Neuraxial Anesthesia and Analgesia in Patients with Preexisting Central Nervous System Disorders

James R. Hebl, MD

Terese T. Horlocker, MD

Darrell R. Schroeder, MS

Historically, the use of regional anesthetic techniques in patients with preexisting central nervous system (CNS) disorders has been considered relatively contraindicated. The fear of worsening neurologic outcome secondary to mechanical trauma, local anesthetic toxicity, or neural ischemia is commonly reported. We examined the frequency of new or progressive neurologic complications in patients with preexisting CNS disorders who subsequently underwent neuraxial blockade. The medical records of all patients at the Mayo Clinic from the period 1988 to 2000 with a history of a CNS disorder who subsequently received neuraxial anesthesia or analgesia were retrospectively reviewed. One-hundred-thirty-nine (n = 139) patients were identified for study inclusion. Mean patient age was 60 ± 17 yr. Gender distribution was 86 (62%) males and 53 (38%) females. An established CNS disorder diagnosis was present a mean of 23 ± 23 yr at the time of surgical anesthesia, with 74 (53%) patients reporting active neurologic symptoms. Spinal anesthesia was performed in 75 (54%) patients, epidural anesthesia or analgesia in 58 (42%) patients, continuous spinal anesthesia in 4 (3%) patients, and a combined spinal-epidural technique in 2 (1%) patients. Bupivacaine was the local anesthetic most commonly used in all techniques. Epinephrine was added to the injectate in 72 (52%) patients. There were 15 (11%) technical complications, with the unintentional elicitation of a paresthesia and traumatic needle placement occurring most frequently. A satisfactory block was reported in 136 (98%) patients. No new or worsening postoperative neurologic deficits occurred when compared to preoperative findings (0.0%; 95% confidence interval, 0.0%–0.3%). We conclude that the risks commonly associated with neuraxial anesthesia and analgesia in patients with preexisting CNS disorders may not be as frequent as once thought and that neuraxial blockade should not be considered an absolute contraindication within this patient population.

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Patients with preexisting disorders of the central nervous system (CNS), such as multiple sclerosis (MS), amyotrophic lateral sclerosis, or postpolio syndrome (PPS), present a unique challenge to the anesthesiologist. Historically, the use of regional anesthetic techniques within this patient population has been relatively contraindicated for fear of worsening neurologic outcome (1–5). Several theoretical factors contribute to this belief, including an increased risk of neurologic injury from needle- or catheter-induced mechanical trauma, local anesthetic toxicity, neural ischemia secondary to local anesthetic additives, personal biases from the patient, and potential medicolegal implications. However, it is unclear if these risk factors are associated with deteriorating neurologic status in patients suffering from chronic neurologic compromise.

Upton and McComas (6) first described the "double-crush" phenomenon and suggested 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 mechanical (needle- or catheter-induced trauma), ischemic (epinephrine-induced vasoconstriction), or toxic (local anesthetic neurotoxicity) risk factors commonly associated with regional anesthetic techniques. Osterman (7) emphasized that not only are two low-grade insults along a peripheral nerve worse than a single-site insult but the damage of dual-injury far exceeds the expected additive damage caused by each isolated insult. Therefore, the performance of a neuraxial technique in patients with preexisting CNS disorders may theoretically increase the risk of a double-crush phenomenon. This investigation examined the frequency of new or progressive neurologic complications in a large patient

From the Department of Anesthesiology, Department of Health Sciences Research, Mayo Clinic College of Medicine, Rochester, Minnesota.

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Address correspondence and reprint requests to James R. Hebl, MD, Department of Anesthesiology, Mayo Clinic College of Medicine, 200 First Street, S.W., Rochester, MN 55905. Address e-mail to hebl.james@mayo.edu.

