates perivascular lymphocytic inflammation consistent with a microvasculitis.[23] This causes significant axonal loss and is associated with a protracted recovery. However, the prognosis is generally good as this is usually a monophasic process (90% recovery by 3 years in Parsonage-Turner syndrome).[82] Patients with a multifocal or difficult to localize postoperative deficit, associated severe pain disproportionate to the expected perioperative course, progressive deficits, or deficits developing after a period of documented return to neurologic baseline should be evaluated for the possibility of a postoperative inflammatory neuropathy with early neurologic consultation. Corticosteroid therapy in these cases is unproven as the postoperative inflammatory neuropathy spectrum has yet to be fully elucidated, but is mechanistically rational based on a microvasculitic pathology and commonly practiced.

TABLE 3. Indications for Early Neurologic Consultation for PNI

If neurologic deficits are as follows:

- Severe
- Functionally limiting
- Progressive
- Multifocal or difficult to localize
- Unexplained neurologic impairment outside the block region or region of common compression
- Associated with severe pain (disproportionate to typical postoperative course)
- Associated with an intervening return to neurologic baseline after surgery before development of PNI

Role of Electrophysiology

The role of electrodiagnostic studies (nerve conduction studies and electromyography) in the setting of PNI is to confirm the suspected neurogenic process, localize it, exclude mimickers (eg, radiculopathy or brachial plexopathy mimicking an ulnar neuropathy), identify subclinical disease, confirm conduction block or focal slowing for mononeuropathies at common sites of compression, and to define the degree of axonal loss (pertinent to expected recovery time).[84–86] Most nerve injuries are related to compression or transient dysfunction of myelin in a focal area of nerve (neurapraxia), which can be identified with nerve conduction studies acutely as conduction block or focal slowing. Sensory nerves are more susceptible to injury. Clinically, patients with predominant sensory symptoms and/or evidence of conduction block or focal slowing on electrodiagnostic studies have an excellent prognosis with expected complete recovery within 3 months.[3,80,84,85] When there is more severe nerve injury damaging the axons, it becomes important to differentiate whether the injury is only to the axon (axonotmesis) or whether connective tissue strata around the axon (the neural tube) has been damaged as well (neurotmesis) such as in transection. Peripheral nerve axons will regenerate if the neural tube is intact (axonotmesis), but not in neurotmesis. Electrodiagnostic studies cannot differentiate these 2 possibilities with a single study. However, in axonotmesis, serial studies performed every 2 to 3 months will show axonal regeneration and reinnervation into muscles adjacent to the area of injury initially and proceeding distally with time. Electrodiagnostic evidence of axonal recovery will precede clinical motor improvement. In cases of more severe injury (neurotmesis), no recovery will be seen on serial studies (Table 4). As soon as a lesion is judged to have insufficient potential for spontaneous recovery (no evidence of axonal regeneration on serial studies), patients should be referred to a peripheral nerve neurosurgeon for surgical options. Neurologic functional outcome is improved if surgical intervention occurs no later than 6 to 9 months from the time of injury.[76,84,87]

The role of electrodiagnostic studies is limited in the acute perioperative period. Although evidence of neurapraxia (conduction block or focal slowing) can be identified acutely, axonal damage is not definitively evident until Wallerian degeneration has occurred and there has been muscle denervation (up to 3 weeks from the time of injury). As such, electrodiagnostics in the acute perioperative period are limited in utility to confirming neurapraxia at a common site of compression and defining preexisting neurologic disease. Outside these indications, electrodiagnostic studies will be more useful when performed 14 to 21 days after the nerve injury to localize the injury and define its severity and

TABLE 4. Temporal EMG Findings for Types of Nerve Injury

	Pathology	Able to Be First Identified	Nerve Conduction Study Findings	Earliest Electromyography Findings	Serial Study Findings
Neurapraxia	Localized myelin dysfunction	Acutely	Conduction block, focal slowing	Reduced recruitment MUPs	Usually full recovery
Axonotmesis	Axonal damage with intact neural tube	3 wk after injury	Low amplitude or absent responses	Fibrillations, reduced recruitment of large, complex MUPs; if severe—no activation in first weeks/months after injury	Reinnervation
Neurotmesis	Axonal and neural tube damage	3 wk after injury	Absent responses	Fibrillations, no activation MUPs	No reinnervation

MUP indicates motor unit potential.

prognosis.[84–86,88] Importantly, although electrodiagnostics localize a lesion, they do note elucidate the cause of the injury.

Symptom Management

Unfortunately, once an active process has been excluded (vascular, compressive, inflammatory), there is nothing that can be done to significantly improve the neurologic outcome (ie, nerve function) for a postsurgical nerve injury (central or peripheral). However, patient education, expectations, pain, and functional assistance through physical and occupational therapy can be managed while assuring appropriate neurologic follow-up is in place. Directly addressing injuries openly and proactively addressing symptom management may positively influence patient attitudes toward a postsurgical injury with medicolegal implications.

Initiation of rehabilitation in a dedicated SCI rehabilitation center within 30 days of acute trauma leads to improved functional outcomes in spinal cord–injured patients.[89]

Neuropathic Pain Management in the Pain Clinic

The role of the multidisciplinary pain clinic physician(s) and staff in managing neurological injuries is essentially that of both detective and counselor. In academic settings, it is possible that some written (electronic or print medical record) or oral communication between the operating surgeon, regional anesthesia/acute pain team, and pain clinic has occurred, but this may be less likely between private practitioners at small to regional sized medical centers. Patients may have had very little communication as to why they have motor/sensory deficits and pain by the time they reach the outpatient pain clinic. Patient expectations of full functional recovery are often high, and the true extent of neurological injury may have been underestimated by the practitioners involved in providing care. Consider the example of a patient who had received a popliteal sciatic nerve catheter placement for anesthesia and analgesia before an ankle surgery using intraoperative tourniquet. When the patient develops foot drop, loss of foot eversion, and signs and symptoms of CRPS with severe allodynia, edema, hyperhidrosis, and lost functionality, the patient rightfully will want to understand why. Obviously, the cause may still be unclear, and multiple rational differential diagnoses include (1) the use of a regional technique causing nerve injury; (2) local anesthetic or adjuvant drug toxicity; (3) tourniquet compression/ischemia; (4) surgical factors; (5) patient premorbid factors; and (6) idiopathic factors, for example, inflammatory neuropathy. More often than not, the patients have been advised that these are likely temporary effects that will go away with time. A thorough pain clinic evaluation that includes neurological, musculoskeletal, general system, and psychological examinations is mandatory, as is an equally thorough history and review of systems (Table 5). Neurodiagnostic evaluations are now appropriate, if not already done, to stage the extent of injury, and also to try to pinpoint the location. In the present example, if the electromyography demonstrated that the injury occurred at the level of the sciatic bifurcation, it would be far more likely attributable to the regional block than to the tourniquet-induced ischemia or a direct surgical injury. The results of these diagnostic tests should be carefully conveyed to the patient, while also discussing them with the providers involved. The manner in which these communications are handled is critical, not only therapeutically for patients, but medicolegally for risk avoidance, and also for future relationships with referring physicians. The patient, at this time, should begin a complete algorithm of potential therapies for the condition and be assured that the pain clinic will see those therapies through to their logical conclusion.

Chronic Persistent Postsurgical Pain

Perkins and Kehlet[90] outlined the problem of persistent postsurgical pain several years ago. Since that time, the emphasis has shifted to use strategies that may mitigate the long-term problem of persistent pain. Efforts have centered on ways to improve our research strategies,[91] and to find ways to predict which patients are at risk.[92] A growing number of cancer survivors have various pain syndromes such as postmastectomy pain (intercostobrachial nerve), postthoracotomy (intercostal nerve), and post amputation (phantom/stump) pain among many others. In some studies, procedural therapies seemed to help prevent the development of persistent pain. One example is the use of paravertebral blocks for breast cancer surgeries.[93] There are also some studies suggesting that the perioperative use of medications may be preventative to future development of chronic pain. Pregabalin has been evaluated

TABLE 5. Indications for Early Pain Clinic Consultation for PNI

If pain is one of the following:

- Severe
- Functionally limiting
- Progressive
- Multifocal or difficult to localize (may indicate comorbidity such as anxiety, or CRPS)
- Unexplained neurologic impairment outside the block region or region of common compression; eg, CRPS
- Associated with severe pain (disproportionate to typical postoperative course)
- Associated with allodynia, edema, hyperhidrosis, uninvolved extremity
- Failure to respond to step 1 and 2 therapies
- Increasing or problematic opioid escalations

for perioperative prevention of pain after total knee arthroplasty. In the study by Buvanendran and colleagues,[94] a relatively large dose (300 mg) of pregabalin was used for 3 weeks beginning immediately preoperatively with long-term outcomes demonstrating reduction in postoperative (as well as chronic) pain. In other studies,[95] a single 600-mg dose of gabapentin before thoracotomy in the setting of good multimodal therapy including thoracic epidural infusions and PCA opioids had no effect on the future presentation of persistent pain.

These neuropathic pain syndromes may arise in the setting of concomitant regional anesthetic techniques, thus clouding the differential diagnosis.

Evidence-Based Pharmacologic Treatment of Neuropathic Pain

Regardless of the etiology, all patients who present to the pain clinic with postsurgical neuropathic pain should have treatment initiated using an evidence-based guideline for oral and topical medications. Several groups have assembled these algorithms for the treatment of chronic neuropathic pain. These include the International Association for the Treatment of Pain and their Neuropathic Pain Special Interest Group,[96,97] and the European Federation of Neurological Societies.[98] These guidelines have also been compared in publications.[99] It must be emphasized that many of the prospective, blinded, randomized studies that form the basis for these recommendations were performed in painful diabetic neuropathy or postherpetic neuralgia populations, and therefore may not be generalizable to PNIs from other causes. All of the guidelines are similar, and essentially follow a tiered approach progressing from first-line single agents, to multiple first-line agents, followed by use of second- and third-line agents when patients are not achieving care goals. First-line agents include secondary amines from the tricyclic antidepressant class (nortriptyline, desipramine) or selective serotonin-norepinephrine reuptake inhibitors (duloxetine), anticonvulsant agents acting at the α-2-δ ligand neuronal calcium channel (gabapentin and pregabalin), and topical 5% lidocaine. Opioids such as oxycodone or combination agents such as tramadol or tapentadol may be used either as second-line or sometimes first-line agents as well (Table 6, adapted from Dworkin et al[96,97] with permission). Third-line agents have much lower quality studies, contradictory evidence from well-designed trials, or other shortcomings. These agents should only be used when first- and second-line agents have failed.

TABLE 6. Management of Neuropathic Pain

Step 1

Assess pain, establish cause and probable neuropathic mechanism, and identify comorbidities

Step 2

Initiate therapy with first-line agent:

- Secondary amine tricyclic antidepressant (nortriptyline, desipramine)
- Calcium channel α2-δ ligand (gabapentin, pregabalin)
- Topical lidocaine for localized peripheral neuropathic conditions, alone or combined with other primary agents
- Nonpharmacologic therapies, when indicated
- Opioid analgesics may be used, generally in combination

Step 3

- Reassess and continue if efficacious
- Consider addition of other first line agents or combinations for partial/incomplete responders

Step 4

- Consider referral to specialty pain clinic or neurological subspecialist if ongoing poor response

Modified from Dworkin et al[96,97] with permission. Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

TABLE 7. Summary Recommendations—Diagnosis

- In the setting of neuraxial anesthesia, any concern of spinal cord dysfunction requires emergent neuroimaging (Level I).
- MRI is the preferred imaging modality. However, imaging should not be delayed to arrange MRI or to get neurologic consultation. CT or CT myelography are acceptable as initial imaging to exclude a compressive lesion (Level I).
- Diagnosis of a compressive lesion (epidural hematoma or SEA) within or near the neuraxis demands emergent neurosurgical consultation for consideration of decompression (Level I).
- Neurologic consultation is recommended for complete nerve injuries (complete absence of nerve function), incomplete injuries with moderate to severe functional limitations, or progressive neurologic dysfunction (Level I).
- An inflammatory postsurgical neuropathy should be considered if there are multifocal, progressive deficits, unexplained excessive pain despite standard perioperative analgesia, and neurologic deficits developing after a period of return to neurologic baseline postoperatively. Neurologic consultation should be considered (Level II).
- Electrodiagnostic studies (EMG and nerve conduction studies) may help confirm neurapraxia with conduction block or define preexisting disease when performed acutely. Axonal loss (prognostic) and the extent of a perioperative neurogenic injury will be better clarified by electrodiagnostic studies performed 3 wk after injury (Level I).

Procedural Therapies for Neuropathic Pain

Patients with postoperative nerve injuries and neuropathic pain may be understandably reticent to have a nerve or plexus "blocked" again when they may attribute causation to the original anesthetic procedure or surgery. In some cases, however, there may be either diagnostic or therapeutic indications for pain interventions. In a study of 520 patients who received interscalene brachial plexus blocks or catheters, there were a total of 41 and 20 patients at 1 and 3 months, respectively (nonacute), who had ongoing pain or paresthesias not felt to be related to the surgery. Of these, 8 were diagnosed as sulcus ulnaris syndromes, 5 CRPS, 4 carpal tunnel syndromes, and 1 each with plexus neuropathy and severe plexus neurological damage. The authors do not state what types of treatments were provided to these patients, but clearly medical, procedural, and surgical treatments may have been used.[78] In particular, one would consider a diagnostic/therapeutic stellate ganglion block to be a reasonable procedure in the cases of CRPS, and it is also possible that ulnar or median nerve blocks could have been used in these cases. Two notable concepts may be inferred from this study: (1) this 1- to 3-month period would coincide well with likely times for pain clinic referrals after a perioperative injury; and (2) all but one of these patients (brachial plexus injury) had improved by 9 months' time, suggesting that the combination of healing time and specific therapies had been effective. Medical therapies used for persistent neuropathic pain might also have included physiotherapy and pharmaceutical therapies. In this study, it is unlikely that the cases

TABLE 8. Summary Recommendations—Treatment

- Outcomes for compressive lesions (epidural hematoma or SEA) are dependent on the severity of neurologic impairment and the duration of symptoms at the time of neurosurgical decompression. Neurologic recovery is improved with early decompression (<8–12 h from symptom onset in epidural hematoma and <36 h from symptom onset for SEA) and with milder preoperative neurologic deficits (Level I).
- Neuropathic pain is reasonably treated pharmacologically with step 1 and 2 agents from Table 6 (Level I).
- Functional deficits from neurological injuries should be rehabilitated in concert with rehabilitation specialists (Level II).
- Nerve lesions that fail to resolve 3 to 5 months after initial neurologic evaluation should prompt consideration of consultation with a peripheral nerve neurosurgeon (Level II).
- The role of corticosteroids in postoperative neuraxial complications is unknown, but widely used in other causes of SCI and could be considered if the associated risks are acceptable (Level III).
- The role of lumbar drains in postoperative/interventional pain spinal cord ischemia is unknown, but widely used to treat surgical spine ischemia and seems safe in the setting of SCI (Level III).

of sulcus ulnaris (cubital tunnel) or carpal tunnel had anything to do with the nerve block therapy. Other reports[100] have described the occurrence of idiopathic brachial neuritis (Parsonage-Turner syndrome) after brachial plexus block. This condition might lead to pain clinic referral for symptomatic management.

Neurostimulation Therapies for Chronic Pain

Although there are many case series and anecdotal reports of success for both spinal cord stimulation (SCS) and peripheral nerve stimulation (PNS) therapies for PNIs, the evidence is inconclusive. The difficulty in studying these technologies relates to difficult sham comparator groups and the fact that most of the time they are applied when all other therapies (eg, pharmacologic) have failed.[99] Of the 2 major indications for SCS (CRPS and postlaminectomy pain syndrome), CRPS is the most applicable to this discussion. The European Federation of Neurological Societies guidelines found evidence to support the use of SCS for CRPS, and inconclusive evidence for PNS.[101] In cases where 1 peripheral nerve is involved, PNS may be considered.[102] Older trials of PNS noted improved outcomes in patients with CRPS[103] and PNIs.[104] Larger, well-designed studies are needed to answer the role for these modalities in PNI patients.

CONCLUSIONS

Fortunately, neurologic injury after regional anesthesia or pain medicine interventions is extremely rare. Most perioperative nerve injuries consist of mild sensory symptoms, which can be appropriately managed with patient reassurance, education, and scheduled follow-up to assure symptom resolution. Neurologic complications in the setting of neuraxial anesthesia require urgent evaluation as delay in the diagnosis of epidural hematoma, epidural abscess, or SCI contributes to long-term morbidity. In the setting of PNIs, early neurologic evaluation should be considered when deficits are severe, progressive, or difficult to localize. Unfortunately, once an active process has been excluded, little can be done to improve the neurologic outcome of a perioperative nerve injury; however, proactive rehabilitation and pain management can improve patient function and quality of life.

We propose an algorithm for the clinical approach (Fig. 1) and evidence-based recommendations on the diagnosis and treatment of postoperative nerve injury (Tables 7 and 8).

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Anatomy and Pathophysiology of Spinal Cord Injury Associated With Regional Anesthesia and Pain Medicine
2015 Update

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Background and Objectives: In March 2012, the American Society of Regional Anesthesia and Pain Medicine convened its second Practice Advisory on Neurological Complications in Regional Anesthesia and Pain Medicine. This update is based on the proceedings of that conference and relevant information published since its conclusion. This article updates previously described information on the pathophysiology of spinal cord injury and adds new material on spinal stenosis, blood pressure control during neuraxial blockade, neuraxial injury subsequent to transforaminal procedures, cauda equina syndrome/local anesthetic neurotoxicity/arachnoiditis, and performing regional anesthetic or pain medicine procedures in patients concomitantly receiving general anesthesia or deep sedation.

Methods: Recommendations are based on extensive review of research on humans or employing animal models, case reports, pathophysiology research, and expert opinion.

Results: The pathophysiology of spinal cord injury associated with regional anesthetic techniques is reviewed in depth, including that related to mechanical trauma from direct needle/catheter injury or mass lesions, spinal cord ischemia or vascular injury from direct needle/catheter trauma, and neurotoxicity from local anesthetics, adjuvants, or antiseptics. Specific recommendations are offered that may reduce the likelihood of spinal cord injury associated with regional anesthetic or interventional pain medicine techniques.

Conclusions: The practice advisory's recommendations may, in select cases, reduce the likelihood of injury. However, many of the described injuries are neither predictable nor preventable based on our current state of knowledge.

What's New: Since publication of initial recommendations in 2008, new information has enhanced our understanding of 5 specific entities: spinal stenosis, blood pressure control during neuraxial anesthesia, neuraxial injury subsequent to transforaminal techniques, cauda equina syndrome/local anesthetic neurotoxicity/arachnoiditis, and performing regional anesthetic or pain procedures in patients concomitantly receiving general anesthesia or deep sedation.

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Injury to the neuraxis associated with regional anesthesia or pain medicine procedures is ultimately linked to anatomic and/or physiologic damage to the spinal cord, the spinal nerve roots, or their blood supply. Mechanisms of injury are sometimes identifiable, as in the case of epidural hematoma or abscess, but can also be exceedingly difficult to pinpoint, as exemplified by most cases of presumed spinal vascular injury. The goal of our original advisory on this topic and the updated material contained herein is to provide an anatomic and pathophysiologic basis from which to build an understanding of neuraxial complications associated with regional anesthesia and pain medicine.

Consistent with a recent editorial call to focus practice advisory and consensus conference updates on new material,[1] we have crafted this review in 2 sections. First, to provide perspective, we will briefly review those topics and associated recommendations for which no substantially new knowledge has emerged. To provide consistency over time or when appropriate, the current review will present text and especially recommendations that are essentially verbatim from those of our original work. Interested readers can find the detailed explanations and their specific literature-based citations by revisiting those 2008 articles.[2,3] The second section will focus on 5 topics that either have significantly new information to add to our previous understanding and/or we believe deserve more extensive discussion than was provided in the first iteration of this practice advisory.

METHODS

Standard search engines and cross-referenced citations identified the literature basis for the updated material contained within this review. PubMed and Ovid were searched from 2006 forward to identify new material by using MeSH terms as individual headings or in relevant combinations: "spinal cord injury," "hypotension," "neurotoxicity," "transforaminal," "cauda equina syndrome," "anterior spinal artery syndrome," "needle injury," "spinal stenosis," "spinal cord ischemia," and "spinal cord infarction."

As specifically noted in our 2008 review, "The strength of scientific evidence that is used to arrive at these recommendations is not easily measured by traditional stratification methodologies such as the United States Agency for Health Care Policy and Research structure for ranking Statements of Evidence and Grades of Recommendation.[4] Because of the extreme rarity of the specific complications that are addressed in this article, traditional methodologies such as randomized controlled trials, meta-analysis, or large human case series rarely exist and are unlikely to exist in the future. Our recommendations are therefore based on methodologies that are necessarily less robust, such as anatomic or pathophysiologic studies of human cadavers or animals, nonrandomized trials, retrospective series, case reports, or expert opinion. The grading of recommendations offered by this practice advisory has been modified from an American College of Cardiology/American Heart Association construct that classifies the strength of guidelines for perioperative cardiac evaluation."[2]

Readers of this article are reminded that practice advisories are created when data on a subject are limited or nonexistent.

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Advisories rely on limited clinical and animal data, and as such, the synthesis and interpretation of data by 1 group of experts may differ from conclusions by another set of equally qualified experts. Thus, practice advisories represent a level of recommendation that is less than that offered by standards or clinical practice guidelines.[5] The recommendations contained herein do not define standard of care. They are not intended to replace clinical judgment as applied to a specific patient scenario. "These recommendations are intended to encourage optimal patient care, but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge of specific complications advances."[6]

REVIEW OF PREVIOUS RECOMMENDATIONS

Mechanical Injury

Some neuraxial anesthetic complications are secondary to mechanical injury of the spinal cord, spinal nerve roots, or the spinal nerves as they exit the intervertebral foramina. Injury to these structures may involve direct needle or catheter trauma or lesions within the vertebral canal that compress neural structures and thereby cause ischemic injury. These various mechanisms ultimately lead to loss of anatomic and/or physiologic neural integrity and can result in permanent injury.[7] We have not changed the majority of recommendations related to mechanical injury (Table 1).

