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REVIEW

Management of Postoperative Pain in Patients Following Spine Surgery: A Narrative Review

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Abstract: Perioperative pain management is a unique challenge in patients undergoing spine surgery due to the increased incidence of both pre-existing chronic pain conditions and chronic postsurgical pain. Peri-operative planning and counseling in spine surgery should involve an interdisciplinary approach that includes consideration of patient-level risk factors, as well as pharmacologic and non-pharmacologic pain management techniques. Consideration of psychological factors and patient focused education as an adjunct to these measures is paramount in developing a personalized perioperative pain management plan. Understanding the currently available body of knowledge surrounding perioperative opioid management, management of opioid use disorder, regional/neuraxial anesthetic techniques, ketamine/lidocaine infusions, non-opioid oral analgesics, and behavioral interventions can be useful in developing a comprehensive, multi-modal treatment plan among patients undergoing spine surgery. Although many of these techniques have proved efficacious in the immediate postoperative period, long-term follow-up is needed to define the impact of such approaches on persistent pain and opioid use. Future techniques involving the use of precision medicine may help identify phenotypic and physiologic characteristics that can identify patients that are most at risk of developing persistent postoperative pain after spine surgery.

Keywords: postoperative pain, spine, surgery, opioid sparing, regional anesthesia, ketamine, lidocaine

Introduction

Pain management after spine surgery represents a unique challenge. Patients undergoing complex spine surgery often present with pre-existing chronic pain and dependence on chronic opioid therapy. Tolerance to conventional opioid doses often results in heightened and prolonged opioid therapy and associated adverse effects. Despite the current opioid crisis and increased efforts to minimize excess postoperative opioid prescribing, adequate acute and long-term pain management after spine surgery remains an important priority. More than half of adults undergoing back surgery continue to report moderate pain 6 months after their operation.[1] Among adolescents undergoing spine fusion, there is a 40% incidence of chronic postsurgical pain.[2] Exact estimates of the incidence of persistent postsurgical pain after spine surgery are challenging given heterogeneity in the definition of the outcome, and the high prevalence of preoperative pain. Postoperative pain may be a continuation of preoperative existing pain or may represent the development of a new chronic pain condition. Risk factors for the development of persistent postoperative pain after spine surgery include elevated anxiety, depression, pain catastrophizing, pain sensitivity, preoperative opioids use, and female gender.[3] As these risk factors can be assessed before surgery, patients at high-risk for the development of persistent postsurgical pain can be identified prior to surgery with implementation of comprehensive pain management planning.[3] Inadequate postoperative analgesia in and of itself can lead to adverse events including cardiac and pulmonary complications, chronic postsurgical pain, decreased patient satisfaction, and increased morbidity and mortality.[4] There is a paucity of literature outlining the evidence base for pain management in the perioperative period for spine surgery. As such, the goal of this narrative

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review is to outline the current body of knowledge supporting various pain treatments in the context of perioperative pain management for spine surgery (Table 1). In this narrative review, we will discuss perioperative opioid management, non-opioid medications, behavioral interventions, ketamine and lidocaine infusions, and regional and neuraxial techniques to consider for patients undergoing spine surgery.

Opioid Management

Opioids remain a mainstay therapy for patients undergoing spine surgery. However, opioid therapy can also result in a number of adverse effects including nausea, vomiting, constipation, ileus, urinary retention, sedation, and respiratory depression.[5] Given increased attention to opioid-related adverse effects including persistent postoperative opioid use, opioid misuse, and diversion of surplus opioid prescriptions, there has been a significant shift towards optimizing non-opioid multimodal pain regimens and precision postoperative opioid prescribing. Spine surgery may result in intense postoperative pain and high postoperative opioid consumption particularly for patients with pre-existing chronic pain or opioid use prior to surgery.[6,7] In turn, these patients are at greater risk of adverse surgical outcomes including increased length of hospital stay, increased surgical site infections[8] and increased reoperations.[2,9,10] Approximately 9% of patients continue to use opioids one year after spine surgery.[11] Risk factors for persistent opioid use after spine surgery include preoperative opioid use, depression, anxiety, chronic pain diagnoses, use of non-opioid pain medications, lower socio-economic status, and younger age.[11,12] Careful consideration of these patient-level characteristics is warranted when formulating a multimodal pain regimen prior to surgery. In addition, extended intraoperative times and 4 or more levels of lumbar fusion further increase the likelihood of chronic opioid use after spine surgery,[12] and postoperative pain management regimens should be continuously modified to optimize non-opioid pain control as patients recover from surgery. Given the multitude of opioid-related adverse effects and the risks of new-onset depression and anxiety associated with chronic postoperative opioid use,[13] multimodal analgesic regimens optimizing non-opioid pain therapy have been proposed to reduce postoperative opioid requirements. Regional anesthetic techniques including spinal or epidural analgesia, ketamine infusions, lidocaine infusions, and non-opioid oral analgesics (gabapentin, NSAIDs, acetaminophen) can all be considered to optimize pain relief and minimize opioid-related adverse effects after spine surgery and will be discussed in this review.[14]