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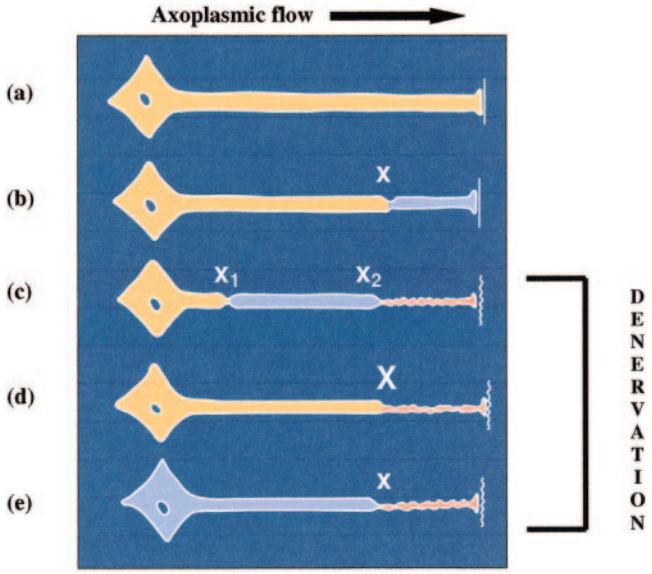

Figure 1. The double-crush phenomenon. Axoplasmic flow is indicated by the degree of shading. Complete loss of axoplasmic flow results in denervation (c,d,e). a) Normal neuron. b) Mild neuronal injury at a single site (x) is insufficient to cause denervation distal to the insult. c) Mild neuronal injury at two separate sites (x_1 and x_2) may cause distal denervation (i.e., double crush). d) Severe neuronal injury at a single site (X) may also cause distal denervation. e) Axon with a diffuse, preexisting underlying neurologic 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 (i.e., double crush).

population with preexisting CNS disorders who subsequently underwent neuraxial anesthesia or analgesia. Common risk factors of neurologic injury, such as local anesthetic toxicity and neural ischemia secondary to local anesthetic additives, were also examined.

METHODS

After IRB approval and written informed patient consent, the medical records of all patients from the period 1988 to 2000 with a history of a CNS disorder who underwent a subsequent neuraxial block were retrospectively reviewed. Neurologic diagnoses were limited to those of the CNS and did not include patients with peripheral neuropathies and/or pathology of the spinal canal. All neurologic conditions were diagnosed or confirmed by a neurologist or neurosurgeon before study inclusion.

Demographic data including age, gender, height, and weight were collected. The date of each neurologic diagnosis and details, such as the presence or absence of: 1) motor deficits; 2) sensory deficits; 3) paresthesias or dysesthesias; or 4) hyperreflexia at the time of their subsequent spinal or epidural anesthetic, were collected for each patient. Neurologic symptoms at the time of their procedure were further classified as: 1) acute (exacerbation of symptoms within the last 30 days); 2) subacute (exacerbation of symptoms within the last 1–6 mo); or 3) chronic/stable (no change in symptoms within the last 6 mo).

Indications for neuraxial anesthesia or analgesia were defined as surgical anesthesia, labor analgesia, or postoperative analgesia only. If a surgical indication occurred, it was classified as 1) orthopedic; 2) urologic; 3) general/abdominal; 4) cesarean delivery; or 5) other. Neuraxial blockade was categorized as: 1) epidural; 2) single-injection spinal; 3) continuous spinal; or 4) combined spinal-epidural. Details of each neuraxial technique, including awake placement (yes or no), approach (midline, paramedian, both), number of attempts (number of needle passes), and local anesthetic(s) used were all collected. The use of epinephrine and other local anesthetic additives was also noted. Technical complications noted at the time of block placement, such as difficulty identifying the epidural space, difficulty advancing an epidural or subarachnoid catheter, traumatic block placement (evidence of blood), unplanned dural puncture, difficulty obtaining cerebral spinal fluid, paresthesia elicitation, or unintended "total" or "high" spinal, were identified. Block efficacy was categorized as 1) satisfactory (surgery performed without additional intervention); 2) unilateral anesthesia or analgesia; 3) segmental or incomplete anesthesia or analgesia; or 4) no block/block failure.

New or progressive postoperative neurologic deficits (motor or sensory deficits, painful paresthesias, or bowel or bladder dysfunction) were identified in the daily progress notes of the primary surgical service and/or the anesthesia pain service. Complications were also noted during the patient's surgical follow-up visit(s). The presence of infectious (neuraxial abscess) or hematologic (neuraxial hematoma) complications was also documented. All recorded complications were followed until complete resolution or until the last documented date of evaluation.

RESULTS

One-hundred-thirty-nine (n = 139) patients were identified as having a preexisting CNS disorder, who subsequently underwent neuraxial anesthesia or analgesia (Table 1). A single CNS diagnosis before neuraxial blockade was present in all patients, with the exception of a single patient who had a diagnosis of both MS and PPS. Although the majority of patients (n = 114; 82%) had no neurologic history other than their primary CNS disorder, 25 (18%) patients had a coexisting radiculopathy, disk herniation, peripheral sensorimotor neuropathy, or history of spinal stenosis. Three patients (2%) had multiple (≥3) neurologic diagnoses in addition to their primary CNS disorder.