Iatrogenic Spinal Cord Trauma

The incidence of spinal cord–related needle/catheter trauma is unknown, but decidedly rare. Anesthesiologist-reported or quality-assurance databases may well underreport this complication, whereas medicolegal databases are likely to skew data in the opposite direction. For instance, direct spinal cord injury was noted in 6 (0.73%) of 821 neuraxial claims from the American Society of Anesthesiologists (ASA) Closed Claims database, which does not provide a denominator of total cases.[7] Conversely, direct needle trauma was detected in only 9 of 1.7 million neuraxial anesthetics (0.0005%) over a 10-year period in Sweden,[12] and only 1 case was reported in a 2000 survey from French spinal cord rehabilitation centers (from an estimated 1 million neuraxial anesthetics performed that year in their catchment area).[13]

Three anatomic characteristics of the human neuraxis contribute to its potential for sustaining needle or catheter injury. First, although the conus medullaris is typically described as terminating at the L1–2 vertebral interspace in adults (and terminates more caudad in the first few months of life), its terminus varies widely from T12 to L4. When this variation is coupled with practitioners' inaccurate determination of which spinal interspace they are palpating,[14] it is not surprising that needle injury to the spinal cord has been reported in instances where the conus medullaris terminated more caudad than expected.[12] Indeed, a recent study demonstrated that in 40% of term parturients, the perceived vertebral level identified by palpation at the intercristal line was in reality at the L3 interspace or higher.[15] Neuraxial ultrasonography may improve estimation of the vertebral level because it is more accurate than palpation for identifying surface landmarks, especially in challenging anatomic scenarios,[16] such as obesity, scoliosis, or previous spinal surgery.[17] Second, the customary expectation of encountering resistance prior to entering the epidural space is not always fulfilled in those individuals in whom the ligamentum flavum has failed to fuse in the midline, a condition that is more prominent in the upper thoracic (4%–21% midline gaps at T3–4 and above) and cervical neuraxis (51%–74% midline gaps).[18] Unanticipated congenital dysraphisms can also contribute to accidental entry into the spinal cord.[19] Third, the margin for error during needle advancement is significantly diminished as one proceeds from the lumbar posterior epidural space with its 5- to 13-mm dorsal-to-ventral dimensions, to the 2- to 4-mm thoracic posterior epidural space, to the average 0.4-mm cervical posterior epidural

TABLE 1. Recommendations: Factors That May Limit Neuraxial Injury

These recommendations are intended to encourage optimal patient care, but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

Anatomic factors

- 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 of the spinal cord. Clinicians are advised to be aware of these anatomic conditions, particularly in patients with challenging surface anatomy (*eg, as may occur with obesity, kyphoscoliosis, and other conditions*). Ultrasonography or fluoroscopy could be considered as an adjunct for accurate determination of vertebral level in these challenging patients. (Class I)
- Surgical positioning, severe spinal stenosis, and specific space-occupying extradural lesions (eg, epidural lipomatosis, ligamentum flavum hypertrophy, synovial cysts, 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-versus-benefit when contemplating neuraxial regional anesthetic techniques. (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)
- For patients receiving neuraxial injection for treatment of pain (eg, cervical epidural injection of steroids via an interlaminar route), radiologic imaging studies such as computed tomography (CT) 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)

Physiologic factors

- 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 American Society of Regional Anesthesia and Pain Medicine Practice Advisories. Such conditions include concurrent or imminent anticoagulation, the use of multiple anticoagulants, improper aseptic technique, and needle placement during untreated active infection.[8–11] (Class I)

Recommendations contained within Table 1 have been modified minimally from the authors' 2008 advisory.[2] Significant changes are in italics.

space. Indeed, because the epidural space is a potential space, the cervical posterior epidural space may be nonexistent, particularly at higher vertebral levels.[20–22]

Mass lesions can also lead to spinal cord injury. Intradural or extradural lesions compete for cross-sectional space within the spinal canal and in so doing potentially decrease spinal cord perfusion pressure (SCPP) by inhibiting arterial inflow, inhibiting venous outflow, or elevating cerebrospinal fluid (CSF) pressure ([SCPP = mean arterial pressure − spinal cord CSF pressure][23]; in rare circumstances, direct venous outflow pressure may also impact regional SCPP.) If SCPP is sufficiently diminished, it can lead to spinal cord ischemia that in more severe instances can produce infarction. Epidural hematoma and abscess are commonly recognized complications of neuraxial anesthetic or pain medicine techniques, and they can lead to consequential mass lesions.[8,24] Less well appreciated is the potential for transient pressure elevations secondary to excessive volumes of local anesthetic[25] (especially in infants),[26] compromised egress of local anesthetic or blood through stenotic intervertebral foramina,[27] or unusual mass lesions such as tumors, granulomas from chronic intrathecal morphine administration,[28] epidural lipomatosis,[29,30] synovial cysts,[13] or ependymoma. Many of these conditions are occult to patient and practitioner and become relevant only when blood, pus, or local anesthetic competes for limited cross-sectional area within the vertebral canal. The presence of increased volume within the vertebral canal, whether by fluids or mass lesions, can have a "Starling resistor" effect on blood vessels, limiting blood ingress into and egress from the affected tissues. Moreover, patients with severe spinal stenosis or other mass effects may be at additional risk of compromised tissue blood flow when surgical field exposure requires certain positions such as extreme lordosis, lithotomy, or the flexed lateral position.[2,31]

Spinal Nerve Root and Spinal Nerve Trauma

The spinal nerves are protected during midline or paramedian approaches to the neuraxis because of their lateral position and the partial protection afforded by the vertebral laminae, transverse processes, and facet joints. Therefore, midline procedure-related injury to the spinal nerve, or to the anterior or posterior ramus outside the intervertebral foramen, occurs only when needles deviate laterally. Spinal nerves can also be contacted unintentionally during procedures such as paravertebral or psoas compartment block when the needle is directed too medially. Needles medial to the facet within the lateral recess may unintentionally contact the dorsal nerve roots[2] (Fig. 1).

As concluded in our 2008 review, "mechanical injury to the neuraxis can arise consequent to direct needle trauma or to space-occupying lesions whose mass effect compromises spinal cord blood flow (SCBF). Evidence to support contribution to injury varies with the mechanism of injury. In the case of epidural hematoma or abscess, extensive literature supports causation. Conversely, neuraxis injury in the setting of rare extraspinal mass lesions or relatively common surgical positions only establishes association or chance occurrence."[2] Limited additional information since our 2008 publication has not altered this conclusion (Table 1), except for new information on the association of spinal stenosis with neuraxial injury, as will be presented subsequently.

Spinal Cord Ischemia and Vascular Injury

Disruption of SCBF can occur from a variety of mechanisms, including needle trauma affecting the spinal vasculature (Fig. 2), compressive mass lesions (Fig. 3), or vascular spasm (Fig. 4). Spinal cord blood flow may also be compromised from low-flow states, such as might occur from significant and prolonged systemic hypotension, embolic phenomena, or vascular stenosis. The frequency of spinal cord ischemia is distinctly rare and our understanding limited. Our previous article[2] extensively reviewed the human spinal cord blood supply. The spinal cord and cauda equina receive two-thirds of their blood supply from the anterior spinal artery, which cannot be injured directly by midline or paramedian needles without first traversing the spinal cord (Fig. 2). Damage to the spinal cord's posterior blood supply is largely mitigated by the redundancy of the posterior spinal artery system. However, the segmental or spinal branch arteries are exposed to needle-related trauma when the needle deviates far laterally or is intentionally placed near a segmental artery (such as during perispinal techniques or celiac plexus block).[33] Radicular arteries can sustain needle injury during a transforaminal approach, which can be important if that artery is 1 of the few radicular arteries that continue on to become a medullary artery supplying the spinal cord (Fig. 5). Disruption of SCBF might also occur from procedure-induced hematoma or drug-induced vasospasm associated with neurolytic procedures such as celiac plexus block (Fig. 4), although clear proof of these mechanisms is lacking.[2]

Within the category of vascular injury to the neuraxis, the majority of our previous recommendations remain intact (Table 1). However, we will henceforth discuss 2 topics for which new information justifies strengthening of previous advice: blood pressure control during neuraxial anesthesia and central nervous system (CNS) injury during transforaminal pain medicine procedures.

Neurotoxicity

Our previous review concluded, "Neuraxial local anesthetics, opioids, adjuvants, and preservatives in clinically recommended doses are remarkably safe in the vast majority of patients. Nevertheless, a patient may rarely be vulnerable to local anesthetic and adjuvant neurotoxicity even in normal clinical situations. Clinical evidence comes from case reports of patients who sustained neuraxis injury that was presumed secondary to a neurotoxic mechanism, even though they received standard doses of spinal or epidural local anesthetic with or without adjuvant. Neurotoxicity is more likely to occur in conjunction with physical disruption of the blood–spinal cord barrier by needle or catheter trauma, or from iatrogenic conditions leading to maldistribution and/or overdosing of neuraxial local anesthetics."[2] While our previous recommendations have not substantially changed (Table 1), we will henceforth discuss newer information concerning cauda equina syndrome (CES), arachnoiditis, and clinical experience with intrathecal 2-chloroprocaine (2-CP).

NEW RECOMMENDATIONS FROM THE SECOND PRACTICE ADVISORY

Spinal Stenosis

Spinal hematoma, abscess, tumor spread, epidural lipomatosis, spinal arachnoid cysts, ankylosing spondylitis,[12,34] or extreme surgical positioning such as hyperlordosis or extreme lateral flexion[31,35] are mechanical causes that can contribute to the development of spinal cord ischemia or infarction in the perioperative period. Recent literature has focused on degenerative spinal stenosis and its association with various manifestations of neuraxial injury in the setting of regional anesthesia. Degenerative spinal stenosis is caused by osteoporosis and/or hypertrophy of the ligamentum flavum and bony elements of the spinal canal that effectively reduces spinal canal cross-sectional area and competes with the spinal cord and nerve roots for space. Similar mechanisms might contribute to local anesthetic neurotoxicity by causing maldistribution and/or

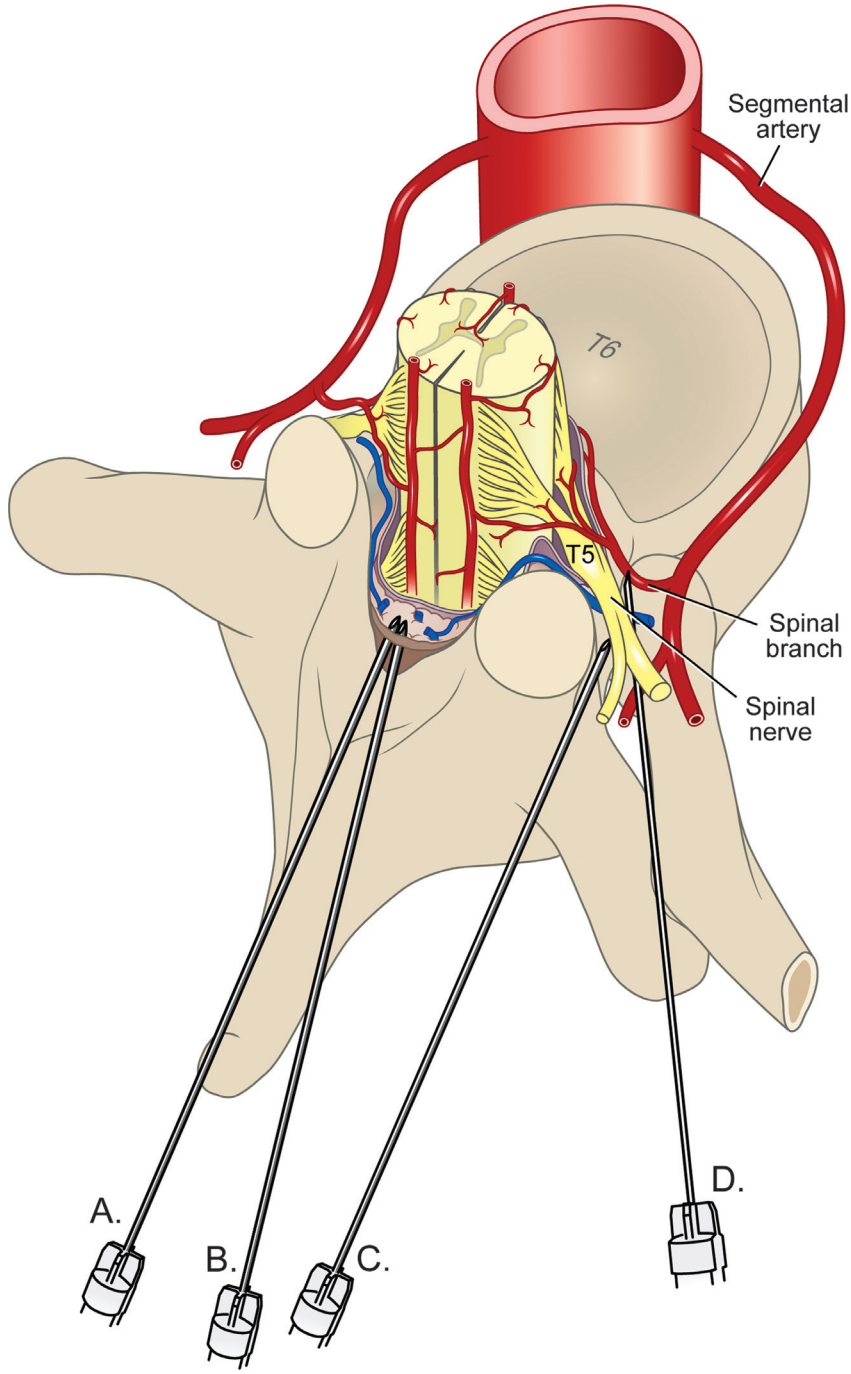

FIGURE 1. Midline or paramedian approaches (needles A and B) may directly traumatize the spinal cord, whereas unintentional lateral deviation of the needle (C) may contact the spinal nerve or the anterior or posterior primary ramus outside the foramen. Intentional lateral approaches, for example, transforaminal approach (needle D), have the potential to come in close proximity to the spinal nerve or a spinal artery. Note that transforaminal approaches are typically at the cervical or lumbar levels, not the T6 level as illustrated. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell, *Complications in Regional Anesthesia and Pain Medicine*.[32]

reduced clearance of relatively undiluted drug.[36,37] Degenerative changes may also cause narrowing of the vertebral foramina, which compromises egress of fluids[22,38] and consequently results in an increase in vertebral canal pressure[27] and transiently diminished neural blood flow.[39] Spinal stenosis represents a continuum of severity, from mild and inconsequential to severe; 19% of patients in their 60s will have absolute spinal stenosis (<1-cm anteroposterior diameter of the spinal canal).[40] Although commonly discovered during imaging for the diagnosis of back pain, there are subsets of patients with undiagnosed spinal stenosis that is discovered only during workup of injury after a neuraxial anesthetic.[12]

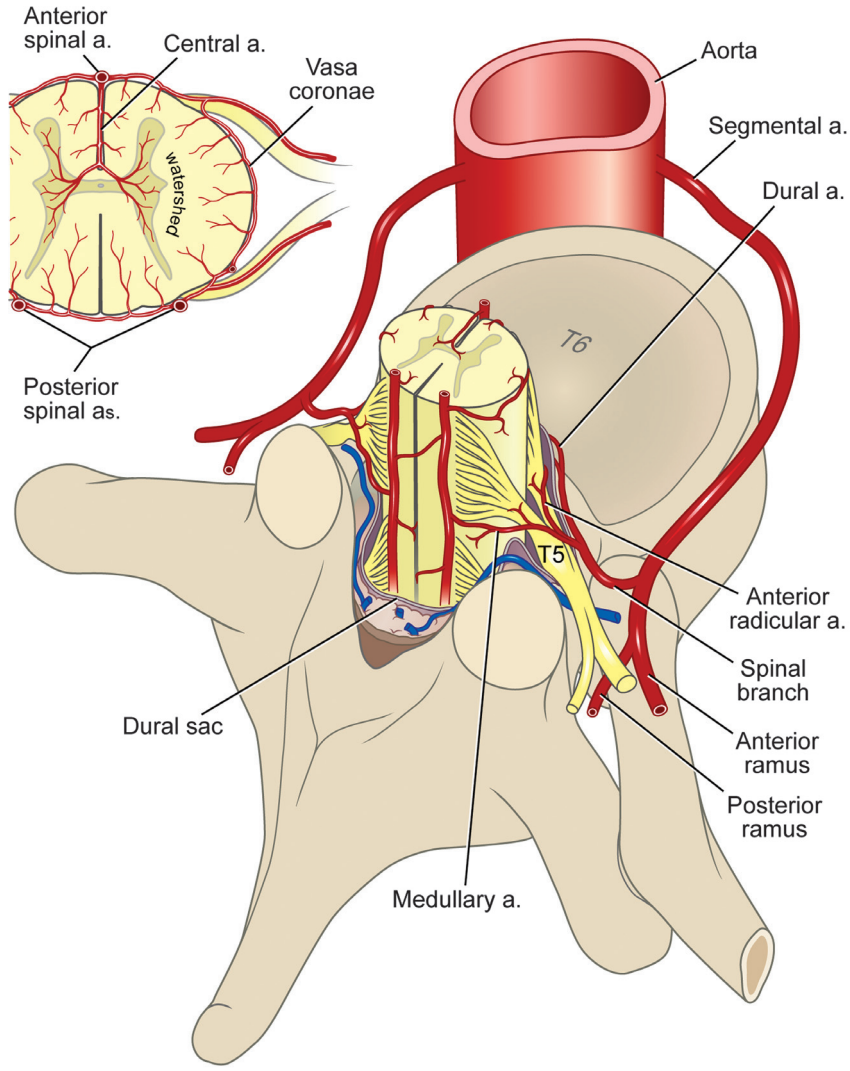

FIGURE 2. Midline or paramedian approaches may directly traumatize the posterior spinal arteries, whereas unintentional lateral deviation of the needle may contact the spinal branch artery. Direct injury to the anterior spinal artery would require placement of a needle or catheter through the spinal cord. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell, *Complications in Regional Anesthesia and Pain Medicine*.[32]

The potential for spinal stenosis to cause or worsen neuraxial injury in the setting of a regional anesthetic has been the object of speculation for decades.[41] However, the first strong signal of the relationship between spinal pathology and increased risk of neuraxial injury was identified in Moen and colleagues'[12] report of the association between spinal stenosis and neuraxial injury in 1.7 million neuraxial anesthetics conducted in Sweden between 1990 and 1999. Of the 33 cases of spinal hematoma, one-third were associated with coagulopathy or thromboprophylaxis (in one-third of those cases, thromboprophylaxis was administered in accordance with published guidelines). This report contrasted the extreme rarity of spinal hematoma in young women who received neuraxial anesthesia for childbirth (1:200,000) versus the 1:22,000 incidence of spinal hematoma in elderly women undergoing hip fracture repair or 1:3600 incidence in those elderly women receiving total joint arthroplasty. During diagnostic imaging, 6 of the 33 cases were noted to have previously undiagnosed spinal stenosis or ankylosing spondylitis. These conditions may have compromised spinal cord circulation to a greater extent in the mostly elderly women who constituted the majority of this cohort, as compared with younger obstetric patients with an uncompromised spinal canal who likely would have experienced a lesser degree of circulatory impairment from a similarly sized hematoma.[12,42]

Since the Swedish publication, confirmatory reports have emerged.[13,43] For example, a retrospective analysis of neuraxial anesthetics performed in patients with *known* spinal canal pathology (spinal stenosis or lumbar disc disease) observed a 1.1% incidence of neuraxial complications, which was higher than expected for patients without spinal canal pathology who underwent similar surgeries at the same institution.[44] While this study corroborates observations from previous investigations and points to a higher incidence in those patients with known spinal stenosis compared with those with unsuspected disease, it also points to the difficulties in firmly establishing spinal canal pathology and subsequent neuraxial injury as cause and effect, rather than association. Case reports and large registries do not provide a general anesthetic control group and cannot distinguish whether