Preoperative Assessment

Prior to surgery, it is vital to assess current opioid intake,[5] use of opioid replacement therapy for opioid use disorders,[15–17] psychological distress, and additional patient-level characteristics that are associated with persistent opioid use after surgery. Among patients presenting for spine surgery, the incidence of preoperative opioid use approaches 50%.[15] As such, thoughtful pre-surgical formulation of tailored perioperative pain management regimens is likely to improve a patient's perioperative pain care and ultimately reduce the development of persistent postoperative pain and opioid use. Preoperative

Table 1 Key Non-Opioid Pain Management Strategies for Patients Undergoing Spine Surgery

Non-Opioid Medications	• Nonsteroidal anti-inflammatory drugs. • Acetaminophen (IV or oral). • Gabapentin or pregabalin (monitor for adverse effects including dizziness and somnolence).
Ketamine Infusion	• Intraoperative 0.1–0.5 mg/kg bolus followed by infusion of 0.1–0.6 mg/kg/h. • Postoperative subanesthetic infusion of 0.1–1 mg/kg/h.
Lidocaine Infusion	• 1 mg/kg/h based on adjusted body weight. • Monitor plasma lidocaine concentrations every 8–12 hours during the course of therapy.
Regional and Neuraxial Techniques	• Local anesthetic wound infiltration or catheter. • Spinal anesthesia, epidural analgesia or combined spinal-epidural anesthesia. • Thoracolumbar interfascial block. • Erector spinae plane block.

interventions include patient education regarding opioids and pain management, referral to an addiction specialist for undiagnosed or untreated opioid use disorder, and initiation of non-opioid pain medications. Patient education regarding proper storage and disposal of unused opioid medications after spine surgery combined with conservative opioid prescribing are important measures to combat the surplus of prescribed opioids that can contribute to opioid diversion and misuse.[18–20] In a prospective study of 140 patients undergoing spine surgery, 73% had unused opioid pills, 92% reported unsafe opioid storage, and 47% reported improper opioid disposal 6 months after surgery.[18]

Inpatient Management

If the patient's perioperative care includes hospitalization, experts recommend the use of intravenous opioid boluses in the immediate postoperative period for analgesic titration with close monitoring, and when able, a transition to oral short-acting opioid regimens.[7] In addition to optimization of non-opioid therapy, research has examined the varied effects of intraoperative opioid administration. For example, methadone is a potent μ-opioid receptor agonist with a long half-life.[21] It exerts additional analgesic effects through inhibition of the N-methyl-D-aspartate (NMDA) receptors, and inhibition of serotonin and norepinephrine reuptake.[22,23] Murphy et al describe a parallel-group, blinded, randomized trial of 115 patients undergoing elective posterior lumbar, thoracic, or lumbothoracic spinal fusion surgery comparing methadone 0.2mg/kg at the start of surgery to hydromorphone 2mg at surgical closure. Median postoperative IV hydromorphone use was reduced in patients receiving methadone on postoperative days 1 to 3, with significant reductions in reported pain intensity.[24] The analgesic benefits of this single dose of intraoperative methadone were still observed 3 months after surgery, as participants who had received methadone reported significantly reduced frequency of chronic pain and fewer subjects required opioid therapy at 3 months. However, no differences were observed with assessment at 6 and 12 months.[25]

Subacute Management

After surgery, frequent follow-up visits or assessments facilitate assessment of opioid intake,[18] single provider opioid prescribing, and suggestions for opioid tapering. Among patients undergoing spine surgery, lower postoperative opioid dosages promote a faster rate of opioid cessation.[26] Regardless of preoperative opioid use, patients prescribed an initial postoperative opioid daily dosage of less than 50 oral morphine milligram equivalents (MME) were significantly more likely to discontinue postoperative opioid use than those receiving greater than 90 oral morphine milligram equivalents daily.[26] As the duration of postoperative opioid use increases, patients undergoing spine surgery report less improvements in extremity pain, axial pain, and disability highlighting the important link between prolonged postoperative opioid use and pain after spine surgery.[26] Although postoperative opioid cessation is an important goal, prolonged postoperative opioid use signals a need for interdisciplinary pain management and specialist referral is warranted.

Opioid use with spine surgery requires a coordinated effort from different specialists and spans from preoperative to the post-operative periods to minimize adverse effects. During hospital admission, opioids are an important component in multimodal analgesia, but after discharge patients on opioids require frequent assessment, education on opioid use, and the provider(s) managing postoperative pain have appropriate opioid stewardship. Patients should receive education on the expected duration of pain that requires medications and understand the plan for tapering off. In this way, risks of opioids (ie, overdose, misuse, dependence, diversion) can be lowered, and the likelihood of chronic opioid use may be reduced.