Patient demographics included a mean patient age of 60 ± 17 yr, height of 170 ± 11 cm, and weight of 76 ± 17 kg. Gender distribution was 86 (62%) males and 53 (38%) females. At the time of surgical anesthesia, an established neurologic diagnosis had been present a mean of 23 ± 23 yr, with the most recent severe exacerbation being 39 ± 109 mo. Motor weakness was

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Table 1. Central Nervous System Diagnoses

Neurologic diagnosis	Number of patients (*N*)*	Percentage (%)
Post-poliomyelitis	79	56.4
Multiple sclerosis	35	25
Traumatic spinal cord injury	13	9.3
Amyotrophic lateral sclerosis	5	3.6
Guillain-Barré syndrome	3	2.1
Meningomyelocele	2	1.5
Cauda equina syndrome	1	0.7
Huntington's chorea	1	0.7
Neurosyphilis with paraplegia	1	0.7

* One patient had a diagnosis of both multiple sclerosis and prior poliomyelitis.

the most common neurologic deficit, followed by painful paresthesias or dysesthesias (Table 2). Although 130 patients had a stable neurologic examination over the 6 mo before block performance, active neurologic signs or symptoms (motor or sensory deficits, dysesthesias/paresthesias, or hyperreflexia) at the time of surgery or obstetrical delivery were documented in 74 patients (Table 2).

The type of neuraxial blockade included spinal anesthesia in 75 (54%) patients, epidural anesthesia or analgesia in 58 (41.7%) patients, continuous spinal anesthesia in 4 (2.9%) patients, and a combined spinal-epidural technique in 2 (1.4%) patients (Table 3). Eleven patients underwent extended postoperative epidural analgesia with a mean duration of 2.4 ± 1.0 days. The majority of these patients (n = 8; 73%) did not receive local anesthetic within their postoperative infusion. Bupivacaine was the local anesthetic most commonly used for both spinal and epidural anesthesia. Drug concentrations ranged from 0.125% to 0.75% (Table 4). Spinal lidocaine was used in only 5 (4%) patients, with doses ranging from 50–75 mg. Epinephrine was added to the injectate in 41 (71%) patients undergoing epidural and 31 (38%) patients undergoing spinal anesthesia.

There were 15 (11%) technical complications (Table 3). Eight occurred in patients undergoing epidural anesthesia or analgesia, and the remaining 7 in patients receiving spinal anesthesia. The most common technical complication was the unintentional elicitation of a paresthesia (n = 8), followed by traumatic (evidence of heme) needle placement (n = 3). A satisfactory block was reported in 136 (98%) patients; all 3 segmental or inadequate blocks occurred in patients undergoing an epidural technique. There were no new or worsening postoperative neurologic deficits documented during follow-up when compared with preoperative findings (0.0%; 95% confidence interval, 0.0%–0.3%). The mean

Table 2. Neurologic History of Patients with Preexisting Central Nervous System Disorders

Neurologic feature(s)	Number of patients (N = 139)	Percentage (%)*
Neurologic history		
Motor deficits	105	80
Sensory deficits	57	44
Paresthesias/dysesthesias	72	55
Hyperreflexia	33	25
Disease status at time of block placement		
Acute exacerbation (<30 days)	4	3
Subacute exacerbation (1-6 mo)	2	1
Chronic/Stable (>6 mo)	130	96
Unknown	3	—
Disease progression within last 12 mo		
Yes	26	20
No	103	80
Unknown	10	—
Active symptoms at time of neuraxial block		
Yes	74	73
No	28	27
Unknown	37	—

* Percentages based on those patients with available data.