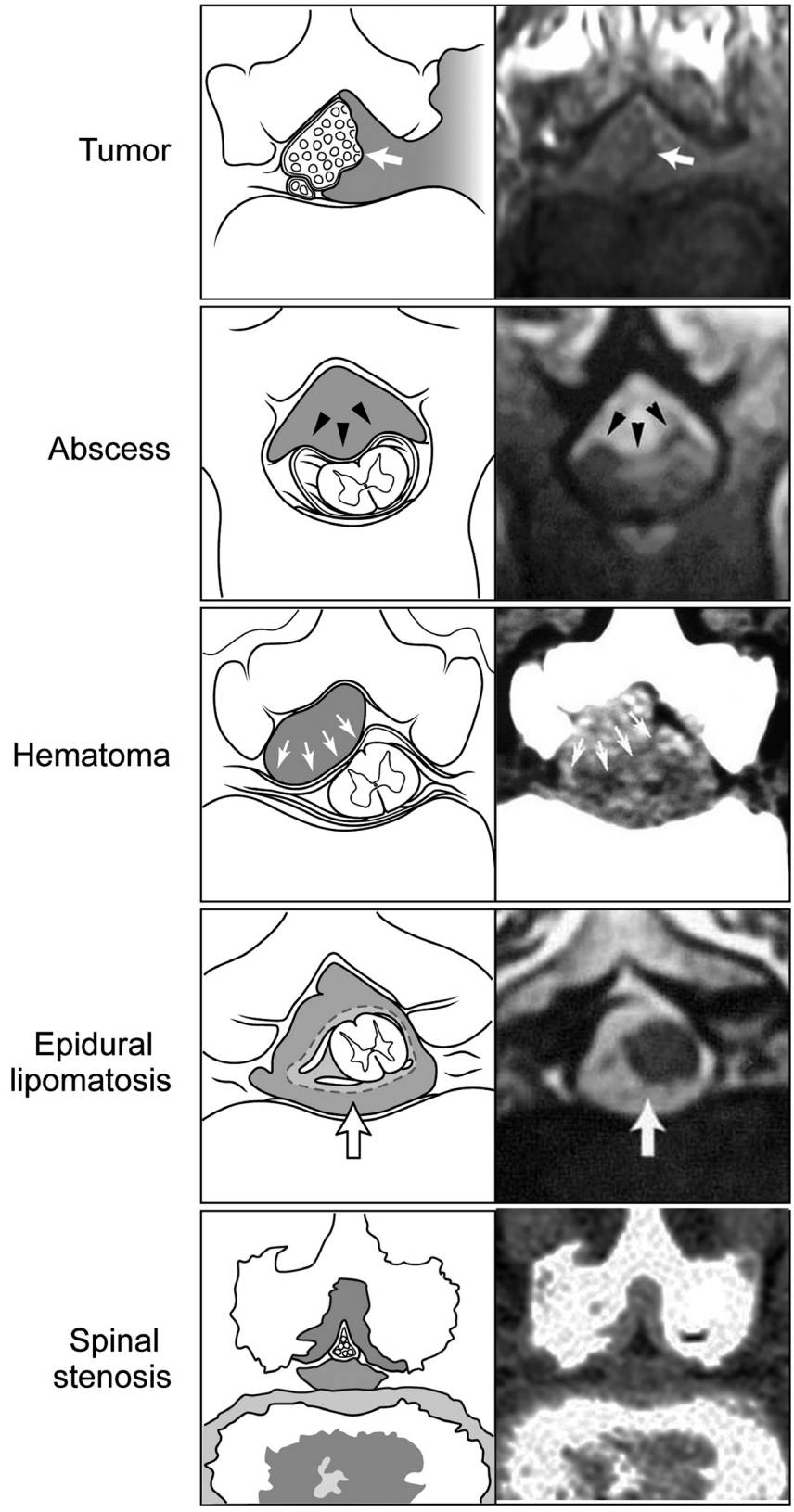

FIGURE 3. Extradural mass lesions. Note how various conditions can reduce spinal canal cross-sectional area and either directly compress the spinal cord or the cauda equina (arrows) or increase epidural space or CSF pressures through their mass effect. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell, *Complications in Regional Anesthesia and Pain Medicine*.[32]

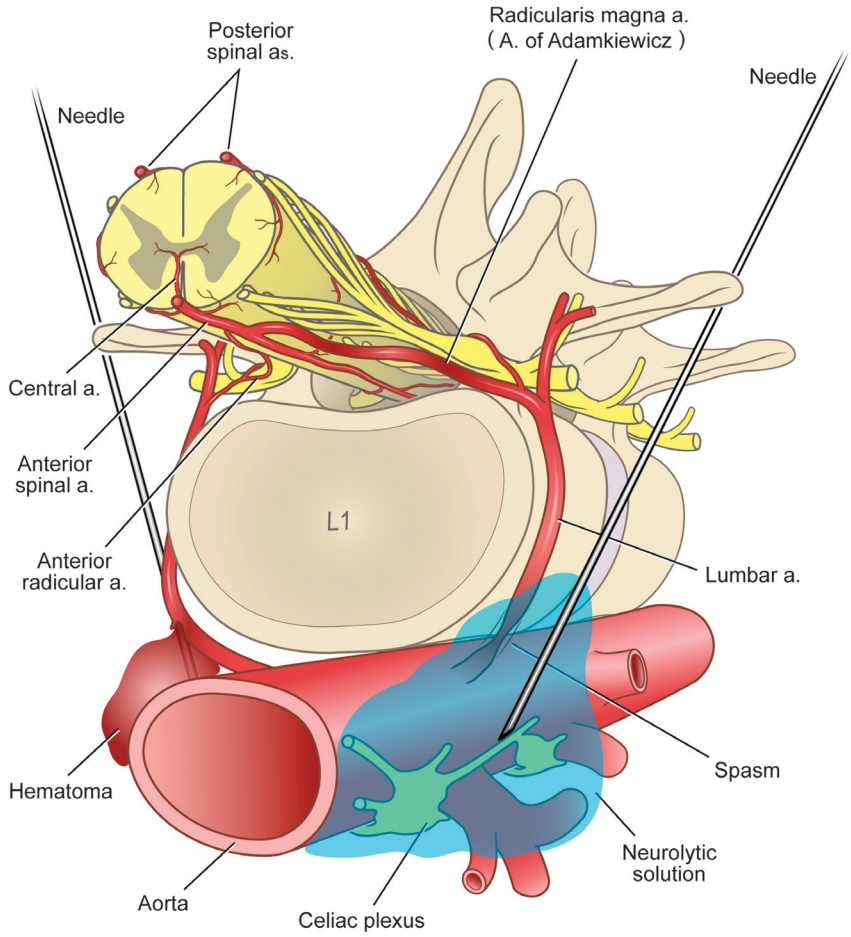

FIGURE 4. Proposed mechanisms of direct injury to reinforcing arteries supplying the spinal cord. On the left, a needle can potentially disrupt a segmental artery or precipitate a hematoma. On the right, needle irritation or injected phenol or alcohol (as used in neuroablation procedures) can cause vasospasm. These proposed mechanisms have not been proven in humans. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell, *Complications in Regional Anesthesia and Pain Medicine*.[32]

the observed injury results from underlying spinal canal pathology, disease progression, surgical factors, patient positioning, or a combination thereof.

The advisory panel therefore acknowledges growing evidence of an association between spinal stenosis or other spinal canal pathology and a higher incidence of complications after neuraxial blockade.[12,13,41,44] However, causation cannot be established definitively. To this point, the panel also acknowledges that a multitude of neuraxial regional anesthetics and interventional pain medicine procedures are performed daily on patients with varying degrees of spinal stenosis. In some of these cases, spinal stenosis has been diagnosed and may indeed be the indication for intervention. Furthermore, spinal stenosis can contribute to neurologic injury from surgery or positioning even in the absence of neuraxial anesthetic techniques.[45,46] Based on details gleaned from the limited literature on this topic and in accordance with the double-crush theory,[47] we believe it reasonable to speculate that patients with moderate to severe spinal stenosis might be more vulnerable to injury if there are coexisting conditions such as neuraxial surgery, preexisting neurologic disease, mucopolysaccharidosis,[48] nonneutral patient positioning, or conditions known or unknown that compete for limited cross-sectional area within the spinal canal. Although the preponderance of spinal stenosis has been associated with epidural and combined spinal-epidural techniques,[12] association with spinal anesthesia has also been reported.[35,44] As noted previously, the presence of spinal stenosis may be unknown to the clinician and the patient. However, those patients who report neurogenic claudication with symptoms that progress with ambulation are likely to have severe stenosis, even if not formally diagnosed. Recommendations for spinal stenosis are found in Table 2.

Blood Pressure Control During Neuraxial Anesthesia

Spinal cord ischemia or infarction associated with neuraxial regional anesthesia is a decidedly rare event that may present as anterior spinal artery syndrome (ASAS), posterior spinal artery syndrome, watershed infarction, or an ill-defined injury consistent with critically reduced or absent SCBF. For perspective, only 10 of 821 medicolegal claims for neuraxial injury contained within the ASA Closed Claims database were alleged to have resulted from ASAS or variations of spinal cord ischemia.[7] A study of long-term outcomes after acute spinal cord ischemia documented that only 1 of 54 patients had actually received a neuraxial anesthetic.[49] This should not be surprising, as the highest risks for perioperative spinal cord infarction are associated with specific operations, for example, aortic, cardiac, thoracic, or spine surgeries. Even

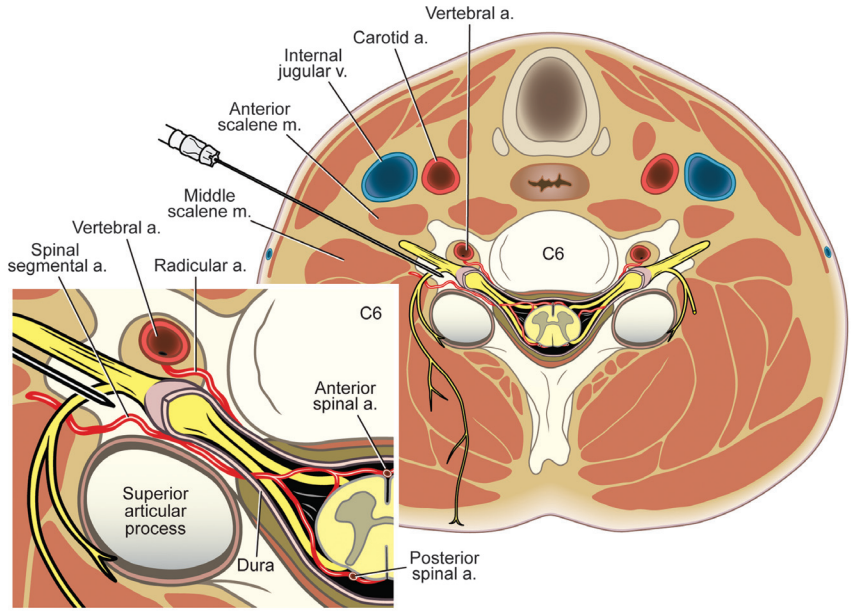

FIGURE 5. The transforaminal approach to the neuraxis may allow the needle to contact either the spinal nerve or the spinal artery. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell, *Complications in Regional Anesthesia and Pain Medicine*.[32]

though autoregulation of SCBF mirrors that of cerebral blood flow[50] (Fig. 6), spinal stroke is apparently much less frequent than the estimated 0.1% incidence of perioperative cerebral stroke in patients undergoing noncardiac, nonneurologic surgery.[51] Spinal cord ischemia and infarction are rarely reported even after clinical scenarios of prolonged low mean arterial pressure (MAP), such as during cardiopulmonary bypass or induced hypotension to a MAP of 60 mm Hg or less.[52–55] While it is relatively rare for survivors of cardiac arrest to develop spinal cord ischemic injury, 46% of those who died of cardiac arrest or a severe hypotensive episode manifested ischemic spinal cord myelopathy at autopsy.[56] Despite the expectation that ischemic myelopathy would be most prevalent within the thoracic spinal cord watershed areas (because the thoracic spinal cord classically is supplied by fewer medullary arteries than either the cervical or lumbosacral spinal cord), 95% of cases in the previously noted postmortem study involved

TABLE 2. Recommendations: Patients With Spinal Stenosis

These recommendations are intended to encourage optimal patient care, but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- Spinal stenosis represents a continuum of spinal canal encroachment by hypertrophied ligamentum flavum, bony overgrowth, and/or degenerative changes such as from osteoporosis or herniated nucleus pulposus. Patients with spinal canal pathology (eg, spinal stenosis, lumbar disk disease) may have clinical or subclinical evidence of a preexisting neurologic deficit due to neural compromise from the disease state. However, even moderately severe spinal stenosis is not always symptomatic; many patients (or their healthcare providers) are unaware that they have the condition. (Class I)
- When neuraxial anesthesia is complicated by the development of mass lesions within the spinal canal (eg, hematoma or abscess), resultant postoperative neurologic complications may be more likely or more severe in patients with spinal stenosis or other obstructive spinal canal pathology, including changes brought on by patient positioning. (Class I)
- In patients with known severe spinal stenosis or symptoms suggestive thereof, we recommend that risk-to-benefit analysis be considered prior to performance of neuraxial anesthesia because of the association of spinal stenosis with neurologic complications in the setting of neuraxial blockade. If neuraxial blockade is performed, we recommend heightened perioperative vigilance for symptoms suggestive of neural compromise. (Class II)
- There is no firm linkage to injury if spinal stenosis is at a site distant from the level of neuraxial block placement. (Class III)
- If neuraxial anesthesia is planned, the practitioner may consider reducing the total mass (volume × concentration) of local anesthetic in an effort to reduce segmental spread and local anesthetic neurotoxicity (which is related to concentration) and/or facilitate neurologic assessment by earlier block resolution. While we are unaware of routinely administered volumes of local anesthetic being associated with injury in patients with spinal stenosis, reports have postulated linkage between high volumes and neuraxial injury in the setting of other mass lesions such as epidural lipomatosis. (Class III)
- The literature has established an association between spinal stenosis and injury after neuraxial blockade, most often affecting patients in whom the diagnosis of spinal stenosis was made during workup for the injury. There is no clear evidence that spinal stenosis per se caused these injuries. (Class II)
- Currently, it is unclear whether the development of new or worsening neurologic symptoms after neuraxial anesthesia or analgesia is due to surgical factors, the anesthetic technique, the natural progression of spinal pathology, or a combination of these factors. (Class II)

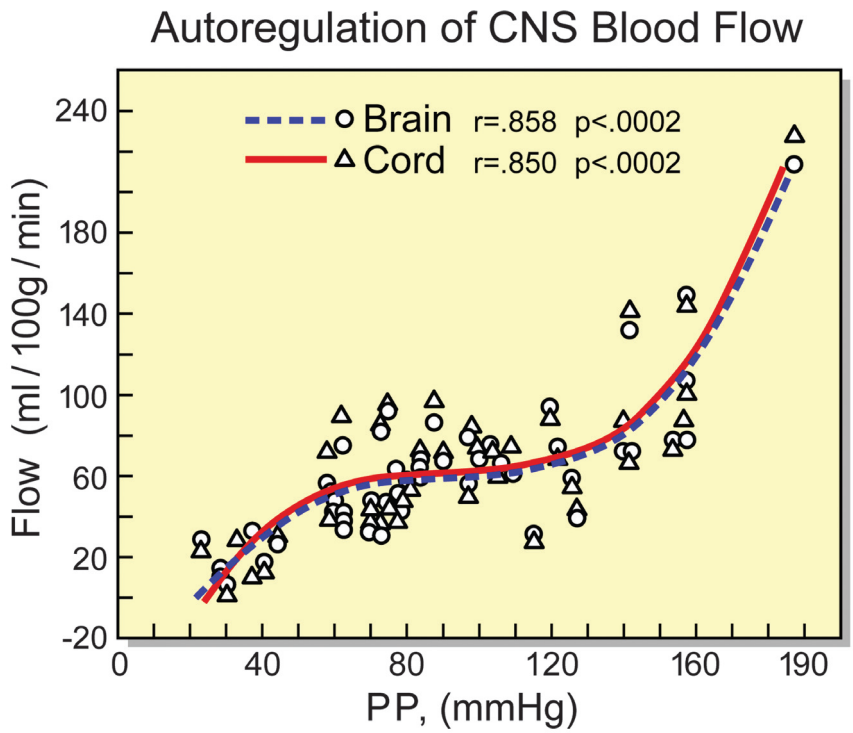

FIGURE 6. The autoregulation of SCBF (red) mirrors that of the brain (blue dashed line). Illustration by Gary J. Nelson. Modified from Hickey et al[50] and reproduced with permission from Neal and Rathmell, *Complications in Regional Anesthesia and Pain Medicine*.[32]

the lumbosacral spinal cord,[56] whereas nearly 50% of cases reported in a neuroradiologic study occurred at the cervical level.[57]

Although local anesthetics and especially adjuvants are often implicated as contributory to spinal cord ischemia, our 2008 advisory[2] summarized that—inherent to an anesthetized spinal cord—neither class of compounds reduces SCBF out of proportion to metabolic demand.[58–61] Conversely, reduction in $CMRO_2$ out of proportion to blood flow does not reliably predict cerebral protection,[62] and it presumably has the same relationship in the spinal cord. Thus, neither local anesthetics nor adjuvants would be expected to influence cord injury based on an uncoupling of SCBF and metabolic rate, regardless of the direction of that uncoupling, in part because the magnitude of the uncoupling would be small. Vasoactive drugs such as epinephrine and phenylephrine do not adversely affect SCBF, whether delivered as an intrathecal adjuvant or in clinically appropriate intravenous doses.[61,63,64]

The Argument for Avoiding Significant Hypotension During Neuraxial Anesthesia

This advisory expands previous recommendations regarding blood pressure control during neuraxial anesthetics. These modifications are predicated by 2 developments: (1) an evolving understanding of brain and spinal cord lower limit of autoregulation (LLA) and (2) a growing body of literature and medicolegal experience that suggests the existence of an extremely rare subset of patients (including young patients with no increased cerebrovascular risk) who suffered spinal cord ischemia or infarction in clinical settings wherein the only or most likely abnormality was an extended period of marginally low blood pressure.[65–67]

With regard to our evolving understanding of CNS LLA, previous animal studies suggested that SCBF is autoregulated within a MAP range of 50 to 60 mm Hg to 120 to 135 mm Hg, assuming (1) an intact blood–spinal cord barrier[50,68] and (2) the LLA for the spinal cord behaves in a similar manner as the LLA of the brain. In recent years, Drummond et al[66,67] and others[61,69,70] have challenged the previously accepted dictum of MAP 50 mm Hg representing a relevant and consistent cerebral LLA in humans and have instead presented evidence that cerebral LLA varies widely among individuals and is likely closer to 60 to 65 mm Hg in normotensive, unanesthetized adults. These experts remind us that CNS blood flow does not stop upon reaching the LLA but that there is a range between baseline MAP, the LLA, and the blood pressure below which irreversible cell damage occurs. The limits of this "physiologic reserve" (between the LLA and the pressure at which cells manifest injury) are unknown but are speculated to be 30% to 40% below baseline MAP.[67,71,72] Whereas physiologic reserve probably affords some degree of spinal cord protection against low-flow states, such protection is likely mitigated by the presence of vascular stenosis, embolic phenomena, erythrocyte sludging (eg, sickle cell disease), or when abnormal vascular anatomy impairs normal blood flow, as has been described in cases of focal cerebral ischemia.[73] This last phenomenon is likely to exist with spinal vasculature anomalies as well.

Clinical support for these concepts can be gleaned from both animal and human studies. The bulk of these studies involve cerebral blood flow rather than SCBF, but the parallel autoregulatory curves of both systems argue that extrapolation from one to the other is reasonable[50] (Fig. 6). For example, in a clinical study that precisely measured cerebral LLA in patients undergoing cardiopulmonary bypass, the mean LLA was a MAP of 66 mm Hg and ranged widely (95% prediction interval, 43–90 mm Hg). In this study, preoperative MAP was not predictive of brain LLA, and only preoperative systolic blood pressures in excess of 160 mm Hg correlated with a higher LLA.[69] Another study noted that patients undergoing shoulder surgery frequently reached the cerebral LLA at a MAP of 65 to 70 mm Hg, especially when in

the beach-chair (ie, semisitting) position (BCP).[70] Similarly, in a study of dogs administered spinal anesthesia and then acutely hemorrhaged, SCBF began to decrease at a MAP of 66 mm Hg.[74]

Circumstantial support for the injurious role of hypotension can also be found in spinal deformity surgery, wherein the correction of hypotension has been reported to reverse electrophysiologic signs of spinal cord dysfunction.[75]

With regard to the duration of hypotension, a case-control study of 48,241 patients undergoing noncardiac, nonneurologic surgery reported that those patients whose MAP was 30% or greater below preoperative baseline had a significantly higher risk of perioperative ischemic cerebral stroke, which also correlated with the duration of hypotension.[71] Moreover, it is possible that prolonged periods of lesser degrees of hypotension (or, alternatively, local tissue hypoperfusion) may also be significant, as inferred from the observation that some patients with ASAS developed symptoms over time; that is, not all presented with sudden flaccid paralysis.[49]

In summary, this advisory's new admonition to avoid significant hypotension (especially of prolonged duration) during neuraxial blockade is based on evolving evidence that the LLA of cerebral blood flow and SCBF appears to be higher than previously accepted. Furthermore, there is an increasing awareness that the range of cerebral and spinal cord LLA is wide in humans, and that at least a subset of patients with otherwise "low normal" MAPs can manifest signs of spinal cord ischemia or sustain injury. Large clinical studies directly linking low blood pressure to spinal cord injury are lacking. Instead, we have only association gleaned from case reports or extrapolated from limited human studies of surrogate end points, for example, measuring cerebral LLA during cardiopulmonary bypass or reversal of electrophysiologic deficits during spinal surgery consequent to correction of low blood pressure.

Perspective on Blood Pressure Control During Neuraxial Anesthesia

Despite concerns over prolonged, significant hypotension as a risk factor for spinal cord ischemic injury, the rarity and nature of such injury make it impossible to assume cause and effect. In most reported cases, the absence of clinical details or the existence of other potentially confounding etiologies precludes cause and effect.[76] Multiple studies point to the relative safety of prolonged hypotension in humans during general and/or regional anesthesia. For instance, clinical studies of prostaglandin-induced hypotension during spinal surgery note the absence of cord injury during prolonged periods of 60 mm Hg MAP.[55] Yet, in a different model, devastating brain or cervical spinal cord injuries and death have been speculated to be causally related to hypotension in otherwise healthy patients undergoing shoulder surgery in the BCP.[65] These injuries are extremely rare and arguably fall within the expected rate of perioperative cerebral stroke.[51] Three series that total more than 9300 patients operated on in the BCP reported no cerebral or cervical spinal cord ischemic injuries despite approximately half of patients in both studies experiencing a hypotensive episode (defined as 30% to 40% reduction of baseline MAP, systolic pressure <90 mm Hg, decreased cerebral oxygen saturation, and/or MAP <66 mm Hg). The duration of hypotension experienced by these patients was relatively limited (only 5%–7% of operative time [15–18 minutes]).[77–79] Laflam et al[70] reported in a prospective study that patients operated on in the BCP often experience diminished autoregulation over a wide range of MAP (70 mm Hg; interquartile range, 55–80 mm Hg), yet did not exhibit evidence of brain injury. Overall, these results can be interpreted as supporting the concept of a physiologic reserve that protects the vast majority of patients from injury, even when limited periods of low MAP occur at the brain or cervical spinal cord level while in the BCP.