Table 3. Block Characteristics of Patients with Preexisting Central Nervous System Disorders Undergoing Subsequent Neuraxial Anesthesia or Analgesia

Block characteristic	Epidural (N = 58)	Spinal (N = 81)
Indication		
Labor analgesia	8 (14)	0 (0)
Postoperative analgesia only	11 (19)	0 (0)
Surgical	39 (67)	81 (100)
Orthopedic	27 (69)	44 (54)
Urologic	5 (13)	23 (28)
Intraabdominal	2 (5)	5 (6)
Cesarean delivery	1 (3)	0 (0)
Other	4 (10)	9 (11)
Postoperative epidural analgesia (N = 11)		
Local anesthetic used	3 (27)	—
Opioid only	8 (73)	—
Duration of indwelling catheter (days)		
Mean ± SD	2.4 ± 1.0	—
Median (range)	3 (0-3)	—
Technical Complications		
Unable to reach epidural space	1 (1.7)	0 (0)
Unable to advance neuraxial catheter	2 (3.4)	0 (0)
Unplanned dural puncture	1 (1.7)	0 (0)
Unable to obtain cerebral spinal fluid	0 (0)	0 (0)
Unintended "high" spinal	0 (0)	0 (0)
Traumatic (blood)	1 (1.7)	2 (2.5)
Unintentional paresthesia	3 (5.2)	5 (6.2)
Block efficacy		
Satisfactory	55 (95)	81 (100)
Unilateral	0 (0)	0 (0)
Patchy or segmental	1 (2)	0 (0)
No block (block failure)	2 (3)	0 (0)

Data are presented as n (%) unless otherwise indicated.

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Table 4. Local Anesthetic and Epinephrine Use During Neuraxial Anesthesia or Analgesia

Local anesthetic	Epidural anesthesia ($N = 58$)	Spinal anesthesia ($N = 81$)
Bupivacaine 0.125%		
Number of patients (N)	5	0
Initial dose (mg)	19 ± 8	—
Range (mg)	8.75–31	—
Bupivacaine 0.25%		
Number of patients (N)	5	0
Initial dose (mg)	22 ± 3	—
Range (mg)	20–25	—
Bupivacaine 0.5%		
Number of patients (N)	30	4
Initial dose (mg)	79 ± 42	12 ± 2
Range (mg)	25–200	10–15
Bupivacaine 0.75%		
Number of patients (N)	7	58
Initial dose (mg; mean ± SD)	137 ± 39	14 ± 2
Range (mg)	60–173	7.5–22.5
Lidocaine 2% (isobaric)		
Number of patients (N)	26	0
Initial dose (mg; mean ± SD)	343 ± 94	—
Range (mg)	160–560	—
Lidocaine 5% (hyperbaric)		
Number of patients (N)	0	5
Initial dose (mg)	—	65 ± 11
Range (mg)	—	50–75
Procaine 10%		
Number of patients (N)	0	10
Initial dose (mg)	—	89 ± 18
Range (mg)	—	50–110
Tetracaine 1%		
Number of patients (N)	0	14
Initial dose (mg; mean ± SD)	—	10 ± 4
Range (mg)	—	5–20
Chloroprocaine 3%		
Number of patients (N)	2	0
Initial dose (mg)	375 ± 106	—
Range (mg)	300–450	—
Epinephrine use		
Yes (%)	41 (71)	31 (38)
No (%)	17 (29)	50 (62)

Values are mean ± SD unless otherwise indicated. Patients often received more than one local anesthetic and/or multiple initial doses.

duration of postoperative follow-up was 46 ± 38 days. In addition, there were no infectious (neuraxial abscess) or hematologic (neuraxial hematoma) complications noted.

DISCUSSION

The recommendations of Vandam and Dripps in 1956 (4) to avoid spinal anesthesia in patients with preexisting CNS disorders has greatly influenced the clinical management of these patients for the last several decades. The theoretical risk of needle- or catheter-induced mechanical trauma, local anesthetic toxicity, or neural ischemia, combined with chronic, underlying neural compromise, was thought to place these patients at increased risk of further neurologic injury (1–4). However, the etiology of postoperative neurologic deficits is often difficult to evaluate because of the many patient, surgical, and anesthetic risk factors that may play a role. For example, the extremes of age or patient body habitus (8), intraoperative surgical trauma (9), tourniquet inflation pressures (10), prolonged or difficult labor, improper patient positioning (8), or anesthetic technique (11) may all be contributing factors. Furthermore, progressive CNS disease processes such as MS may coincidentally worsen perioperatively, independent of anesthetic or surgical technique. Therefore, the abundance of contributing factors makes it extremely difficult for clinicians and investigators alike to reliably isolate the effect of anesthetic technique on neurologic outcome.