Perhaps more apropos to patients undergoing neuraxial regional anesthesia, Sharrock and colleagues[80] reported decades of experience with hypotensive epidural anesthesia for total hip arthroplasty, in which their goals were to reduce blood loss and to improve acetabular prosthetic component adherence. Their work can be summarized as induced hypotension to a MAP of 45 to 55 mm Hg that was typically maintained for 30 to 120 minutes, but occasionally longer. Sharrock et al[80] reported that this regimen did not adversely affect renal function, cognitive function,[81] or cardiac function, even in elderly patients with preexisting ischemic cardiac disease and/or hypertension.[82] Of critical importance is understanding that Sharrock and colleagues' intraoperative routine involved much more than using dense epidural anesthesia to induce hypotension. Their regimen included meticulous attention to details such as maintaining neutral spine position, central venous pressure, and cardiac output. With regard to cardiac function, their use of low-dose epinephrine infusion (1–4 μg/min) preserved central venous pressure, heart rate, cardiac stroke volume, cardiac output, and cardiac index. They reported that epinephrine is superior for maintaining these vital parameters, rather than phenylephrine, which adversely affected heart rate and cardiac index.[83,84] Thus, we can infer that, despite prolonged low MAP, Sharrock and colleagues' clinical regimen promoted forward blood flow and avoided excessive cardiac afterload.

To place our argument for increased awareness of blood pressures during neuraxial anesthesia into perspective, the rate of cerebral and spinal cord injury during all surgeries is remarkably low, even under potentially "physiologically stressful conditions" such as the BCP and induced hypotension. The vast majority of patients appear to tolerate limited periods of marginal hypotension. We nevertheless posit that an extremely small subset of patients either lack a physiologic reserve or have a higher set point for their individual LLA, which we speculate increases their susceptibility to a spinal cord ischemic event. Furthermore, positioning in other than the neutral supine position may enhance the vulnerability of these patients to new-onset spinal cord ischemia, whether the positioning alterations are the result of preincision surgical positioning or alterations in local or regional anatomic relationships that result from surgical retraction.

One of the arguments to allow blood pressure to decline, or even to pharmacologically reduce blood pressure to below the patient's baseline values, is a desire to lessen blood loss in the surgical field. The literature is conflicting as to whether this approach results in clinically meaningful reductions in blood loss, especially that requiring blood transfusion.[85] We advise that the relative benefits of general anesthesia versus neuraxial anesthesia be carefully weighed for those patients who may benefit from induced hypotension and that the potential risks of prolonged hypotension be considered for each individual patient.

Recommendations

Recommendations for blood pressure control during neuraxial regional anesthesia are summarized in Table 3. Our previous advisory emphasized the rarity of blood pressure–related CNS injury, but noted that if spinal cord ischemia or infarction occurs the chance for recovery is extremely poor.[86] This current advisory acknowledges scientific and medicolegal reports of ischemic spinal cord injury in patients without obvious risk factors other than a prolonged period of frank or borderline hypotension. Although lower blood pressures are apparently safe in the vast majority of patients, there appears to exist an unpredictable

TABLE 3. Recommendations: Blood Pressure Control During Neuraxial Anesthesia

These recommendations are intended to encourage optimal patient care, but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- Local anesthetics, adjuvants, and their combination have variable effects on SCBF. Reduction of SCBF in the presence of local anesthetics and adjuvants typically mirrors reduction in metabolic demand secondary to spinal cord anesthesia. There is no evidence that either intravenous or intrathecal epinephrine or phenylephrine adversely affects SCBF. (Class I)
- Our understanding of the lower limits of autoregulation of SCBF has evolved recently, based on inferences gained from cerebral LLA studies. Rather than the previously accepted cerebral LLA at a MAP of 50 mm Hg in humans, many experts now believe the cerebral LLA in unanesthetized adults is 60 to 65–mm Hg MAP. There is a wide variability of LLA among subjects. Preexisting hypertension appears to be a poor predictor of LLA except at the extremes of hypertension, eg, systolic pressure >160 mm Hg. (Class II)
- Case reports attest to an extremely small subset of patients who have sustained cerebral or spinal ischemia associated with periods of severe or prolonged low blood pressure. These rare events stand in stark contrast to the common perioperative occurrence of relative hypotension that does not result in spinal cord ischemia. Presumably, injury does not manifest in these patients because of a physiologic reserve that exists between the LLA and blood pressure thresholds below which neurologic injury occurs. (Class III)
- When the LLA of SCBF is approached, specific patient conditions may increase the risk of injury. Such conditions include reduced blood oxygen-carrying capacity, impairment of SCBF from obstructing anatomic lesions, and/or increased spinal cord CSF pressure. (Class I)
- In the absence of compelling reasons to manage a patient otherwise, we recommend that blood pressures during neuraxial anesthesia be maintained in normal ranges or at least within 20%-30% of baseline MAP. When MAP goes below these parameters, we recommend that it not be allowed to persist at those levels. While these recommended parameters are arbitrary, they are inferred based on large population studies that have linked both degree and duration of hypotension to perioperative cerebral, renal, or myocardial injury. (Class II)
- When neuraxial anesthesia or analgesia is followed by unexpectedly prolonged sensory or motor blockade, recrudescence of weakness or sensory changes after initial block resolution, or neural blockade outside the expected distribution of the intended procedure, the anesthesiologist must rule out reversible causes in an expedient manner. At the physician's judgment, this may entail reduction or discontinuation of local anesthetic infusion and reexamination of the patient within an hour or immediate neuroimaging to exclude a compressive process (hematoma or abscess). If imaging is ordered, magnetic resonance imaging is preferable to CT, but the diagnosis should not be delayed if only CT is available. However, if CT rules out a compressive lesion, subsequent magnetic resonance imaging will be necessary if spinal cord ischemia is suspected. (Class I)
- If imaging rules out an operable mass lesion and spinal cord ischemia is suspected, practitioners should ensure at least normal blood pressure or consider inducing high-normal-range blood pressure. The efficacy of CSF pressure modulation via lumbar drains in anesthesia/interventional pain medicine–related spinal cord ischemia is unknown, but the technique is widely used to treat surgery-related spinal ischemia and appears safe in the setting of ischemic spinal cord injury. (Class III)
- The role of corticosteroids in anesthesia-related injuries is unknown. Corticosteroids may have a beneficial effect after direct spinal cord trauma resulting from interventional procedures. However, the potential benefits for these patients should be balanced against the associated risk of corticosteroid-associated hyperglycemia; ie, hyperglycemia worsens brain (and presumably spinal cord) ischemic injury. We do not recommend the use of corticosteroids for ischemic spinal cord injury. Definitive diagnosis and treatment are best determined in consultation with neurology or neurosurgery colleagues. (Class III)

subset of patients who are at risk of spinal cord injury when low blood pressure is associated with spinal stenosis,[13,66,87] anemia (reduced oxygen-carrying capacity),[66] hypocapnia, raised intrathoracic pressure (eg, during mechanical ventilation in lung-injured patients), extremes of patient position, chronic hypertension, unrecognized vascular abnormalities, variation in the LLA, or as yet undiscovered conditions. The panel therefore recommends that anesthesiologists strive to maintain blood pressure within 20% to 30% of baseline and that persistent hypotension be treated, especially in the absence of neuromonitoring that could identify any new-onset insults. This may be especially true in pediatric patients, particularly infants, who normally have lower baseline MAPs than adults and who manifest higher epidural space pressures upon injection of fluid.[26,30]

Diagnosis and Treatment

If signs and symptoms of spinal cord ischemia occur, rapid intervention is mandatory to rule out potentially correctable causes such as spinal hematoma or abscess. Based on clinical presentation, the anesthesiologist may elect to reduce or stop the local anesthetic infusion and reevaluate the patient within an hour or alternatively proceed directly to imaging to rule-out a treatable intraspinal mass. For diagnosing ischemia, magnetic resonance imaging scan may be normal within the first few hours of symptoms, but hours to days later, it may reveal focal cord swelling or hyperintensities on T2-weighted images.[57,88,89]

If ischemia is suspected, normalizing or inducing high-normal-range blood pressure and/or CSF drainage have been recommended, but their effectiveness is not fully supported by the literature.[51] While limited data support the role of CSF lumbar drainage in aortic aneurysm surgery[90] and its use is generally safe,[91] there are no data specific to its efficacy in anesthesia- or pain medicine procedure–related injuries.

Likewise, there are no data specific to the role of corticosteroids in anesthetic or pain medicine intervention–associated neuraxial injury; we are thus left to extrapolate the literature of brain and spinal cord traumatic injury, and cerebrovascular ischemia, to anesthesia-related injuries. Although controversial,[92] corticosteroid drugs have Cochrane Review–level evidence for improving outcome after acute traumatic spinal cord injury.[93] Conversely, corticosteroids have been shown not advantageous for acute head injury[94] or cerebral stroke.[95] Furthermore, a considerable and growing body of literature reports that corticosteroids can be directly injurious (ie, glucose independent) to hypoxic/ischemic animal spinal cords,[96] neurotoxic to human brains after traumatic brain injury,[97] and secondarily neurotoxic as a result of increases in blood glucose concentrations.[92,98,99] While fully acknowledging this conflicting literature and the absence of studies directly related to anesthesia-related injuries, the advisory panel suggests that administration of corticosteroids may be beneficial in cases of direct spinal cord trauma related to interventional procedures. However, because steroid administration has been shown in animals and humans to worsen outcome in the setting of neurologic

ischemia, we recommend that corticosteroids not be used in suspected cases of spinal cord ischemia or infarction. In either case, maintenance of normoglycemia (such as through administration of insulin in a previously hyperglycemic patient) is advised. We recommend neurologic consultation to help evaluate the nature and mechanisms of any insults and to coordinate possible treatments.

Establishing "Baseline Blood Pressure"

There are no reliable historical or diagnostic criteria that identify patients susceptible to spinal ischemia in the setting of neuraxial regional anesthesia. Furthermore, most studies have failed to link baseline hypertension to an increased risk of anesthesia-associated ischemic cerebral or spinal cord injury. Just as there are no firm guidelines for what constitutes the SCBF LLA and for what duration blood pressures less than the LLA become injurious, the determination of "baseline blood pressure" in an individual patient is difficult. A recent study[100] observed that MAP of less than 55 mm Hg, particularly if lasting longer than 20 minutes, predicted a higher rate of adverse cardiac and renal (not cerebral) outcomes in 33,000 noncardiac surgery patients. Nevertheless, we agree with the editorial opinion[101] that such results cannot be extrapolated to an individual patient. Moreover, recent studies have discovered that average preoperative blood pressures are not predictive of the LLA.[69,70]

Despite the unclear relationship of baseline blood pressure to LLA, anesthesiologists nevertheless often wish to ascertain a patient's baseline MAP. A study that sought to correlate perioperative blood pressures to true baseline found that a normal blood pressure obtained on arrival in the operating room closely approximated that patient's true baseline. However, if the first operating room blood pressure was hypertensive, it was less likely to represent baseline. Instead, an average of ambulatory blood pressures over the past 7 months or a preoperative blood pressure obtained 1 to 30 days prior to surgery more accurately reflected that patient's baseline.[102]

Transforaminal Pain Medicine Procedures

We have previously detailed the emerging evidence linking use of particulate steroids with catastrophic neural injuries when administered for treatment of painful conditions via the transforaminal route. Reported complications include spinal cord infarction, cortical blindness, paralysis, and death.[103–105] As noted in our 2008 advisory, "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,[106,107] thoracic, lumbar, and sacral portions of the spine (Fig. 5). Subsequent injection of particulate steroid preparations can result in occlusion of the distal arterioles within the spinal cord or brain and lead to infarction.[104] In the interim since the 2008 practice advisory, a collaboration between the US Food and Drug Administration's Safe Use Initiative and a group with representation from numerous specialties with interest and expertise in treating spinal disorders led to the publication of an article that reviews the existing evidence regarding transforaminal injections and catastrophic neural injuries and puts forward a series of expert opinions meant to improve safety.[108] We will henceforth summarize the newer evidence that has emerged regarding transformational injections.

Additional evidence has emerged that direct traumatic injury to the spinal cord can and rarely does occur during cervical transforaminal techniques,[109,110] but the cardinal neurologic complications of this procedure are infarctions of the spinal cord, brainstem, cerebrum, or cerebellum.[111–121] A review of closed claims identified 9 instances of spinal cord infarction, although the overlap with the published case reports could not be determined.[110] The literature reporting paraplegia following lumbar transforaminal injections has also grown.[122–126] Particulate steroids were used in all cases, and the suspected mechanism of injury was either injection of steroids into a radiculomedullary artery or spasm of an artery when disturbed by a needle.

The role of particulate steroids as causative agents in producing neurologic injury after intra-arterial injection has been further clarified. In vitro studies note that methylprednisolone has the largest particles, betamethasone the smallest, and dexamethasone has no particulate matter.[127] Animal studies have clearly demonstrated that injection of particulate methylprednisolone into the vertebral artery or internal carotid artery can lead to strokes similar to those seen in published human case reports.[128,129] Such injuries did not occur after the injection of the nonparticulate steroid dexamethasone. The amassing evidence strongly suggests that intra-arterial injection of particulate steroids is a mechanism underlying some spinal or cerebrovascular complications of cervical transforaminal injections. In virtually all case reports of infarction following cervical transforaminal injection of steroids, particulate steroids were used. There is now evidence from small studies that demonstrates the effectiveness of dexamethasone is not significantly less than that of particulate steroids.[130,131] Further studies comparing particulate, nonparticulate, and other injectates are much needed, because many practitioners still strongly believe that particulate steroids are associated with more profound pain relief that is of longer duration than that provided by the nonparticulate steroid dexamethasone.

Our 2008 recommendations regarding transforaminal injections[6] have been modified to align with the 2015 US Food and Drug Administration's Safe Use Initiative.[108] These revised recommendations are presented in Table 4.

TABLE 4. Recommendations: Transforaminal Injection Techniques

These recommendations are intended to encourage optimal patient care, but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.
• To avoid direct injection into critical structures, final position of an immobile needle during transforaminal injection should be confirmed by injecting contrast medium under real-time fluoroscopy and/or digital subtraction imaging, using an anteroposterior view, before injecting any substance that may be hazardous to the patient. (Class III)
• Because of the significantly higher risk of catastrophic neurologic injuries associated with cervical transforaminal injections, particulate steroids should not be used in therapeutic cervical transforaminal injections. (Class III)
• Although the risk of neurologic injury is markedly lower when performed at lumbar levels, a nonparticulate steroid (eg, dexamethasone) should be used for the initial injection in lumbar transforaminal epidural injections. (Class III)
• Particulate steroids can be considered under some circumstances for lumbar transforaminal injections, eg, after failure to respond to treatment with a nonparticulate steroid. (Class III)

Cauda Equina Syndrome, Local Anesthetic Neurotoxicity, and Arachnoiditis

Our previous article emphasized the unique anatomic and physiologic attributes of the cauda equina that might make it particularly vulnerable to local anesthetic–induced neurotoxicity.[2] These attributes include neural elements that are not fully protected by myelin, have a large surface-to-volume ratio, may experience reduced drug clearance because of limited vascular supply,[132] and may have limited CSF dilutional capacity when local anesthetic is injected into a dural root sleeve[133] (Fig. 7). This current practice advisory addresses 3 topics not fully explored in the first iteration: CES, transient neurologic symptoms (TNS) associated with 2-CP, and arachnoiditis. We have chosen to arbitrarily combine these topics because of a shared presumed mechanism of injury that involves neurotoxicity.

Cauda Equina Syndrome

Similar to emerging concerns regarding spinal canal mass lesion pathologies, CES has been associated with spinal stenosis. In Moen and colleagues'[12] study of 1.7 million neuraxial anesthetics, there were 32 cases of CES, 9 of which occurred in patients with previously undiagnosed spinal stenosis. In theory, a tight spinal canal, perhaps exacerbated by extreme surgical positions, might result in pressure-induced spinal cord ischemia or reduced vascular clearance, either of which might increase cauda equina susceptibility to local anesthetic neurotoxicity. Of the 18 cases of CES associated with spinal anesthesia, 8 patients received lidocaine 5%, 10 received bupivacaine, and 1 received a mixture of the 2.

Of perhaps greater concern from Moen and colleagues'[12] study is that 23 of 32 cases were associated with nothing extraordinary in terms of spinal canal diameter, local anesthetic dosing, potential needle trauma, or abnormal postinjury imaging, all of which emphasize the unclear etiology of this syndrome. Although there are several known risk factors for the development of CES, we will offer 2 additional speculative mechanisms. With regard to known risk factors, data from the French surveillance studies[134,135] and reports of CES associated with microcatheter continuous spinal anesthesia[136] strongly suggest that CES can result from supernormal doses of intrathecal local anesthetics and/or maldistribution of local anesthetic spread within the caudad intrathecal sac. Based on a limited understanding of the mechanism of CES injury, we speculate that, in addition to supernormal dose

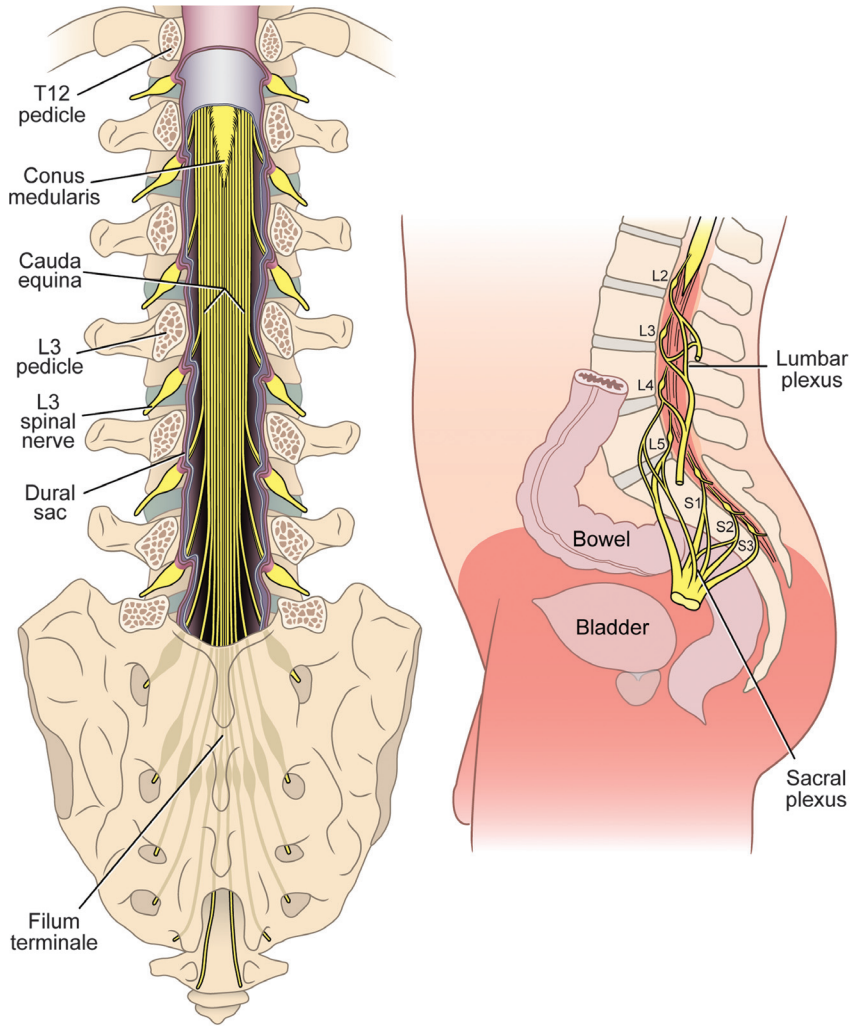

FIGURE 7. The cauda equina may be particularly prone to local anesthetic neurotoxicity because of the large surface area afforded by the long travel distance of nerve roots that have only partial or absent myelin covering. Illustration by Gary J. Nelson. Reproduced with permission from Neal and Rathmell, *Complications in Regional Anesthesia and Pain Medicine*.[32]

and maldistribution of local anesthetic, (1) an extremely small subset of humans may be predisposed to neurotoxicity from clinically appropriate doses of local anesthetic. Alternatively, we speculate that (2) abnormal neural inflammation may occur in response to exposure to local anesthetic, adjuvant, needle trauma,[12,137] or other factors unrelated to the anesthetic. While the majority of cases of CES occur in patients with no known risk factors or no identified improper anesthetic technique, clinicians are advised to carefully weigh the risks to benefits of subarachnoid anesthesia in patients with known moderate to severe lumbar spinal stenosis and to avoid redosing failed, partial, or maldistributed spinal anesthetics (or at least not exceed the total recommended maximum dose).[138]

Local Anesthetic Neurotoxicity

Transient neurologic symptoms after spinal anesthesia were the subject of significant scientific inquiry nearly 2 decades ago.[139] Experts continue to debate the etiology of TNS and whether it represents a forme fruste of neurotoxicity. At the time of our first advisory, several laboratory studies had examined for possible 2-CP–related neurotoxicity,[140–142] but there was limited clinical research to confirm or refute whether 2-CP might indeed be neurotoxic in humans.[143,144] Within the past few years, several reports have described the apparently safe use of low-dose (40–50 mg) spinal 2-CP in terms of TNS,[145–147] albeit the patient numbers are too small to adequately judge overall safety for an event as rare as CES. Indeed, a study comparing 2-CP to lidocaine for ambulatory transurethral prostate resection described a case of incomplete CES (confirmed by positive nerve conduction study and electromyographic deficits) that resolved completely after several weeks in a subject who received 2-CP.[148] Intrathecal 2-CP remains an off-label indication in the United States; however, in 2013, a 1% 2-CP solution was approved for intrathecal use in Europe. Based on the absence of appropriately powered studies for rare events, we cannot offer a recommendation with regard to intrathecal 2-CP and CES. However, we acknowledge a growing research literature that attests to acceptably low risk of TNS after low-dose intrathecal 2-CP.

Arachnoiditis

Arachnoiditis was not addressed in our previous advisory. This poorly understood entity describes diffuse inflammatory reaction of the 3 meningeal layers that manifests clinically in a spectrum from pain and disability to hydrocephalus and death. Historically, arachnoiditis has been associated with infection, trauma, intrathecal blood, contrast media, neuraxial hypertonic saline,[149] and multiple back surgeries.[150] Two potential etiologies are especially pertinent to the regional anesthesiologist and pain physician. While allergic, inflammatory, or idiosyncratic reactions to local anesthetics have been entertained as an etiologic factor for arachnoiditis, reasonably large studies suggest that if this association exists it is exceedingly rare.[12,151–153] Attention has also been paid to the role of skin disinfectants. The latter concern stems from case reports[154,155] of severe arachnoiditis after spinal or epidural anesthesia in which the "most likely mechanism" involved contamination by chlorhexidine. Many of these cases presented with remarkable similarity—headache or extremity burning immediately after injection of the local anesthetic, followed days later by evidence of increased intracranial pressure from hydrocephalus that required shunting, followed weeks later by progressive motor and sensory impairment to the point of paraplegia and chronic pain. This delay in major symptoms confounds identification of these cases by typical anesthesia surveillance mechanisms, but also argues for an idiosyncratic mechanism that might stem from an early, minor inflammatory reaction of the meninges in response to a drug, disinfectant, or other triggers.

The role of chlorhexidine/alcohol mixtures in the etiology of arachnoiditis is unclear and circumstantial. Numerous contemporary studies point to the clear superiority of chlorhexidine for skin asepsis as compared with povidone-iodine. This has resulted in the American Society of Regional Anesthesia and Pain Medicine,[9] the ASA,[156] the Centers for Disease Control and Prevention, and the Royal College of Anaesthetists[152] recommending chlorhexidine as the skin disinfectant of choice. A retrospective cohort study of 12,465 spinal anesthetics in which 2% chlorhexidine gluconate in isopropyl alcohol was used for skin antisepsis did not find increased risk of any neuraxial complication over historical controls (57 cases lasting <30 days; 0.04%; 95% confidence interval, 0.00%–0.08%).[157] An in vitro study of human neuronal and rat Schwann cells found that chlorhexidine was no more cytotoxic than povidone-iodine at relevant clinical concentrations. Furthermore, the amount of dried antiseptic carried by a needle tip from skin-to-subarachnoid space was calculated to undergo a 1:145,000 dilution.[158]

Based on the superiority of chlorhexidine as an antiseptic and the extremely low likelihood that it would cause arachnoiditis under normal clinical conditions, the advisory panel continues to recommend it as the disinfectant of choice for neuraxial and peripheral nerve block techniques. Nevertheless, practitioners are advised to physically and temporally separate chlorhexidine from the block procedure itself. This implies allowing the solution to completely dry prior to needle placement (2–3 minutes). Steps should be taken to avoid chlorhexidine contamination of the block tray and/or drugs intended for intrathecal administration, as might occur from splashing or dripping the disinfectant, disposal of the applicator device near the block setup area, or pouring liquid chlorhexidine into receptacles where it could be mistaken for other drugs.

Recommendations regarding CES, local anesthetic neurotoxicity, and arachnoiditis are presented in Table 5.

TABLE 5. Recommendations: CES, Local Anesthetic Neurotoxicity, and Arachnoiditis

These recommendations are intended to encourage optimal patient care, but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.
• 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. In addition, maldistribution (usually sacral) of local anesthetic spread should be ruled out prior to redosing single-injection or continuous subarachnoid blocks. (Class I)
• The risk-to-benefit analysis of neuraxial techniques should be considered in patients known to have moderate to severe spinal stenosis, especially if within the vertebral territory of the intended injection. (Class II)
• The incidence of TNS after 40–50 mg intrathecal 2-CP appears to be remarkably low. The number of 2-CP spinal anesthetics reported in the literature is insufficient to determine the risk of CES or other manifestations of neurotoxicity. (Class III)
• Physically and temporally separate chlorhexidine use from block trays and instruments during neuraxial procedures. Allow the solution to completely dry on skin prior to needle placement (2–3 min). Care should be taken to avoid needle or catheter contamination from chlorhexidine spraying or dripping, or from applicator device disposal, onto aseptic work surfaces. (Class II)

Neuraxial Procedures on Anesthetized or Deeply Sedated Patients

"We define the *anesthetized patient* as one who is under general anesthesia. A *deeply sedated patient* is one who is sedated to the point of being unable to recognize and/or report any sensation that the physician would interpret as atypical during block placement."[3] In either case, the patient's state of wakefulness is insufficient to support cognizance of potentially deleterious events during the procedure. The appropriateness of performing regional anesthesia and interventional pain medicine procedures in unresponsive patients continues to be debated. Indeed, this topic is an outstanding example of how individuals of similar expertise can arrive at different recommendations after review of the same, albeit limited, data set. For example, some European experts endorse (particularly peripheral) regional blockade in anesthetized or deeply sedated patients,[159,160] whereas the majority of North American experts advise against this practice in adult patients.

We previously reviewed the pathophysiology of this issue in detail. A substantial body of literature points to divergent descriptions of how patients report needle–to–spinal cord contact. Some reports describe paresthesia or abnormal sensation when a needle enters the spinal cord, especially if accompanied by injection; injury, if it occurred at all, often was associated with these warning signs. Conversely, there also exist reports of fully awake or minimally sedated patients who sustained neuraxial injury but reported no unusual sensations during needle placement.[2,3] Thus, one may argue that because "the neuroanatomy of the spinal cord and its coverings cannot be consistently relied upon to provide warning or indication of needle or catheter-induced trauma,"[2,161] so too wakefulness cannot be relied upon as critical to the detection of impending injury. Nevertheless, our 2008 practice advisory categorized wakefulness as a potentially useful monitoring tool when used during adult, but not pediatric, neuraxial anesthesia, or pain medicine procedures. Importantly, wakefulness is not limited as a monitor of nerve injury but may also play a role in recognizing neuraxial-related complications such as high spinal anesthesia or evolving local anesthetic systemic toxicity.[30,162]

Neuraxial Anesthesia in the Anesthetized or Deeply Sedated Pediatric Patient

Although the absolute risks in either scenario are unknown, as stated in our 2008 practice advisory, "the argument to perform neuraxial anesthesia in anesthetized or deeply sedated children is predicated on the likely higher risk of injuring a moving and/or uncooperative child during placement of a neuraxial-directed needle versus the (presumably) much lower risk of injuring the spinal cord even in the absence of patient feedback."[3] Emerging data from large-scale pediatric registries have strengthened the evidence base for our previous recommendation. These large registries—2 from the French-Language Society of Pediatric Anaesthesiologists[163,164] and one each from the Association of Pediatric Anaesthetists of Great Britain and Ireland[165] and the (North American) Pediatric Regional Anesthesia Network (PRAN)[166,167]—include more than 100,000 pediatric patients who underwent some form of regional anesthesia, with more than 95% of these procedures performed under general anesthesia. The strengths of these studies include their large numbers, relatively robust follow-up, and practitioner experience. The weaknesses include a large number of caudal anesthetics and admixing of an increasing number of peripheral nerve blocks. Nevertheless, overall analysis points to very few long-term neuraxial injuries, with an incidence similar to the "expected" 0 to 2 injuries per 10,000 blocks. Thus, performing neuraxial regional blockade in anesthetized pediatric patients does not appear to place these patients at increased risk of injury that is higher than baseline expectation. Indeed, there is some evidence that general anesthesia may reduce some injuries as compared with those recorded in awake children.[167] Nevertheless, these data should not be interpreted as a license to lower one's vigilance during these procedures. A case series described 3 permanent neuraxial injuries and 1 unrecognized high spinal anesthetic in children who had thoracic epidural anesthesia placed during general anesthesia by experienced pediatric anesthesiologists.[30] These cases emphasize that neuraxial procedures carry inherent risk regardless of patient wakefulness.

Neuraxial Anesthesia in the Anesthetized or Deeply Sedated Adult Patient

Just as new data are supportive of our previous recommendations regarding pediatric patients, our 2008 recommendation to not routinely perform neuraxial regional anesthesia in anesthetized or deeply sedated adults gained further support from the ASA Closed Claims project.[110] An analysis of injuries associated with cervical procedures for chronic pain noted that general anesthesia or deep sedation was used in 67% of those cervical procedure *claims* wherein the cervical spinal cord sustained injury, but only 19% of those cervical procedure *claims* that were not associated with cord injury. Of those patients who were nonresponsive during the cervical procedure, 25% sustained injury to their cervical spinal cord. This is compared with only 5% of responsive patients sustaining a cord injury associated with their

TABLE 6. Recommendations: Performing Neuraxial Techniques in Anesthetized or Deeply Sedated* Patients

These recommendations are intended to encourage optimal patient care, but cannot ensure the avoidance of adverse outcomes. As with any practice advisory recommendation, these are subject to revision as knowledge advances regarding specific complications.

- Monitoring and prevention: There are *no data to support the concept that ultrasound guidance of needle placement reduces the risk of neuraxial injury* in patients under general anesthesia or deep sedation. (Class II)
- 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 deep sedation removes any ability for the patient to recognize and report warning signs. This suggests that neuraxial regional anesthesia *or interventional pain medicine procedures* should be performed rarely in adult patients whose sensorium is compromised by general anesthesia or deep sedation. *Adult patients with specific conditions (eg, developmental delay, multiple bone trauma) may be appropriate exceptions to this recommendation after consideration of risk versus benefit. (Class III)*
- Pediatric neuraxis: The benefit of ensuring a cooperative and immobile infant or child *likely outweighs* the risk of performing neuraxial regional anesthesia in pediatric patients during general anesthesia or deep sedation. The overall risk of neuraxial anesthesia should be weighed against its expected benefit. *(Class I)*

**Anesthetized* refers to patients under general anesthesia. *Deep 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.

Recommendations contained within Table 6 have been modified from our 2008 advisory.[3] Significant changes are in italics.

cervical procedure. While analysis of legal claims can establish neither incidence nor cause and effect, this information nevertheless suggests that conducting neuraxial procedures (at least around the cervical spine) in unresponsive patients may increase the likelihood of subsequent neuraxial injury.

An often-misunderstood recommendation from our 2008 practice advisory was that interscalene blocks not be performed routinely in anesthetized or deeply sedated adults or children. We speculate that confusion on this topic occurred because the recommendation was based on medicolegal concerns rather than specific scientific evidence that interscalene blocks per se are more or less risky than other peripheral nerve blocks in anesthetized or deeply sedated patients. Our primary intent was to emphasize the existence of literature that describes cervical spinal cord injury in patients who underwent interscalene block during general anesthesia and sustained significant cervical spinal cord injury.[168] Whether general anesthesia was a contributor to these injuries will never be known with certainty, but a similar body of "plaintiff-friendly" literature does not exist for other blocks. In the interim since our last advisory, the PRAN registry reported no postoperative neurologic symptoms associated with 390 pediatric interscalene blocks (upper limit of 95% confidence interval, 0.77%).[169] This report appears to corroborate findings from recent pediatric regional anesthesia registries—that regional blocks in anesthetized or deeply sedated children may be no more risky that regional anesthesia in awake adults. However, the number of interscalene blocks reported in PRAN is insufficient for us to make a definitive recommendation on this issue.

Recommendations for performing procedures on anesthetized or deeply sedated patients are summarized in Table 6.

Summary

This practice advisory offers additional information and recommendations on selected topics from our 2008 advisory. Despite this new information, our summary of the topic has not changed: "The pathophysiology of neuraxis injury associated with regional anesthesia and pain medicine procedures presumes that a mechanical, vascular, neurotoxic, or a combination insult has occurred. With the exception of epidural hematoma or abscess, the linkage of patient injury to a specific anesthetic procedure or perioperative event is mostly one of association rather than causation. Importantly, many of the factors that may contribute to neuraxis injury cannot be identified prospectively, which suggests that a large portion of these injuries are unpreventable based on our current knowledge. Fortunately, neuraxis injuries associated with regional anesthesia or pain medicine procedures are exceedingly rare."[2]

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APPENDIX 1. Strength of Recommendations

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

This classification system is significantly modified from the American College of Cardiology/American Heart Association construct for classifying strength of evidence.[170]

Regional Anesthesia in Patients With Preexisting Neurologic Disease

Sandra L. Kopp, MD, Adam K. Jacob, MD, and James R. Hebl, MD

What's New: Since publication of initial recommendations in 2008, there is limited new information regarding the performance of regional anesthesia in patients with preexisting neurologic diseases. However, the strength of evidence has increased since 2008 regarding (1) the concern that diabetic nerves are more sensitive to local anesthetics and perhaps more susceptible to injury and (2) the concern that performing neuraxial anesthesia and analgesia in patients with preexisting spinal canal pathology may increase the risk of new or worsening neurologic symptoms. This increased evidence reinforces our initial recommendations. In addition, since the initial recommendations in 2008, the concept of postsurgical inflammatory neuropathy has been described and is potentially a contributor to postoperative neurologic dysfunction.

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Preexisting disorders of the peripheral nervous system (hereditary neuropathies, diabetic polyneuropathy [DPN], chemotherapy-induced neuropathies, inflammatory neuropathies), central nervous system (multiple sclerosis [MS], postpolio syndrome [PPS], amyotrophic lateral sclerosis [ALS]), and spinal canal pathology present a challenge to patients and anesthesiologists who desire to use regional anesthetic techniques. Because each of these clinical conditions involves compromise to neural structures, the concern is that further insult from surgical (eg, intraoperative stretch or compression, tourniquet ischemia, hemorrhage) or anesthetic (eg, mechanical trauma, vasoconstrictor-induced ischemia, local anesthetic toxicity) causes may result in new or worsening postoperative neurologic deficits.

Regardless of the underlying etiology, the presence of chronic neural compromise secondary to mechanical (eg, spinal stenosis or compressive radiculopathy), ischemic (eg, peripheral vascular disease), toxic (eg, vincristine or cisplatin chemotherapy), metabolic (eg, diabetes mellitus [DM]), or autoimmune (eg, MS) derangements may theoretically place patients at increased risk of further neurologic injury.[1–3] Upton and McComas[1] were the first to describe the double-crush phenomenon, which suggests that patients with preexisting neural compromise may be more susceptible to injury at another site when exposed to a secondary insult (Fig. 1). Secondary insults may include a variety of surgical or anesthetic risk factors—including regional anesthetic techniques. Osterman[2] emphasized that not only are 2 low-grade insults along a peripheral nerve trunk worse than a single site but also that the damage of the dual injury far exceeds the expected additive damage caused by each isolated insult. It may be further postulated that the second insult need not be along the peripheral nerve trunk itself but rather at any point along the neural transmission pathway. Therefore, the performance of peripheral or neuraxial regional techniques in patients with preexisting neurologic disorders may theoretically place them at increased risk of a double-crush phenomenon.

Unfortunately, the rarity of these disease processes results in a paucity of clinical data that are often conflicting in their outcomes and conclusions. As a result, definitive recommendations can rarely be made from the existing scientific literature (Table 1). However, the following commentary provides a comprehensive review of the available literature on the topic so that patients and clinicians can make an informed decision on the potential neurologic risk of performing regional anesthesia in the presence of preexisting neurologic disorders.

METHODS

Standard search engines and cross-referencing material contained therein provided the literature basis for updated material contained within this review. PubMed and Ovid were searched from 2006 onward to identify new material since our original practice advisory search. MESH terms included individual headings and their relevant combinations, including "regional anesthesia," "peripheral nerve blockade," "spinal anesthesia," "epidural anesthesia," "peripheral neuropathy," "Charcot-Marie-Tooth disease," "diabetic polyneuropathy," "chemotherapy-induced peripheral neuropathy," "Guillain-Barré syndrome (GBS)," "postsurgical inflammatory neuropathy," "post-polio syndrome," "multiple sclerosis," "amyotrophic lateral sclerosis," "traumatic spinal cord injury," "spinal stenosis," "lumbar radiculopathy," and "lumbar disk disease." All prospective randomized controlled trials, retrospective studies, case-controlled cohort studies, case series, and case reports were included for review.

PERIPHERAL NERVOUS SYSTEM DISORDERS

The peripheral nervous system is composed of numerous cell types that serve diverse sensory, motor, and autonomic functions. Signs and symptoms of impaired function depend on the distribution and severity of the injury, in addition to the specific element of the nerve that is affected. More than 100 types of peripheral neuropathy have been identified, each with its own pathophysiology, symptoms, and prognosis.[4]

Hereditary Peripheral Neuropathy

Inherited neuropathies represent a heterogeneous group of diseases that often share the features of an insidious onset and indolent course across years to decades. A wide range of genotypes may result in phenotypes ranging from mild symptoms and subclinical disease to severe debilitating conditions. The most common inherited neuropathies are a group of disorders collectively

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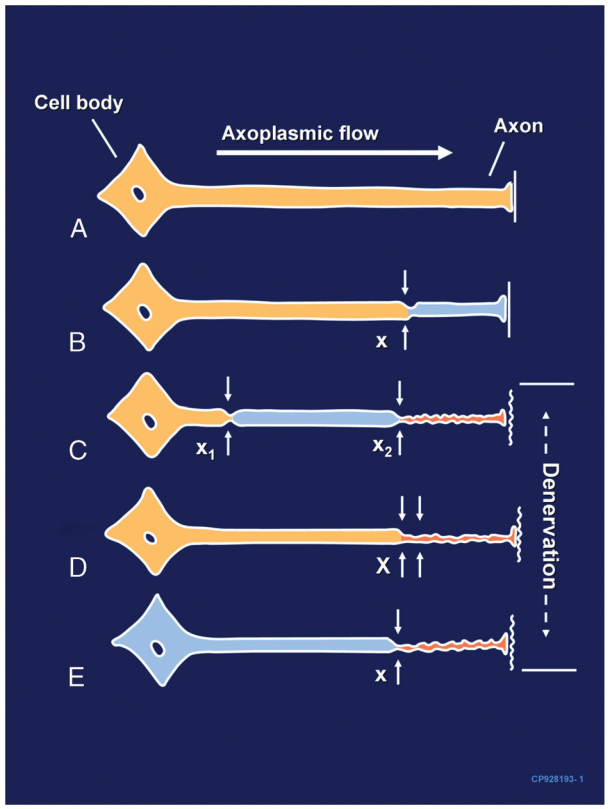

FIGURE 1. Neural lesions resulting in denervation. Axoplasmic flow is indicated by the degree of shading. Complete loss of axoplasmic flow results in denervation (C, D, E). A, Normal neuron. B, Mild neuronal injury at a single site (x) is insufficient to cause denervation distal to the insult. C, Mild neuronal injury at two separate sites (x_1 and x_2) may cause distal denervation (ie, double crush). D, Severe neuronal injury at a single site (X) may also cause distal denervation. E, Axon with a diffuse preexisting underlying disease process (toxic, metabolic, ischemic) may have impaired axonal flow throughout the neuron that may or may not be symptomatic but predisposes the axon to distal denervation after a single minor neural insult at x (ie, double crush) (by permission of Mayo Foundation for Medical Education and Research).

referred to as Charcot-Marie-Tooth (CMT) disease. Charcot-Marie-Tooth disease affects approximately 1 in 2500 people, often beginning during childhood or adolescence.[5] Charcot-Marie-Tooth neuropathies are caused from mutations in more than 30 genes responsible for manufacturing neurons or the myelin sheath.[6] Typical signs and symptoms include extreme motor weakness and muscle wasting within the distal lower extremities and feet, gait abnormalities, loss of tendon reflexes, and numbness within the lower limbs.

The reported use of peripheral[7,8] or central[9–12] regional anesthetic techniques in patients with CMT disease has been limited to small case series and anecdotal case reports. All patients made uneventful recoveries without worsening of their neurologic conditions. Of note, 2 cases involving single-injection regional techniques (epidural anesthesia using 18 mL of 0.75% ropivacaine[10] and supraclavicular analgesia using 30 mL of 0.5% bupivacaine[7]) reported a prolonged effect (12 hours and 30 hours, respectively) of the regional technique compared with the anticipated duration. In both cases, the use of higher concentrations of local anesthetic may have contributed to the delayed recovery.

Hereditary neuropathy with liability to pressure palsy (HNPP) is another rare inherited demyelinating peripheral neuropathy in which individuals have repeated motor and sensory neuropathies (pressure palsies) after a brief nerve compression or mild trauma. Discovered in the early 1990s, HNPP has been linked to a mutation on the *pmp-22* gene, resulting in reduced myelin production. Evidence discussing the use of any regional technique in the setting of HNPP has been limited to a single case report. Lepski and Alderson[13] reported the successful use of labor epidural analgesia in a 24-year-old parturient with HNPP. The patient made an uneventful recovery without worsening of her neurologic condition.

Based on the lack of clinical evidence, definitive recommendations cannot be made about safety and use of regional anesthesia in patients with preexisting inherited peripheral neuropathies. However, isolated case reports would suggest that peripheral and central regional techniques *may* be used without worsening a patient's stable neurologic condition. However, caution should be used to minimize other surgical and anesthetic risk factors for perioperative nerve injury when considering the use of regional anesthesia within this patient population.