Our results do not support the recommendations of Vandam and Dripps (4). None of the 139 patients with a confirmed, preexisting CNS disorder undergoing neuraxial anesthesia or analgesia had a new or progressive postoperative deficit documented within the medical record. This is despite the fact that nearly three fourths of patients (74%) reported active neurologic symptoms (sensorimotor deficits, paresthesias, dysesthesias, or hyperreflexia) at the time of surgery. Furthermore, all patients received standard doses of local anesthetic, with no apparent reduction in dose(s) for fear of worsening neurologic outcome. Although the current investigation may be the largest case series to date, previous investigators have described similar results in smaller anecdotal reports. Crawford (12) reported no neurologic deficits in parturients with MS ($n = 7$), spina bifida ($n = 7$), paraplegia ($n = 1$), or hemiplegia ($n = 1$) undergoing labor analgesia. Similarly, Confavreux et al. (13) reported that epidural analgesia did not increase the risk of progressive neurologic deficits in parturients with MS. However, the majority of patients in both the Crawford (12) and Confavreux et al. (13) series were parturients receiving small-dose local anesthetics for labor analgesia. In contrast, only 11 (8%) of the 139 patients in our series received small-dose local anesthetics for labor analgesia or postoperative pain management. The remaining 128 (86%) patients received standard doses of local anesthetics commonly used for surgical anesthesia. Furthermore, although ischemic nerve injury secondary to local anesthetic additives is also commonly cited as a risk factor of regional anesthesia (14,15), none of the 72 (52%) patients receiving epinephrine additives experienced new or progressive neurologic deficits. Clearly, the current study does not allow definitive recommendations to be made regarding the use of epinephrine in patients with underlying neurologic compromise. However, our results do not

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suggest that the use of epinephrine within this patient population should be considered to be contraindicated.

The most commonly encountered CNS disorders in our investigation were PPS ($n = 79$; 56%) and MS ($n = 35$; 25%). PPS refers to new, late-appearing manifestations of acute poliomyelitis infection. The pathogenesis of PPS consists of decompensation of a chronic denervation and reinnervation process to the extent that the remaining motor neuron(s) can no longer maintain new sprouts; and thus denervation exceeds reinnervation (16). Initial symptoms include fatigue, muscle weakness, joint pain and instability, cold intolerance, and muscle atrophy. The mean onset of symptoms is 30 years after the initial episode of poliomyelitis and involves only those muscle groups previously affected (17). Electromyographic and muscle-biopsy evidence of continuing denervation does not distinguish between stable, nonsymptomatic patients with prior poliomyelitis (i.e., non-PPS patients), and those with new weakness (i.e., PPS) (18). Diagnosis is by exclusion because no test is specific for PPS. The differential diagnosis includes MS, peripheral neuropathies, amyotrophic lateral sclerosis, anterior horn cell disease(s), and myasthenia gravis.

The use of spinal anesthesia in patients with PPS has been described in a single anecdotal case report (19). Higashizawa et al. (19) performed a hyperbaric tetracaine spinal in a 75-year-old man undergoing transurethral resection of the prostate. The patient had paralytic poliomyelitis at the age of 1 year. Postoperatively, there was no progression of the patient's preoperative muscle weakness or atrophy, nor aggravation of his autonomic dysfunction. In our series, no patient experienced new or worsening neurologic deficits when compared to preoperative findings. However, because of the limited number of patients and lack of proper controls, further investigation is necessary to definitively comment on the safety of neuraxial techniques within this patient population.

MS was also commonly identified within the current investigation. MS is a chronic, degenerative disease of the CNS characterized by focal or segmental demyelination within the brain and spinal cord. Demyelination produces a conduction blockade that fluctuates in severity, resulting in a characteristic waxing and waning disease course. Although the cause of MS remains unclear, both an infectious and an autoimmune etiology have been proposed. Signs and symptoms that commonly occur during an exacerbation of MS include diplopia, vision loss, sensory or motor deficits, ataxia, bowel or bladder dysfunction, and sexual impotence. Several factors may adversely influence the clinical course of the disease, including infection, hyperpyrexia, surgery, emotional stress, and pregnancy (20).