Acquired Peripheral Neuropathy

Diabetic Polyneuropathy

The increasing prevalence of DM and its associated comorbidities will likely translate into a larger number of diabetic patients presenting for surgery. However, despite the clinical benefits and widespread use of regional anesthesia (peripheral and neuraxial blockade), there remains concern regarding its use in patients with DM.[14–17] It has been suggested that patients with a history of chronic neural compromise secondary to metabolic conditions such as diabetes may be at an increased risk of worsening neurologic injury after neuraxial or peripheral nerve blockade.[14–17]

Diabetes mellitus is currently the most common cause of systemic polyneuropathy. There are several types of neuropathy associated with DM. However, distal symmetric sensorimotor polyneuropathy is the most common form and generally synonymous with the term "diabetic polyneuropathy." The frequency of DPN ranges from 4% to 8% at the time of diagnosis to more than 50% in patients with long-standing diabetes. Despite the fact that patients may be asymptomatic, nearly all will have evidence of abnormal nerve conduction.[18,19] Furthermore, it is not uncommon for patients to present for surgery with either undiagnosed DM or known diabetes with uncontrolled hyperglycemia.[20]

The pathophysiology of DPN is poorly understood and likely multifactorial. Early symptoms such as numbness, pain, and autonomic dysfunction are caused by damage to small nerve fibers, which occurs before damage to large fibers becomes apparent.[21] There is pathophysiologic evidence of abnormalities in both large and small neural blood vessels, ultimately contributing to multifocal fiber loss. Axonal degeneration is the most prominent feature of DPN and occurs secondary to the reduced delivery of essential nutrients and other components (oxygen, blood, adenosine triphosphate, glucose) to the axon. Proposed mechanisms include (1) sorbitol deposition in the nerve because of glucose accumulation, (2) local tissue ischemia in sensory and autonomic fibers secondary to endoneurial hypoxia, (3) abnormal tissue repair mechanisms caused by excess glucose, and (4) mitochondrial dysfunction within the dorsal root ganglia.[22–24]

Currently, there is an abundance of animal data that suggests diabetic nerves may have an increased risk of neurologic injury after regional anesthesia compared with nondiabetic nerves.[25–27] Kalichman and Calcutt[17] were the first to hypothesize that diabetic

nerve fibers may be more susceptible to local anesthetic neurotoxicity for 2 reasons: (1) the nerve is more susceptible to injury because of chronic ischemic hypoxia and (2) the nerves are exposed to larger concentrations of local anesthetics because of a decreased perineural blood flow. More recently, these findings were supported with both animal and clinical data. Lirk and colleagues [28] used Zucker diabetic fatty rats exposed to hyperglycemia to demonstrate that, although the overall neuronal survival difference was low, in vitro local anesthetic neurotoxicity was more pronounced in neurons from diabetic animals. The authors also reported that preexisting subclinical neuropathy led to substantial prolongation of the block duration in vivo. Kroin and colleagues[26] also reported that the duration of sciatic nerve block with lidocaine 1% or ropivacaine 0.5% was longer in streptozotocin-induced diabetic rats compared with nondiabetic rats, and that block duration actually correlated with nerve fiber degeneration. In a subsequent study, the same authors also concluded that, with continuous glycemic control, diabetic rats had a block duration that was similar to nondiabetic rats and 40 minutes shorter than rats without glycemic control.[25] Interestingly, acute glycemic control did not lessen the nerve block duration, suggesting that diabetic neuropathy is not rapidly reversed within this animal model. Currently, it is unclear whether the results from animal studies using experimentally induced hyperglycemia can be used to make recommendations about patients with long-standing DM.[29]

Although animal studies have consistently found that diabetic nerves are more sensitive to local anesthetics and potentially more susceptible to neural injury, it is unclear whether diabetic patients have a higher incidence of neurologic injury after regional anesthesia.[17,25,26,30] There is limited clinical data suggesting that the success of peripheral nerve blockade (supraclavicular brachial plexus) may be higher in diabetic patients independent of other predictors of success (eg, body mass index) compared with nondiabetic patients.[31,32] Gebhard and colleagues[30] propose several theories for this finding, including (1) a higher sensitivity of diabetic nerve fibers to local anesthetics, (2) possible unknown intraneural penetration before injection, and (3) preexisting DPN with accompanying decreased sensation. Preexisting pathology has long been reported to play a role in the development of postoperative neurologic dysfunction.[33–35] A recent case report described a persistent postoperative femoral neuropathy after discontinuing a femoral nerve catheter in a patient with a preexisting subclinical diabetic neuropathy that was undiagnosed preoperatively.[36]

In patients with DM, a decreased sensitivity to electrical stimulation combined with diminished sensory function and an increased sensitivity to local anesthetic toxicity may increase the risk of intraneural injection during peripheral nerve blockade using a peripheral nerve stimulator.[37–39] Currently, there is a lack of clinical evidence suggesting that the use of ultrasound guidance is safer than peripheral nerve stimulation within the general population.[40,41] However, this lack of clinical benefit may be less clear for diabetic patients. For example, there are a limited number of animal and clinical studies that suggest ultrasound guidance may be a more desirable method of neural localization in diabetic patients. Animal studies have shown that low-threshold electrical stimulation may not offer protection from intraneural injection in the presence of hyperglycemia. Rigaud and colleagues[42] demonstrated that all needle insertions within a hyperglycemic dog model resulted in intraneural injection (6 of 6); whereas only one (1 of 18) intraneural injection occurred among control dogs. Sites and colleagues[39] also concluded that ultrasound guidance may be a preferred method of neural localization in diabetic patients after failing to elicit a motor response or paresthesia in 2 patients undergoing sciatic nerve blockade using peripheral nerve stimulation. The authors describe a very weak motor response in both diabetic patients with a stimulating current of more than 2.4 mA despite perineural placement of the stimulating needle using ultrasound guidance. Another potential application of ultrasound technology is the ability to use the cross-sectional area of a peripheral nerve to identify a clinical or subclinical peripheral neuropathy; a diagnosis that historically would require complex nerve conduction studies.[43,44]

Findings of spinal cord involvement in diabetic patients suggest that the same or similar mechanism of injury may affect not only peripheral nerves but also neural elements within the central neuraxis as well.[45,46] Using magnetic resonance imaging, Selvarajah and colleagues[47] described early central nervous system involvement consisting of a significant reduction in spinal cord cross-sectional area in patients with both subclinical and clinically detectable diabetic peripheral neuropathy. A case report of a diabetic patient experiencing a persistent lower-extremity neuropathy after what appeared to be an uneventful epidural analgesia reinforces concerns that diabetic patients may be at an increased risk of neurologic injury after neuraxial anesthesia.[48] A retrospective review also evaluated neurologic complications in patients with preexisting peripheral sensorimotor neuropathy or DPN who subsequently underwent neuraxial anesthesia or analgesia.[22] Of the 567 patients studied, 2 (0.4%; 95% confidence interval [CI], 0.1%–1.3%) experienced new or progressive postoperative neurologic deficits when compared with preoperative findings. The authors concluded that, although the risk of severe postoperative neurologic injury among diabetic patients is rare, it appears to be higher than that reported for the general population. Although the neuraxial technique could not be definitively implicated as the primary cause of the neurologic insult, it may have been a contributing factor among patients with preexisting neural compromise. Echevarria and colleagues have also reported faster onset times, a longer duration of maximal block levels, and slower regression times of spinal anesthesia in diabetic patients compared with nondiabetic patients.[49]

In summary, patients with DPN likely have neural elements that are more sensitive to the effects of local anesthetic. As a result, diabetic peripheral nerves may be more susceptible to subsequent injury from local anesthetic toxicity or ischemic insults. Ultimately, the decision to use regional anesthesia within diabetic patients should be made on an individual basis after a thorough discussion with the patient regarding the potential risks and benefits of the technique. Consideration should be given to decreasing the concentration or total dose of local anesthetic for both peripheral and neuraxial techniques,[50] particularly in profoundly symptomatic patients. Furthermore, the use of ultrasound guidance may facilitate perineural needle placement and the use of lower local anesthetic volumes in diabetic patients; although definitive data ensuring increased safety with ultrasound guidance are currently lacking.[51] Decreasing the concentration or dose of local anesthetic or eliminating epinephrine additives should also be considered given that diabetic nerves are already at risk of neural ischemia and infarction because of changes within the endoneural microvasculature.[52]

Chemotherapy-Induced Neuropathy

Chemotherapy-induced peripheral neuropathy (CIPN) is a frequent side effect of several commonly used chemotherapeutic agents. It is a dose-limiting side effect that occurs in approximately 30% to 40% of patients.[53] The exact mechanism of injury is unclear, although damage to microtubules, interference with microtubule-based axonal transport, mitochondrial disruption, and cytotoxic effects on DNA are all possible mechanisms.[53,54]

The neurotoxicity depends on the agent used, the duration of administration, and the cumulative dose received. Cisplatin, oxaliplatin, and carboplatin characteristically induce a purely sensory painful peripheral neuropathy, whereas vincristine, paclitaxel, and suramin tend to induce a mixed sensorimotor neuropathy with or without involvement of the autonomic nervous system.[55] Symptoms are often in the "glove and stocking" distribution and consist of pain or paresthesias. Patients at risk of developing CIPN include those with preexisting neural damage secondary to DM, excessive alcohol use, or an inherited peripheral neuropathy. In general, a prolonged period of regeneration is required to restore neurologic function, with incomplete recovery being the most common outcome.[54–56] However, patients who recover from CIPN are at an increased risk of developing progressive neuropathic symptoms if exposed to additional neurotoxic agents. Local anesthetics are potentially neurotoxic, and caution should be used when deciding whether to perform regional anesthesia in patients who have received chemotherapeutic agents known to cause CIPN. It is not uncommon for patients to have a subclinical neuropathy that only presents after a second neurologic insult, such as a peripheral or neuraxial block.[16]

INFLAMMATORY NEUROPATHIES

Guillain-Barré Syndrome

Guillain-Barré syndrome is an acute, inflammatory, demyelinating polyneuropathy characterized by areflexia and diffuse ascending neuromuscular paralysis. The etiology of GBS is unclear, although infection, pregnancy, vaccinations, immunosuppression, systemic illnesses, and transfusion have all been proposed as potential triggers.[57] The degree and distribution of paralysis are variable and can include sensory nerve, cranial nerve, and autonomic nervous system involvement. Symptoms peak approximately 2 to 4 weeks after the initial onset, with most patients experiencing prolonged recovery. Unfortunately, many patients experience moderate-to-severe neurological impairment for years after the initial diagnosis.

There are several reports of GBS occurring in the postoperative period after a variety of surgical procedures and types of anesthetics.[58–60] However, case reports of regional anesthesia use in patients with GBS are generally limited to the obstetric population.[61–64] Some patients with GBS may have autonomic instability and subsequently experience an exaggerated response to neuraxial blockade,[63] whereas other patients exhibit a normal response to neuraxial anesthesia.[61,64] Although there have been reports of successful neuraxial anesthesia in parturients with GBS, the theoretical concern of local anesthetics interacting with peripheral myelin or direct nerve trauma cannot be ignored.[21] There is some evidence to suggest that epidural anesthesia may precipitate or reactivate GBS hours to weeks after surgery.[58,65,66] However, it is difficult to determine if this is caused by the effects of the epidural, the natural progression of the disease, the surgical procedure, or the stress response related to surgery.

Although it has been suggested that acute neuronal inflammation may be a relative contraindication to regional anesthesia, existing data provide little information regarding the safety of neuraxial anesthesia or peripheral nerve blockade in patients with GBS.[21] Ultimately, the decision to perform regional anesthesia should be made on an individual basis after a thorough discussion with the patient regarding the potential risks and benefits.

Postsurgical Inflammatory Neuropathy

Recently, neurologists have become aware that an autoimmune or inflammatory process may be the cause of severe postoperative neurologic deficits. Staff and colleagues[67] recently described a series of 33 patients who developed postsurgical inflammatory neuropathy (PSIN) within 30 days of surgery. The diagnosis was confirmed in most patients after a peripheral nerve biopsy. Postsurgical inflammatory neuropathy is believed to be an idiopathic immune-mediated response to a physiologic stress such as an infectious process, a vaccination, or a surgical procedure.[67] The condition may present as focal, multifocal, or diffuse neurologic deficits in the setting of a negative radiographic imaging. Complicating the diagnosis, the onset of neurologic deficits may not be apparent during the immediate postoperative period; and the deficits may be in an anatomic distribution remote from the surgical site or regional anesthetic technique. Risk factors or potential triggers for PSIN include malignancy, DM, tobacco use, systemic infection, volatile anesthetic use, and recent blood transfusion.[67] Suppression of the immune response with prolonged high-dose corticosteroids or intravenous immunoglobulin is the current treatment of choice. The goal of treatment is to sufficiently blunt the inflammatory response to allow for axonal regeneration. Fortunately, most patients improve with current treatment recommendations, with pain and sensory deficits improving before the motor deficits.[67]

The degree to which inflammatory mechanisms play a role in postoperative neurologic dysfunction is unknown and poorly characterized particularly within the anesthesia literature.[68] As a result, anesthesia providers and surgeons rarely consider this potential etiology of nerve injury when evaluating patients with postoperative deficits. This is problematic because the common approach of watchful waiting and conservative management will not be effective in patients with PSIN. Rather, PSIN is a clinical condition that must be suspected early in the disease process so that a definitive diagnosis can be obtained (nerve biopsy) and aggressive immunotherapy can be initiated to potentially improve neurologic outcome.[67]

CENTRAL NERVOUS SYSTEM DISORDERS

Historically, neuraxial anesthesia techniques have not been offered to patients with preexisting neurologic disorders of the central nervous system (MS, PPS, ALS) for fear of worsening neurologic outcome.[69–72] In fact, many historians believe that the recommendation by Dripps and Vandam[70] in 1956 to avoid regional anesthesia in patients with preexisting neurologic disorders has impacted clinical management for nearly half a century. Several theoretical mechanisms have been proposed based on the double-crush phenomenon, including neurologic injury from needle- or catheter-induced trauma, local anesthetic neurotoxicity, and neural ischemia caused by local anesthetic additives. However, the avoidance of regional anesthesia within this patient population may also be caused by physician and patient biases or potential medicolegal concerns. There are several confounding factors (age, body habitus, surgical trauma, tourniquet times and pressures, positioning, anesthetic technique) that make it difficult to determine the etiology of worsening postoperative neurologic deficits.

A recent review evaluated 139 patients with a history of one or more central nervous system disorders that subsequently underwent a neuraxial anesthetic technique.[71] Preoperative neurologic disorders included primarily PPS, MS, ALS, and traumatic spinal cord injury. In contrast to the findings of Dripps and Vandam several decades ago, the authors identified no new or worsening postoperative neurologic deficits (0.0%; 95% CI, 0.0%–0.3%) within their patient cohort. This was despite the fact that 74% of the patients reported active neurologic symptoms (paresthesias, dysesthesias, hyperreflexia) or sensorimotor deficits during the immediate preoperative period and subsequently

received standard doses of local anesthetics. Two smaller reviews in parturients receiving smaller doses of local anesthetic for labor analgesia have reported similar results.[73,74]

Clearly, further investigations with more patients are needed to make definitive recommendations. However, the current data suggest that the decision to perform neuraxial anesthesia in patients with preexisting central nervous system disorders be based on the risks and benefits for each individual patient. Some authors have postulated that the neurologic risk may be higher in patients who have progressive neurologic deficits when compared with those patients with chronic stable sensorimotor symptoms that have not changed during the course of several months or years.

Multiple Sclerosis

Multiple sclerosis is an inflammatory autoimmune disorder of the central nervous system with a lifetime risk of 1 in 400, making it the most common debilitating neurologic disease in young adults.[75] It is a chronic degenerative disease characterized by focal demyelination within the spinal cord and brain. The demyelination results in a fluctuating conduction block that causes a classic "waxing and waning" of symptoms that is characteristic of the disease. Signs and symptoms include sensory or motor deficits, diplopia or vision loss, bowel or bladder dysfunction, and ataxia. The precise etiology is unclear; however, a combination of genetic risk factors and environmental factors likely plays a role. Twenty-five percent of MS patients are essentially asymptomatic, and their activities of daily living are unaffected. However, up to 15% of patients may become severely disabled, with significant sensorimotor deficits within a short period.[76]

Several factors common to surgery can negatively impact the disease process, including hyperpyrexia, emotional stress, and infection.[77] The mechanism of worsening neurologic function in patients with MS is unclear and may occur coincidentally within the postoperative period independent of the anesthetic technique. Evidence regarding the risk of regional anesthesia in patients with MS is limited. Despite some evidence for demyelination of the peripheral nerves in MS, peripheral nerve blockade has traditionally been considered safe.[78] However, a recent report of severe brachial plexopathy after an ultrasound-guided interscalene block has raised the concern that a segment of MS patients may have subclinical peripheral neuropathy.[79] Several investigators have demonstrated evidence of axonal demyelinating peripheral lesions (sensory > motor) in patients with MS.[80–82] Misawa and colleagues[81] demonstrated that peripheral demyelination may occur in 5% of MS patients, whereas Pogorzelski and colleagues[80] report peripheral demyelination may occur in up to 47% of patients. Similarly, Sarova-Pinhas and colleagues[82] describe nerve conduction abnormalities in up to 14.7% of peripheral nerves within MS patients compared with only 2.4% of nerves within the general population. Despite this evidence, the overall incidence and clinical relevance of this underlying peripheral neuropathy remain undefined in the setting of performing peripheral nerve blockade in patients with MS.

In contrast to peripheral nerve blockade, the potential risk of new or progressive neurologic deficits in MS patients after spinal anesthesia was first described in 1937. Critchley[83] described 3 patients with "disseminated (multiple) sclerosis" that experienced worsening of symptoms after spinal anesthesia. The author concluded that "spinal anesthesia may be a precipitating agent in the evolution of disseminated (multiple) sclerosis." Several subsequent studies demonstrated similar outcomes with the development of new or worsening neurologic deficits or a higher likelihood of symptom exacerbation after spinal anesthesia.[69,72,84,85] In contrast, a more recent study demonstrated no new or worsening neurologic symptoms after spinal anesthesia in 35 MS patients undergoing a variety of surgical procedures.[22]

The safety of epidural anesthesia and analgesia in MS patients has been focused almost exclusively within the obstetric population, which may not accurately represent the nonpregnant MS patient. Pregnancy is frequently associated with a decrease in disease relapses, whereas the postpartum period is often associated with an increased risk of relapse. The transition from cellular immunity to humoral immunity required for the mother's immune system to tolerate the fetus is thought to be protective during pregnancy.[73] However, as cell-mediated immunity rebounds during the postpartum period, patients will often experience transient worsening of neurologic symptoms that could be falsely attributed to recent regional anesthetic techniques.

Confavreux and colleagues[73] have performed one of the few prospective studies evaluating risk factors associated with disease relapse during the postpartum period. They concluded that epidural analgesia during labor and delivery did not contribute to a higher risk of relapse compared with patients not receiving neuraxial techniques. Similarly, Kuczkowski[86] found no association between any form of obstetric regional analgesia and the worsening of MS symptoms among obstetric patients. Epidural anesthesia and analgesia have traditionally been recommended over spinal anesthesia in MS patients because the concentration of local anesthetic in the white matter of the spinal cord is one fourth the level after epidural injection compared with intrathecal injection.[87] It is believed that the lack of myelin may leave the spinal cord susceptible to the neurotoxic effects of local anesthetics.[87] Although definitive studies on the pharmacological effects of local anesthetic concentrations and doses are lacking, many recommend limiting neuraxial local anesthetic doses and concentrations to the lowest level possible. There is some evidence that lidocaine can reversibly worsen symptoms of MS.[88] This is thought to occur when sodium channels in demyelinated areas are blocked enough to unmask lesions that would otherwise be below the level of clinical detection. With regard to the obstetric patient, the risk of neuraxial anesthesia or analgesia needs to be weighed against the increased risk of general anesthesia. A recent survey demonstrated that 99% of obstetric anesthesiologists would perform neuraxial anesthesia for an emergency cesarean delivery in an MS patient after carefully weighing the potential risks and benefits.[89]

In summary, there remains little conclusive evidence to support or refute the use of regional anesthesia in patients with MS. Peripheral nerve blockade has not been definitively shown to be harmful in the setting of MS and, therefore, should not be considered an absolute contraindication. In contrast, given that demyelinated fibers may be more prone to the toxic effects of local anesthetics, epidural anesthesia and analgesia may be considered safer than spinal anesthesia techniques. However, reducing the local anesthetic concentration and total dose to the lowest effective level(s) may be prudent for both peripheral and neuraxial blockade. All decisions regarding the use of regional anesthesia and analgesia in patients with MS need to be made after careful consideration of the potential risks and benefits. Regardless of the anesthetic technique chosen, patients should be informed about the risk of new or worsening neurologic symptoms during the postoperative period because of exposure to multiple exacerbating factors.

Postpolio Syndrome

Postpolio syndrome refers to new-onset neurologic symptoms that develop several years after an acute poliomyelitis infection. The onset of new or progressive symptoms may occur up to

30 years after the initial episode of poliomyelitis. PPS affects anterior horn cells within the anterior portion of the spinal cord and is, therefore, considered a lower motor neuron disorder.[90] Initial symptoms include muscle weakness, fatigue, gait instability, joint pain, and muscle atrophy within muscle groups that were previously affected by the disease. Sensory deficits are generally not characteristic of the syndrome and are only observed if a secondary disorder is present (ie, compression radiculopathy or disk herniation). The muscle effects of PPS are thought to be related to an ongoing process of denervation and reinnervation that ultimately ends when denervation is no longer compensated for by reinnervation.[90]

Postpolio syndrome is the most prevalent motor neuron disease in North America. Furthermore, because acute poliomyelitis continues to occur in developing countries, PPS will likely remain an anesthetic concern for years to come.[21] It is not uncommon for patients with PPS to require orthopedic procedures; therefore, it is important to determine the safety of regional anesthetic techniques under these clinical circumstances. Although patients with PPS have fewer motor neurons than normal, it is difficult to know whether remaining motor neurons are more susceptible to the toxic effects of local anesthetics. There have been no reports of worsening neurologic status after neuraxial anesthesia with normal doses of tetracaine and bupivacaine in patients with PPS.[91,92] However, this does not imply that regional anesthetic techniques are without risk.[93] As with all patients, the potential risk of regional anesthesia must be balanced against the disadvantages of general anesthesia, including a hypersensitivity to sedative or opioid medications, risk of muscle relaxant use, and the risk of hypoventilation and aspiration. The largest series of patients with PPS (n = 79) undergoing neuraxial anesthesia or analgesia demonstrated no worsening of neurologic symptoms during the postoperative period.[71] However, the paucity of clinical data on this topic prevents clear recommendations from being made regarding the safety of neuraxial anesthesia or peripheral nerve blockade in patients with PPS. Ultimately, the decision to use regional anesthesia should be made on an individual basis after a thorough discussion of the potential risks and benefits with each patient. Given the increased sensitivity to opioid and sedative medications within this patient subgroup, these medications should always be used with caution.