The use of neuraxial anesthesia or analgesia in patients with MS has been debated for quite some time. Critchley (1) first suggested in 1937 that spinal anesthesia may worsen demyelinating and other neurologic disorders. Since that time, several reports have suggested that both spinal (2,3,5,21) and epidural (22) anesthesia may worsen the disease course, while others have touted its safety (12,23–28). Regardless, much of the evidence is limited to isolated case reports or small case series. For example, Bamford et al. (5), reported seven patients with MS who underwent spinal anesthesia on nine separate occasions. One patient (11%) had an exacerbation of symptoms during the month after the anesthetic. In contrast, patients undergoing general anesthesia and local infiltration had exacerbation rates of 2.3% and 1.3%, respectively, which are consistent with baseline rates of exacerbation among nonsurgical patients with MS (29). The authors concluded that spinal anesthesia should be avoided in MS patients until the safety of the procedure has been convincingly established by other investigators. In contrast, Bader et al. (26) described the clinical outcomes of 20 women with MS during 32 pregnancies over a 5-year period of time. A postpartum relapse occurred in 9 (28%) of the 32 pregnancies. However, only 5 of these relapses occurred in women receiving epidural anesthesia or analgesia. Overall, relapse rates among women receiving neuraxial anesthesia or analgesia was 36%, whereas the relapse rate of patients not undergoing neuraxial anesthesia or analgesia was 22%. These results were not significantly different. The authors concluded that there is no absolute contraindication to the use of regional anesthesia for labor and delivery in the parturient with MS. Although our overall relapse rates in patients with MS were significantly less than Bader et al.'s (0% versus 36%), caution must be exercised in interpreting these results. For example, Bader et al.'s patient population was restricted to parturients, who have a more frequent relapse rate in the postpartum period regardless of the use of anesthesia (20). In contrast, only 4 (11%) of our 35 patients with MS were parturients, making comparisons quite difficult.

The mechanism by which neuraxial anesthesia may exacerbate MS is unknown. Diagnostic lumbar puncture alone does not seem to be associated with deterioration of symptoms (30). The lack of a protective nerve sheath around the spinal cord and the associated demyelination may render the spinal cord more susceptible to the potential neurotoxic effects of local anesthetics (22). The fact that larger concentrations of local anesthetic contribute to an increased frequency of disease relapses further supports this theory (26). Because local anesthetic concentrations are significantly smaller within the white matter of the spinal cord after epidural administration (22), this modality of neuraxial anesthesia is generally recommended over intrathecal techniques. No patients with MS in our investigation experienced a documented exacerbation or deterioration of symptoms after spinal ($n = 17$) or epidural ($n = 18$) anesthesia. This despite the fact that potentially toxic (local anesthetics) and/or ischemic (epinephrine) solutions were administered directly on compromised cell bodies of the CNS.

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Essentially, these conditions may represent a worst-case-scenario in which cell bodies are placed at increased risk of subsequent neural death and destruction.

Importantly, the limitations of this retrospective investigation must be recognized. First, a selection bias may have occurred in that neuraxial blockade was used in a relatively select group of patients, the majority of whom were neurologically stable (80% non-progressive) during the preceding 12 months. Second, the duration of postoperative follow-up was limited to 6 to 8 weeks. Neurologic deterioration occurring beyond this point, although unlikely, could not have been reliably identified. Third, the patient population examined included a mix of neurologic conditions. Upper versus lower motor neuron lesions and progressive versus non-progressive conditions were collectively examined. Therefore, definitive conclusions for all patients with a specific CNS disorder cannot be made based on these results. Finally, the logistics of performing of a retrospective investigation make it difficult to reliably capture all minor or subclinical complications. This limitation may result in fewer complications or adverse events that may otherwise appear in prospective studies.

In summary, the decision to perform regional anesthesia in patients with preexisting neurologic deficits should be based on the risks and potential benefits of each individual case. For example, many patients with neurologic disorders may have concurrent respiratory or cardiovascular impairments that may benefit from a regional technique. Although this investigation examined a variety of patients with differing comorbidities and neurologic conditions, definitive conclusions cannot be made with regard to the safety of neuraxial anesthesia or analgesia within a specific patient population. However, the investigation does suggest that the risks commonly associated with neuraxial anesthesia and analgesia in patients with preexisting CNS disorders may not be as frequent as once thought (95% confidence interval, 0.0%–0.3%). In fact, it may be prudent to reconsider the long-standing belief that neuraxial anesthesia and analgesia be considered an absolute contraindication within this patient population. However, to make definitive conclusions on the safety of these techniques in patients with CNS disorders requires further prospective study.

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