Amyotrophic Lateral Sclerosis

Amyotrophic lateral sclerosis is a common form of motor neuron disease characterized by adult-onset degeneration of both the upper and lower motor neurons. Unfortunately, in the majority of patients, death from respiratory failure occurs within a few years of disease onset.[94]

The existing evidence, albeit limited, has not supported the fear that neuraxial or peripheral blockade will exacerbate preexisting symptoms in ALS patients.[65,95–99] However, given the potential for worsening respiratory failure after general anesthesia because of the use of muscle relaxants and opioid medications, the ability to avoid airway manipulation may be considered a benefit within this high-risk patient population. Regardless of the anesthetic technique, the possibility of postoperative respiratory or neurologic deterioration is quite high in patients with ALS. Ultimately, the decision to use regional anesthesia should be made on an individual basis after a thorough discussion of the potential risks and benefits with each patient.

SPINAL CANAL PATHOLOGY

Spine and spinal canal pathology has been proposed as a potential risk factor for neurologic complications after neuraxial blockade. Several mechanisms of injury have been proposed, including an ischemic or compressive effect after the injection of large volumes of local anesthetic into a relatively confined space (ie, epidural anesthesia) as well as local anesthetic neurotoxicity (ie, spinal anesthesia). Although the precise mechanism(s) of injury remain unclear, there are several isolated case reports and large case series that are believed to support these hypotheses.

Spinal Stenosis and Lumbar Disk Disease

Spinal stenosis occurs as age-related changes within the intervertebral disks and facet joints result in narrowing of the spinal canal or neural foramina. Changes include disk degeneration, facet joint hypertrophy, osteophyte formation, and infolding of the ligamentum flavum. The precise mechanism by which spinal nerve root compression results in signs or symptoms of spinal stenosis is not completely understood.[100] Classic symptoms include back and leg radicular pain that significantly worsens with extension and is alleviated with flexion. Preexisting spinal stenosis or compressive lumbar disk disease has been proposed as a potential risk factor for neurologic complications after a neuraxial (spinal or epidural) technique. Proposed mechanisms of injury include mechanical trauma,[101,102] local anesthetic neurotoxicity,[103,104] ischemia,[105–107] or a multifactorial etiology.[108,109] Pathophysiologically, patients with spinal stenosis have a reduction in the diameter of the spinal canal, resulting in less anatomic space for fluid collections such as blood or local anesthetic. As a result, small quantities of fluid may result in significant increases in pressure around the neuraxis that would otherwise have no clinical effect in a widely patent spinal canal.

Two relatively large case series and several case reports have been published that suggest undiagnosed spinal stenosis may be a risk factor for neurologic complications after neuraxial blockade.[101,103,105,108,110] The majority of cauda equina cases involved epidural analgesia, which may suggest an ischemic component (mechanical compression of the cord by the infusing local anesthetic) to the injury.[106] Hebl and colleagues[108] performed a retrospective review of patients with preexisting spinal stenosis or lumber disk disease with and without a history of prior spinal surgery and concluded that this cohort of patients was at an increased risk for the development or worsening of neurologic deficits when compared with the general population undergoing a neuraxial technique. In addition, patients with more than one neurologic diagnosis (eg, spinal stenosis, compressive radiculopathy, preexisting peripheral neuropathy) appeared to have an even higher risk of injury. Moen and colleagues[103] also performed a large epidemiologic survey in Sweden that revealed similar trends. During a 10-year study period, 1,260,000 spinal anesthetics and 450,000 epidural blocks were evaluated. Overall, the authors identified 127 serious complications, including 85 (67%) patients with permanent injuries. Although 14 patients had preexisting spinal stenosis, 13 (93%) of these were diagnosed in the postoperative period during the evaluation of the neurologic deficit. The authors concluded that the incidence of severe anesthesia-related complications may not be as low as previously reported, and preexisting spinal canal pathology may be a "neglected risk factor." Finally, although patients with prior spine surgery may have an increased risk of paraplegia after transforaminal epidural steroid injections,[111,112] no similar risk has been found in patients after neuraxial anesthesia or analgesia.

In summary, although it appears that patients with spinal stenosis or compressive lumbar disk disease may be at increased risk of neurologic complications after neuraxial blockade, the existing literature fails to provide a direct comparison of surgical patients with similar spinal pathology undergoing general anesthesia.

Therefore, it is unclear whether the higher incidence of neurologic complications is caused by surgical factors, the anesthetic technique, the natural progression of the disease process, or a combination of these factors.

Neural Tube Defects

Neural tube defects are congenital anomalies of neural development that primarily affect the cranium or spine. Clinical manifestations vary widely and include cranial defects (eg, anencephaly, exencephaly, encephalocele), open spinal dysraphisms, and closed spinal dysraphisms. Open spinal dysraphisms, often referred to as *spina bifida cystica*, occur at a frequency of 0.5 to 8 cases per 1000 live births and include conditions in which neural tissue is exposed to the external environment.[113] The most common open spinal dysraphisms are meningocele (exposed meninges) and meningomyelocele (exposed meninges and spinal cord tissue). In contrast, closed spinal dysraphisms are characterized by unexposed neural tissue with abnormalities ranging from isolated defects in the fusion of the posterior vertebral column (ie, spina bifida occulta) to more serious spinal cord malformations such as diastematomyelia (split cord malformations), tethered spinal cord syndrome, and dural ectasia (lumbosacral widening or caudal displacement of the dural sac).[114] The etiology of neural tube defects are believed to be multifactorial, with both genetic and environmental factors equally implicated.[115]

Open spinal dysraphisms are commonly treated with surgical intervention during the early neonatal period. Clinical outcomes may vary from no neurologic sequelae to sensorimotor deficits, lower extremity paraplegia, and bowel and bladder dysfunction. Four anecdotal case reports have been described in the literature in which epidural analgesia[116,117] or spinal anesthesia[118,119] has been used in parturients during labor and delivery with a history of spina bifida cystica and subsequent surgical correction. In all but 1 case, the authors describe extensive cranial spread of local anesthetic and dense neural blockade with normal or reduced doses of local anesthetic. Limited spread of local anesthetic caudad to the site of surgical intervention was also noted. None of the patients experienced an inadvertent dural puncture, postdural puncture headache, or new or progressive neurologic dysfunction after the regional technique. Tidmarsh and May[120] have also described the use of epidural analgesia in four parturients who previously underwent meningomyelocele repair during infancy. Clinical outcomes included extensive cranial spread of local anesthetic (n = 1), poor sacral analgesia (n = 1), and successful epidural analgesia (n = 2). The authors cautioned that performing neuraxial techniques within this patient population can be technically challenging, with an increased risk of inadvertent dural puncture and unpredictable local anesthetic spread.[120] If neuraxial anesthesia or analgesia is performed under these clinical circumstances, it is recommended that the site of needle insertion occurs at a level above the original lesion because of limitations in local anesthetic spread.[116]

Spina bifida occulta is a common closed spinal dysraphism that is thought to be a normal variant of vertebral column development. Studies report an incidence of 10% to 24% within the general population.[114] *Isolated* spina bifida occulta involves the failure of a single-level vertebral arch (usually the lamina) from fusing, with no clinical signs or symptoms. There is no external lesion, and the spinal cord and meninges are not involved. The use of regional anesthesia in parturients with isolated spina bifida occulta has been reported but is limited to anecdotal case reports[121] and small case series.[120,122] Within this collection of 11 reported cases, successful epidural analgesia was achieved with normal doses of local anesthetic without extensive cranial spread of local anesthetic, sacral sparing, or adverse neurologic sequelae. One patient experienced technical difficulties during block placement, including the elicitation of a transient paresthesia and inadvertent dural puncture.[121] If neuraxial anesthesia or analgesia is performed in patients with isolated spina bifida occulta, it is generally recommended that the site of needle insertion occur at a level above the vertebral abnormality.[116]

In contrast to patients with isolated spina bifida, *complex* spina bifida may occur in conjunction with more severe closed spinal dysraphisms. Patients with spina bifida and (*a*) associated cutaneous manifestations (eg, hairy patch, subcutaneous lipoma, skin sinus), (*b*) involvement of more than one lamina, (*c*) neurologic symptoms, or (*d*) associated bowel or bladder dysfunction commonly have more severe coexisting conditions such as tethered spinal cord syndrome or diastematomyelia.[123] Under these clinical circumstances, neuraxial techniques should be considered contraindicated because neurologic complications have been reported after spinal,[124] epidural,[125] and combined spinal-epidural[126] techniques in patients with previously unrecognized tethered spinal cord syndrome and/or diastematomyelia.

Dural ectasia is the abnormal widening or ballooning of the dural sac, most commonly within the lumbosacral region of the spinal cord. It is common among patients with Marfan syndrome, occurring in 63% to 92% of cases.[127,128] Dural ectasia is also known to occur in patients with Patau syndrome (trisomy 13),[129] Ehlers-Danlos syndrome, neurofibromatosis type I, and ankylosing spondylitis.[130] Several case reports have described inadvertent dural puncture during caudal anesthesia[129,131,132] and incomplete spinal anesthesia[133] in patients with dural ectasia.

In summary, neural tube defects encompass a wide range of spinal cord malformations, ranging from asymptomatic single-level vertebral canal abnormalities (ie, spina bifida occulta) to meningomyelocele with paraplegia after surgical repair. Given the wide spectrum of clinical abnormalities, the varied risk, and the paucity of clinical data for any one diagnosis, definitive recommendations cannot be made regarding the safety of neuraxial anesthesia or analgesia in patients with neural tube defects. However, it is clear that regional anesthesia should be avoided in patients with documented tethered spinal cord syndrome, diastematomyelia, or spina bifida with associated cutaneous lesions, multilevel vertebral body involvement, neurologic deficits, or bowel or bladder dysfunction.

The neuroanatomy of all other neural tube defects (eg, isolated spina bifida occulta, prior meningo-myelocele repair) should be clearly documented with radiographic imaging before neuraxial anesthesia or analgesia is considered. If radiographic imaging can exclude the coexistence of complex closed spinal dysraphisms (eg, tethered spinal cord, diastematomyelia) within these patients, then regional anesthesia may be considered after a comprehensive risk/benefit discussion with the patient, highlighting the risk of technical difficulties, extensive cephalad spread of local anesthetic, sacral sparing, inadvertent dural puncture, and neurologic injury. If neuraxial anesthesia or analgesia is performed under these clinical circumstances, it is recommended that the site of needle insertion occurs at a level above the vertebral abnormality or site of prior surgical repair.[116]

RECOMMENDATIONS

The following recommendations (Table 1) are intended to encourage quality patient care, although observing them cannot guarantee any specific patient outcome. Their value should ultimately be determined by those who use them. The recommendations are subject to revision from time to time, as warranted by the evolution of technology, scientific evidence, and clinical practice. Importantly, the recommendations address only the issue of

TABLE 1. Recommendations: Regional Anesthesia in Patients With Preexisting Neurologic Disease

Peripheral Nervous System Disorders

Hereditary Peripheral Neuropathies

- Patients with Charcot-Marie-Tooth (CMT) disease and hereditary neuropathy with liability to pressure palsy (HNPP) may have a clinical or subclinical evidence of a preexisting peripheral neuropathy caused by neural compromise from the disease state (Class I).
- Anecdotal case reports and small case series suggest that both peripheral and neuraxial regional techniques may be used in patients with stable CMT or HNPP disease states without worsening their neurologic symptoms. However, a careful discussion regarding the potential risks and benefits of performing regional anesthesia in patients with preexisting neural compromise is strongly recommended (Class III).

Acquired Peripheral Neuropathies

- Patients with diabetic peripheral neuropathy or previous exposure to chemotherapy (eg, cisplatin or vincristine) may have a clinical or subclinical evidence of a preexisting peripheral neuropathy caused by neural compromise from the disease state (Class I).
- An abundance of animal data and limited clinical data support the concern that diabetic nerves are more sensitive to local anesthetics and perhaps more susceptible to injury. Therefore, peripheral and neuraxial blockade may theoretically increase the risk of new or progressive neurologic deficits in patients with diabetic peripheral neuropathy (Class II).
- When regional anesthesia is thought to be appropriate in patients with acquired peripheral neuropathy (eg, diabetic peripheral neuropathy or chemotherapy-induced neuropathy), consideration should be given to modify the anesthetic technique (ie, decreasing the concentration of local anesthetic, reducing the total dose of local anesthetic, eliminating or reducing the concentration of vasoconstrictors such as epinephrine) to minimize the potential additive risk (Class II).
- The use of ultrasound guidance may facilitate (a) perineural needle placement and (b) a reduction in the total dose (volume) of local anesthetic administered. However, clinical data demonstrating a reduction in neurologic injury with ultrasound guidance are currently lacking (Class II).

Inflammatory Neuropathies

- Patients with inflammatory neuropathies such as Guillain-Barré syndrome and postsurgical inflammatory neuropathy are at risk of new or worsening neurologic deficits during the postoperative period regardless of anesthetic technique (Class II).
- Neural compromise secondary to acute neuronal inflammation may be a relative contraindication to regional anesthesia. However, the existing literature can neither support nor refute this claim. Therefore, the decision to perform neuraxial or peripheral nerve blockade in patients with inflammatory neuropathies should be made on an individual basis after a thorough discussion of the potential risks and benefits with the patient (Class III).

Central Nervous System Disorders

- Patients with central nervous system disorders (eg, multiple sclerosis, postpolio syndrome, amyotrophic lateral sclerosis) may have clinical or subclinical evidence of a preexisting neurologic deficit caused by neural compromise from the disease state. Furthermore, it is not uncommon for patients with central nerve system disorders to experience worsening of their neurologic symptoms during the postoperative period regardless of the anesthetic technique (Class I).
- Anecdotal case reports and small case series suggest that neuraxial anesthesia and analgesia may be used in patients with stable neurologic symptoms without worsening their neurologic deficits. However, *definitive* evidence supporting this practice is lacking. Therefore, a careful discussion regarding the potential risks and benefits of performing regional anesthesia in patients with preexisting neural compromise is strongly recommended (Class II).

Spinal Canal Pathology

Spinal Stenosis or Lumbar Disk Disease

- Patients with spinal canal pathology (eg, spinal stenosis, lumbar disk disease) may have clinical or subclinical evidence of a preexisting neurologic deficit caused by neural compromise from the disease state (Class I).
- Large case series suggest that the performance of neuraxial anesthesia and analgesia in patients with preexisting spinal canal pathology may result in new or worsening neurologic symptoms. However, *definitive* evidence suggesting an increased risk of neurologic complications is lacking (Class II).
- Currently, it is unclear whether the development of new or worsening neurologic symptoms after neuraxial anesthesia or analgesia is caused by surgical factors, the anesthetic technique, the natural progression of the spinal pathology, or a combination of these factors (Class II).

Previous Spine Surgery

- Prior spine surgery is not a contraindication to the performance of neuraxial anesthesia or analgesia. However, before performing a regional technique, a review of the patient's radiologic imaging or the use of fluoroscopy is recommended to identify the optimal approach to the neuraxis (Class I).
- Under most clinical circumstances, spinal anesthesia may be (a) technically easier to perform and (b) more reliable (ie, higher success rates) than epidural techniques in patients who have previously undergone spine surgery. Patients undergoing neuraxial anesthesia or analgesia after a previous spine surgery do not appear to be at higher risk of new or progressive neurologic deficits (Class II).

Neural Tube Defects

- Neural tube defects encompass a wide range of spinal cord malformations, including both open (eg, meningocele, meningomyelocele) and closed (eg, spina bifida occulta, tethered spinal cord syndrome, diastematomyelia, dural ectasia) spinal dysraphisms. Patients with neural tube defects may have clinical or subclinical evidence of a preexisting neurologic deficit caused by neural compromise from the disease state (Class I).
- Because of the wide range and severity of possible spinal cord and vertebral column malformations, patients with neural tube defects should undergo radiographic imaging to fully evaluate and define the extent of their disease state before considering neuraxial anesthesia or analgesia (Class II).

Continued next page

TABLE 1. *(Continued)*

- Anecdotal case reports and small case series suggest that the performance of neuraxial anesthesia and analgesia in patients with complex closed spinal dysraphisms (ie, tethered spinal cord syndrome or diastematomyelia) may result in new or progressive neurologic symptoms. However, *definitive* evidence suggesting an increased risk of neurologic complications is lacking (Class II).
- Anecdotal case reports and small case series suggest that neuraxial anesthesia and analgesia may be used in patients with *isolated* spina bifida occulta (without associated tethered spinal cord syndrome or diastematomyelia) without an increased risk of neurologic injury. However, *definitive* evidence supporting this practice is lacking. Therefore, a careful discussion regarding the potential risks (technical difficulties, unpredictable local anesthetic spread, inadvertent dural puncture, neural injury) and benefits of performing regional anesthesia in patients with isolated spina bifida occulta is strongly recommended (Class II).

TABLE 2. Strength of Recommendations

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

This classification system is significantly modified from the American College of Cardiology/American Heart Association construct for classifying strength of evidence.[134]

regional anesthesia in patients with preexisting peripheral and neurologic disorders.

The recommendation classification scheme (Table 2) is a modification from the American College of Cardiology/American Heart Association construct for classifying strength of evidence.[134]

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The European Society of Regional Anaesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine Joint Committee Practice Advisory on Controversial Topics in Pediatric Regional Anesthesia

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Background and Objectives: Some topics in the clinical management of regional anesthesia in children remain controversial. To evaluate and come to a consensus regarding some of these topics, The European Society of Regional Anaesthesia and Pain Therapy (ESRA) and the American Society of Regional Anesthesia and Pain Medicine (ASRA) developed a joint committee practice advisory on pediatric regional anesthesia (PRA).

Methods: Representatives from both ASRA and ESRA comprised the joint committee practice advisory on PRA. Evidence-based recommendations were based on a systematic search of the literature. In cases where no literature was available, expert opinion was elicited. Experts selected controversial topics in PRA.

Results: The performance of PRA under general anesthesia or deep sedation is associated with acceptable safety and should be viewed as the standard of care (Evidence B2 and Evidence B3). Because of the difficulty interpreting a negative test dose, the use of test dosing should remain discretionary (Evidence B4). The use of either air–loss of resistance or saline–loss of resistance techniques is supported by expert opinion, but the literature supporting one technique over the other is sparse and controversial; when used appropriately, each technique may be safely used in children. There are no current evidence-based data that the use of RA increases the risk for acute compartment syndrome or delays its diagnosis in children.

Conclusions: High-level evidence is not yet available for the topics evaluated, and most recommendations are based on Evidence B studies. The ESRA/ASRA recommendations intend to provide guidance for the safe practice of regional anesthesia in children.

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The American Society of Regional Anesthesia and Pain Medicine (ASRA) and the European Society of Regional Anaesthesia and Pain Therapy (ESRA) are the primary societies for regional anesthesia in the world, and one of their goals is to create recommendations/guidelines through the collaboration of their experts.

The first result was in 2009, the publication of "The American Society of Regional Anesthesia and Pain Medicine and the European Society of Regional Anesthesia and Pain Therapy Joint Committee Recommendations for Education and Training on Ultrasound-Guided Regional Anesthesia." [1]

The 2 societies worked again together to create The European Society of Regional Anesthesia and Pain Therapy and the American Society of Regional Anesthesia and Pain Medicine Joint Committee Practice Advisory on Pediatric Regional Anesthesia (PRA). Experts from both societies discussed important and controversial topics in PRA and provide guidance, wherever possible, from an evidence-based perspective and on the basis of expert opinion when conclusive evidence is lacking in the literature. Four topics were selected by participant consensus according to the current main areas of PRA controversy: 1) the performance of regional nerve blocks under deep sedation (DS) or GA, 2) the value of a test dose, 3) the use of air versus normal saline for loss of resistance (LOR) for epidural space detection, and 4) regional anesthesia and the risk of obscuring compartment syndromes.

We are unaware of any previous practice advisories that specifically addressed controversial topics in PRA. The ASRA and the ESRA hope that this article will be useful not only to those who work every day in pediatric hospitals but also to all anesthesiologists who care for children less frequently. In addition, we intend to provide guidance and reflection on current controversial clinical issues in PRA practice.

METHODS

Representatives from both ASRA and ESRA comprised the joint committee practice advisory on PRA. Committee members met in workgroups, and decisions on topics to be addressed were made through consensus. The committee used similar methodology on the generation of practice advisories previously described by the American and European anesthesiology societies.[2,3] In brief, an evaluation of availability and strength of the evidence was systematically performed. Scientific evidence was obtained by performing a systematic search of literature. All committee members participated in the expert opinion decisions because all involved have had extensive experience (>20 years) on the topic. No other clinician outside of the committee was consulted.

Published reports evaluating the practice of RA for pediatric patients were searched using the National Library of Medicine's

PubMed database, the Cochrane Database of Systematic Reviews, and Google Scholar inclusive to December 9, 2014. Free text and MeSH terms "block," "regional," "children," "surgery," "anesthesia," "local," and "pediatric" were used individually and in various combinations. No language restriction was used. No date limit was used. The search was limited to articles in subjects younger than 18 years. We reviewed the reference lists from identified studies to identify additional studies not found during our primary search. No search was performed for unpublished studies. The scientific evidence was classified according to the quality of research design as presented in Table 1, similar to what has been previously described in other practice advisories.[2,3]

When the literature search revealed a lack of published studies or when the only evidence was generated from studies with insufficient quality because of methodological constraints, it was deemed as "insufficient literature" and expert opinion from the ESRA/ASRA joint committee was considered.

RESULTS

Performance of Regional Anesthesia Under General Anesthesia or DS

Soon after the first description by August Bier of spinal anesthesia in 1898, this regional anesthesia technique became popular for use in children on both sides of the Atlantic Ocean.[4,5] This was later followed by the seminal publication by Campbell in 1933, which reported the use of caudal blockade for pediatric urologic procedures.[6] However, with the many advances in the development of general anesthesia (GA) between 1940 and 1960, PRA was used only in a few specialized centers until the 1980s.

At that time, a resurgence of interest in PRA took place, perhaps best exemplified by the description of epidural anesthesia in pediatric patients by Ecoffey et al[7] and Murat et al.[8] Epidural anesthesia rapidly became a common modality of regional anesthesia in infants and children and was most often performed under GA. A case report of a devastating neurological complication resulting from multiple attempts at a thoracic epidural blockade performed under GA in an adult, however, provoked controversy about the safety of this practice in children.[9] The contention was based on the supposition that improper needle placement could be detected in the awake patient by paresthesia, pain on injection, or unexpected motor responses—warning signs that would not be detectable under GA or DS (GA/DS) in children. This concern was further increased by a European publication describing serious complications after attempted epidural block placement under GA in 4 pediatric patients.[10]

TABLE 1. Classification of Scientific Evidence

Evidence Class	Study Design
Category A1	Sufficient number of randomized controlled trials to conduct a meta-analysis
Category A2	Several randomized controlled trial but not sufficient to conduct
Category A3	Single randomized controlled trial
Category B1	Observational comparisons between clinical interventions for a specific outcome
Category B2	Observational studies with associative statistics
Category B3	Noncomparative observational studies with descriptive statistics
Category B4	Case reports

In response to those concerns, thought leaders in pediatric anesthesiology opined that it was safe and consistently stated that it was acceptable care to perform PRA under GA/DS in children.[11,12] Nevertheless, objective data were lacking, and the discussion about the safety of PRA during GA/DS was largely based on opinion and anecdote.[12] A 2008 ASRA practice advisory guideline acknowledged the need for performance of regional blockade under GA or DS in children.[13]

Current Evidence Base for the Safety of PRA Performed During GA/DS

Apart from reports of single-center experiences with regard to PRA,[14,15] there are currently 4 major large-scale (>10,000 patients per study) multicenter studies available that specifically have focused on the incidence of complications after PRA.[16–19] A summary of these seminal studies is provided below. None of the studies reported any cases of paralysis after the use of neuraxial anesthesia/analgesia, leading to an incidence (95% confidence interval [95% CI]) of 0 (0%–0.004%) for paralysis.

The first large-scale effort focused on the complications associated with the use of PRA was published by the French-Language Society of Paediatric Anaesthesiologists (ADARPEF) in 1996.[16] At the 38 participating centers, all use of regional anesthesia was prospectively registered during 1 year (May 1993–April 1994), with a special focus on safety issues. There were 24,409 regional anesthetics included in the study, of which 89% were performed under GA. Neuraxial blocks were the most common; caudal blockade was by far the most common individual block performed. Peripheral blocks and local anesthesia techniques were used in only 38% of the registered cases. The overall complication rate was found to be very low (0.9 per 1000 blocks), but neuraxial blocks were found to have a higher complication rate compared with peripheral techniques (1.5 and 0 per 1000 blocks, respectively). None of the observed complications resulted in long-term disability or medicolegal action (follow-up period of 12 months) (Evidence B2).

The second large-scale effort focused on the complications associated with the use of PRA was conducted by the 2007 UK Prospective National Pediatric Epidural Audit.[17] To quantify the risk associated with the use of pediatric epidural analgesia, the Association of Paediatric Anaesthetists of Great Britain & Ireland undertook a prospective audit within its membership, with the aim to include 10,000 epidural infusions. The audit was performed from 2001 to 2005. If an individual patient complication was recorded, a more detailed 12- month follow-up was undertaken. An expert panel adjudicated complications and graded the severity. A total of 10,633 epidurals in all pediatric age groups were included in the study. All but one were placed under GA. Overall, 96 incidents were reported, with the large majority being classified as minor (1:189). Only 5 incidents were recorded as serious (1 of 2000) and an additional 9 as major (1:1100). One child, who had a drug infusion error, experienced persistent paresthesia still present at the 12-month follow-up (1:10,000). Four patients developed compartment syndrome, but the expert panel judged that there was no delay in diagnosis because of the epidural infusion (Evidence B3).

The third large-scale effort focused on the complications associated with the use of PRA was the 2010 ADARPEF study.[18] In this prospective 1-year study (November 2005–October 2006) including 47 different institutions, a total of 29,870 regional blocks were performed under GA and 1262 regional blocks without concomitant GA. Compared with the earlier ADARPEF study, peripheral nerve blocks were used with increasing frequency (66% peripheral vs 34% neuraxial). However, in children younger than

3 years, the use of neuraxial and peripheral blocks was similar, whereas, in older children, peripheral nerve blocks were performed 4 times more frequently than neuraxial blocks. The authors did not analyze differences in complications under GA/DS. Only 41 complications were recorded in this study (1.2:1000), and none resulted in long-term sequelae. Similar to the 1996 ADARPEF study, neuraxial blocks were associated with a 6-fold higher incidence of complications (Evidence B3).

The fourth large-scale effort focused on the complications associated with the use of PRA was the 2014 Pediatric Regional Anesthesia Network (PRAN) report.[19] To allow for prospective and continuous audit of practice trends as well as the incidence of complications, 6 academic centers in the United States pioneered an Internet-based PRAN database in 2006.[20] They reported on 53,564 cases of PRA prospectively collected between 2007 and 2012.[19] They were able to demonstrate that performing a PRA under GA (with or without neuromuscular blockade [NB]) did not increase the risk of immediate or late complications. The incidence of neurological complications (all of which were minor with 1 exception that resolved) in patients under GA without NB was lower than that seen in any other group: 0.62 of 1000 (CI 0.4–0.92) compared with 2.4 of 1000 (CI, 1.6–3.6) in patients under GA with NB, 8.3 of 1000 (4.9–13.3) in sedated and 3.4 of 1000 (CI, 0.7–10.0) in awake patients (Evidence B2). Pediatric regional anesthesia was performed in awake patients most commonly in neonates and infants younger than 6 months (n = 290) and teenagers (n = 515); those in which sedation was used included mainly teenagers (n = 2060).

Cautionary Case Reports

A strong evidence base exists supporting the safety of PRA performed under GA/DS. However, this does not ensure that serious complications cannot occur under certain circumstances. Thus, if PRA is performed with the wrong type of equipment or without basic safety precautions, if the operator has insufficient training and/or skills, or if PRA is used in particularly vulnerable patient categories, serious complications may still occur, a fact that may be especially true in association with the use of epidural blockade.[21–24] Furthermore, there is always a risk of rare complications, often of obscure or unknown etiology, that are unrelated to operator expertise and will not be an adequately identified event in large-scale studies[25] (Evidence B4).

Evidence-Based Conclusions and Clinical Advice

- The performance of PRA under GA/DS is associated with acceptable safety and should be viewed as the standard of care (Evidence B2 and Evidence B3).
- The overall risk for complications is 0.66% (95% CI, 0.6%–0.7%), whereas the risk of paralysis is estimated at 0 (95% CI, 0%–0.004%) (Evidence B2 and Evidence B3).
- Despite the reassuring safety of PRA performed under GA/DS, serious complications may still occur. In the event of an unexpected clinical outcome, especially unanticipated motor blockade during continuous postoperative regional block after the use of PRA, a high index of suspicion for neurological injury is warranted and appropriate diagnostic and therapeutic measures must be performed without delay (Evidence B4).

Test Dose and Intravascular Injection

Because differences exist in both the physiological and clinical conditions under which regional anesthetics are administered in children compared with adults, there is considerable controversy and disparity of practice regarding the use of local anesthetic (LA) test doses in children. The epinephrine-containing test dose initially was designed to be used in awake adults who were not receiving β-blocking agents to detect accidental intravascular injection during epidural anesthesia.[26] In an awake adult, the injection of 3 mL of an LA solution containing 15 μg epinephrine produces hemodynamic effects (mainly tachycardia) if injected intravascularly. Most children, however, have their regional blocks placed while under GA/DS, making the recognition of accidental intravascular injection of LA with epinephrine more difficult.

To detect accidental intravascular injection of an LA solution in children, some practitioners add epinephrine to the LA solution at a concentration of 2.5 or 5 μg/mL, a concentration of 1/400,000 or 1/200,000, respectively. However, a small child's increased resting heart rate, combined with the fact that most regional blocks are performed under GA/DS, means that the utility and accuracy of test dosing remain a matter of controversy among pediatric anesthesiologists.

The volume of a pediatric test dose was empirically defined as a volume of 0.1 mL/kg of an LA solution containing 5 μg/mL of epinephrine, that is, a dose of 0.5 μg/kg epinephrine.[27] This was thought to be sufficient to induce an easily detectable hemodynamic change but also small enough to avoid complications and is supported by a dose-response study.[28]

Incidence of Accidental Intravenous Injection of LA During Regional Anesthesia in Children

In the first prospective study of ADARPEF, 6 of the 25 complications observed were caused by the accidental intravascular injection of the LA[16] (Evidence B3). The second ADARPEF study reported 15 cases of LA toxicity, of which 6 had a negative test dose[18] (Evidence B3). In a prospective study of 1100 caudal blocks, the incidence of unintentional vascular puncture was 6.9% and 8 (0.7%) accidental intravascular (IV) injections, all occurring in infants weighing less than 10 kg, were observed[29] (Evidence B4).

In another prospective study including 742 epidural caudal or lumbar blocks, a 5.6% incidence of unintentional vascular injections was observed. In addition, in 12 cases out of 36, aspiration for blood had been negative before the injection of the epinephrine-containing LA[30] (Evidence B3). In an audited cohort from the PRAN database composed of a total of 26,949 blocks using a test dose, there was a 0.21% incidence of positive test doses, almost all of which occurred during caudal or epidural placement[20] (Evidence B3). There were no positive test doses in other blocks, with the exception of 1 single-injection truncal block, although test doses were less frequently used in non-neuraxial blocks when ultrasound guidance was used.

All the aforementioned studies attested to the importance of dose calculation and staying below the maximum recommended LA dose to avoid complications related to LA toxicity.

Possible Interfering Factors Specific to Efficacy of the Test Dose in Children

One of the main problems is interpreting the hemodynamic response induced by an IV injection of LA mixed with a small dose of epinephrine.[31,32] The following factors have been demonstrated or theorized to alter the reliability of a test dose: 1) the general anesthetic agent used and its dose at the time of injection of the test dose; 2) a higher basal heart rate in infants and small children; 3) a possible age-dependent variation of the reactivity of the cardiovascular system to epinephrine; 4) the premedication received; 5) the LA used; and 6) the GA technique used.[32–36]

In children under sevoflurane anesthesia, the IV injection of 0.1 mL/kg of an LA solution containing 5 or 2.5 μg/mL epinephrine produces (Evidence B3):

1) An early modification (within 20–40 seconds) of the T wave morphology on the electrocardiogram (ECG): the increase in T wave amplitude is more pronounced in younger children.[28] In older children, adolescents, and adults, inversion of the T wave is observed.[35] These modifications are best observed in leads I, II, III, or V5 on the ECG.[37] The pathophysiology of this modification of the T wave is unknown: it can be observed after the accidental IV injection of a large dose of a mixture of lidocaine and bupivacaine without epinephrine but also when a small dose of epinephrine is injected IV without any LA.[38]
2) A change in heart rate: this is most often manifested as a heart rate increase of more than 10 beats/min observed somewhat later than the T wave changes. However, bradycardia or other dysrhythmias may be observed, too, and about 25% of patients may not demonstrate any change in rate.
3) A transient increase in systolic blood pressure: this can be missed during intermittent noninvasive measurement of blood pressure, as is usually the case in routine pediatric anesthesia cases.
4) In children receiving GA with propofol and remifentanil-based total intravenous anesthesia, the T wave amplitude changes are highly inconsistent—elevation is seen in only 25% of cases, whereas no change or depression is seen equally in the remainder.[39] Other hemodynamic criteria need thus to be defined in this context. Diastolic blood pressure elevation, measured between 1 and 2 minutes after injection, was reported to be a highly sensitive indicator and was observed in all cases studied.

Evidence-Based Conclusions and Clinical Advice

- Because of the difficulty interpreting a negative test dose, the use of test dosing should remain discretionary. In clinical practice, if a test dose is used, there may be false-negative results, especially when the test dose is only partially administered intravenously or when the general anesthetic agents can blunt the hemodynamic effects of epinephrine. A negative result after the injection of a test dose therefore is reassuring but does not rule out vascular placement of needle or catheter. Any injection of an LA solution should be performed slowly, in small aliquots (0.1–0.2 mL/kg) and with intermittent aspiration and observation of the ECG tracing (Evidence B4).
- In all experimental studies using the deliberate IV injection of an LA solution containing epinephrine to model accidental IV injection, no false-positive results were observed: any modification of the T wave or of the heart rate within 30 to 90 seconds after the injection of a test dose should thus be interpreted as an accidental IV injection until disproven (Evidence B3).
- Imaging modalities (ultrasound, fluoroscopy) may help to avoid or visualize accidental intravascular needle placement in peripheral blocks, but data are lacking in PRA to determine the value of these techniques (expert opinion).[40,41]

Loss of Resistance

Despite the introduction of ultrasound guidance as a complement to regular LOR, the traditional LOR techniques using air or saline still remain the most widely used techniques for detecting needle placement in the epidural space.[42,43]

In 1995, a case series was published reporting a serious complication after the use of air-LOR in children, which immediately triggered an intense discussion regarding whether saline-LOR is a safer option and therefore should be the only recommended technique[10] (Evidence B4). This discussion has since been ongoing and has divided the pediatric anesthesia community into 2 camps, those in favor of saline-LOR and those who prefer to use air-LOR. Recently, a third option has been advocated as a "compromise"—use of a combination of air and saline.[44]

Air-LOR

Several complications related to the air-LOR technique have been published (nerve root compression, pneumocephalus, incomplete analgesia, and venous air embolism)[8,10,45–48] (Evidence B4). However, all these complications were associated with the total amount of air injected (eg, multiple attempts, large injection volume). Thus, expert consensus is that the amount of air in the syringe should be limited to a maximum of 0.5 to 1 mL and used only to detect the change of resistance, releasing the pressure on the plunger immediately on entry into the epidural space. Restricting the volume of air that is/can be injected will on theoretical grounds substantially limit the risk for any air-related complications. The use of air-LOR is currently the preferred choice in some countries.[49]

Other gases have been tried as alternatives to air for LOR. From a theoretical point of view, CO_2 may offer some theoretical advantages.[50] Carbon dioxide is extremely soluble in blood and therefore will mitigate the risk of air embolism; in addition, CO_2 may possess bactericidal properties. However, the availability of CO_2 is limited in most operating rooms and may therefore be an impractical alternative as compared with either air or saline.

Saline-LOR

The use of saline avoids most of the issues related to the use of air. However, as with air, it is essential to limit the volume of the injectate because excessive amounts of saline may dilute subsequently injected LA, may make the identification of unintentional dural puncture more difficult, and can together with the volume of LAs cause transient reduction in cerebral blood flow in small infants.[51] Despite these issues associated with the use of saline-LOR, the exclusive use of saline has been recommended by some experts and has become the general practice in some countries.[52,53]

Air/Saline-LOR

One publication involving 500 pediatric epidural blocks described the use of saline with a bubble of air in the syringe[44] (Evidence B3). This was reported to permit easy detection of the epidural space with a lower incidence of dural puncture (0.5%) than what has been reported for exclusive use of air or saline.[50]

Evidence-Based Conclusions and Clinical Advice

- The use of either air-LOR and saline-LOR techniques are supported by different international experts, and the literature supporting 1 technique over the other is sparse; as long as either technique is used appropriately, each may be safely used in infants and children. The combination of air and saline may represent a better alternative that will minimize the risk of injecting air and reduce the volume of saline injected. This method is also associated with a low risk for unintentional dural puncture (expert opinion).
- There are insufficient data in children to determine if using LOR to air or saline to detect needle entry into the epidural space will result in clinically significant differences regarding safety, accuracy, and subsequent efficacy of the injected LA (Evidence B3 and Evidence B4). Thus, both the aforementioned alternatives are acceptable if care is taken to keep the injected volume at a minimum.

- In neonates and infants, the volume of air contained in the syringe should be limited to less than 1 mL and air injections should not be repeated if multiple attempts are made to enter the epidural space (expert opinion).
- Although the committee recognizes that an air embolism with hemodynamic consequences is rare when LOR-air is used, enough evidence is lacking regarding the brain safety even for small amounts of air in the presence of a right-to-left cardiac shunt.

Compartment Syndrome

Acute compartment syndrome (ACS) of a limb is caused by high pressure in the closed noncompliant muscle compartment, which leads to compromised circulation, ischemia, and, if unrecognized, to motor and sensory impairment, neuronal death, and myonecrosis.[53] Therefore, the time to diagnosis of ACS is essential because a delay in treatment of more than 4 hours can lead to irreversible limb damage and possible limb loss.

Both adults and children develop this syndrome, which is generally associated with trauma, fracture with subsequent casting, prolonged malpositioning during surgery, or ischemia-reperfusion injury.[54–61] External or internal compression creates excessive pressure in a closed fascial compartment and leads to excruciating pain that cannot be ascribed to the trauma or surgery. A compartment pressure greater than 30 mmHg is the commonly accepted trigger for emergency intervention.[62]

The hypothesis that RA delays diagnosis and treatment of ACS is one that continues to generate debate. Only isolated case reports describe this event, and any evidence-based conclusion is difficult. Moreover, in children, especially in preverbal or nonverbal children, the recognition of ACS is more difficult because of its unreliable warning signs (Evidence B4). Furthermore, several case reports suggest that breakthrough pain in a patient with a previously well-functioning continuous block may be an early warning sign of ACS and enhance its detection if caregivers are vigilant (Evidence B4).

Epidural infusions and peripheral single-dose and continuous LA infusions have been stated to be responsible for delayed diagnosis in children, but without convincing evidence of causation[63–65] (Evidence B4). In many cases, the main root cause was not caused by the regional anesthetic technique but because of inadequate observation or to surgical malposition of the patient. Kanj and colleagues,[66] evaluating 23 children undergoing fasciotomy for ACS of the upper limb, showed that pain and swelling were the main symptoms of excessively high compartment pressure (>30 mmHg) in all but 2 patients, and that diagnosis in children is difficult and "associated with a prolonged clinical time course" (Evidence B4).

Johnson et al[67] reviewed 12 pediatric cases of ACS associated with epidural analgesia reported in the literature. They identified the following clinical signs for impending compartment syndrome in the lower limbs (Evidence B4): 1) increasing pain with increasing need for analgesics, 2) pain remote to the site of surgery, 3) paresthesia that is not attributable to analgesia technique, 4) signs of reduced perfusion of the painful site, 5) local swelling, and 6) pain on passive movement of the limb. Mar et al,[68] correlating ACS and type of analgesia (opioids or regional anesthetics), concluded that "There is no convincing evidence that patient-controlled analgesia, opioids, or regional analgesia delays the diagnosis of compartment syndrome provided that patients are adequately monitored. Regardless of the type of analgesia used, a high index of clinical suspicion, ongoing assessment of patients, and compartment pressure measurement are essential for early diagnosis."

Evidence-Based Conclusions and Clinical Advice

- There is no current evidence that the use of regional anesthetics increases the risk for ACS or delays its diagnosis in children.
- A comprehensive preoperative discussion with the patient's family and the surgical team should be performed to inform them of this rare but serious complication.
- As with many controversies linked to PRA, it is almost impossible to give unequivocal statements or recommendations. We suggest the following "best practice rules " to reduce or avoid the risk of compartment syndrome in children undergoing surgery with perioperative PRA: 1) single shot for both peripheral and neuraxial blocks: use 0.1% to 0.25% bupivacaine, levobupivacaine, or ropivacaine concentrations because they are less likely to mask ischemic pain and/or produce muscle weakness than more concentrated solutions (Evidence B4); 2) for continuous infusions, bupivacaine, levobupivacaine, or ropivacaine concentrations should be limited up to 0.1%; 3) in cases of patients having tibial compartment surgery or other high-risk surgeries for compartment syndrome, restricting both volume and concentration in sciatic catheters is advisable; 4) the use of LA additives should be with caution because they can increase the duration and/or density of the block; 5) high-risk patients should have appropriate follow-up by acute pain services to allow early detection of potential signs and symptoms; and 6) if ACS is suspected, compartment pressure measurements should be urgently assessed.

CONCLUSIONS

Notwithstanding the evidence of the value, safety, and efficacy of PRA, some aspects of it remain controversial. The ASRA and the ESRA have worked together on the main controversies and present their conclusions. High-level evidence is not yet available for these controversies, and most recommendations are based on Evidence B–level studies.

A practice advisory based on consensus should only be considered within its inherent limitations. First, it may become obsolete as new information becomes available from future studies. It is, therefore, likely that this practice advisory will need to be reviewed and updated periodically. It is possible that anesthesiologists practicing PRA may encounter system and individual barriers to implement the proposed recommendations. Nevertheless, the ESRA/ASRA joint commission hopes that barriers to implementation will be overcome with the publication of this international practice advisory.

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