Considerations for Patients with Opioid Use Disorder

Management of patients with opioid use disorder (OUD) presents a clinically challenging scenario for the healthcare practitioner in the perioperative period. Since 1999, greater than 840,000 people have died from drug overdose in the United States.[27] Methadone, buprenorphine, and naltrexone are the three categories of medications approved by the Food and Drug Administration for medication assisted treatment (MAT) of OUD. Studies have repeatedly demonstrated that MAT improves a variety of health outcomes.[28–31] To date, minimal research examines the pain management of patients with OUD undergoing spine surgery. However, existing perioperative research helps to guide recommendations for patients undergoing spine surgery with co-morbid OUD.

Understanding the effectiveness of MAT forms the basis of perioperative management of patients with OUD. As these patients may also have comorbid chronic pain, they are at higher risk of development of chronic postsurgical pain and associated complications, including prolonged hospital admission. These risk factors should be considered in perioperative planning and counseling.[4,32] Multiple guidelines and reviews exist for MAT of OUD.[28,33] Though there is not a consensus for perioperative management of buprenorphine, discontinuation of buprenorphine entails medical risk and burdens on patients and healthcare providers with potential destabilization of OUD treatment and associated risks of relapse and overdose. Buprenorphine MAT can be continued in the perioperative period and opioids with high binding affinity such as sufentanil and hydromorphone can provide adequate acute pain control. Studies have shown conserved μ-opioid receptors available for analgesia at high sublingual doses of buprenorphine as well as a full-agonist effect of buprenorphine for analgesia.[16,28,34–36] Similarly, patients on methadone should continue on their MAT dose. As α-elimination (8 hours) is associated with analgesia, pain control can be improved simply by dividing the daily methadone MAT dose into three divided doses.[37] Naltrexone is an opioid antagonist which should ideally be discontinued prior to surgery to facilitate the analgesia of opioid agonists. Coordination to discontinue therapy will be needed generally 2–3 days prior to surgery for oral naltrexone therapy and 4 weeks prior to surgery for extended release injection formulations of naltrexone.[38]

Beyond management of MAT, all patients with OUD should receive multimodal pain management with consideration of non-opioid medications and interventions discussed in greater detail throughout this review. Further, involvement of addiction medicine specialists throughout the perioperative period is key to patient success and optimal outcomes, as addressing psychological factors prior to surgery can help decrease the risk of prolonged postoperative pain.[39] Advance planning and can result in successful perioperative outcomes for patients with OUD.

Non-Opioid Medications

Enhanced recovery pathways in spine surgery have recognized the utility of non-opioid medications as a key component of a multimodal protocol in managing postoperative pain after spinal surgery. Standard non-opioids prescribed include nonsteroidal anti-inflammatory drugs (NSAIDs), acetaminophen, and gabapentinoids which have all been shown to curb post-operative opioid consumption and improve pain scores following spine surgery.[40] Typically, these medications are initiated perioperatively as part of a comprehensive, multimodal treatment plan to ameliorate acute postoperative pain and the transition to chronic postsurgical pain.

NSAIDs possess anti-inflammatory and analgesic properties by preventing prostaglandin synthesis via inhibition of spinal and peripheral cyclooxygenase (COX-1 and COX-2).[41] Randomized controlled trials examining the efficacy of NSAIDS for postoperative pain control after lumbar spine surgery have shown that NSAIDs have a significant opioid dose-sparing effect and result in lower postoperative pain scores when compared to the sole use of opioids.[42] A recent meta-analysis of eight studies showed NSAID use resulted in significantly better pain scores than placebo after lumbar spine surgery, and the type of operation and specific NSAID examined had a differential effect on postoperative analgesia.[43] Nonselective (COX-1 and COX-2 inhibition) NSAIDs have been implicated in impaired bone formation and healing due to studies in animal models. However recent evidence suggests that the adverse effects on bone healing in humans are likely dose and duration dependent.[5,44]

Evidence for prevention of postsurgical pain with acetaminophen alone after spinal surgery is lacking yet its safety profile and rapid onset of analgesia makes it an effective tool as part of multimodal therapy for post-operative pain management. Intravenous acetaminophen may offer faster onset and better acute analgesia compared to oral formulations but IV and oral formulations reach equivalency in overall effect after repeated doses.[40]

Gabapentinoids interact with the α-2-δ-subunits of voltage-gated calcium channels and are proposed to improve analgesia by decreasing the hyperexcitability of dorsal horn neurons and resultant central sensitization.[45] The oral absorption of pregabalin is proportional to dose and has a more predictable pharmacokinetic profile in comparison to gabapentin. A recent systematic review of randomized controlled trials (RCTs) reported that both gabapentin and pregabalin were efficacious in the management of postoperative pain in the immediate post-operative period.[46] Khurana et al demonstrated that pregabalin is associated with less pain intensity and improved functional outcomes three months after lumbar discectomy compared to gabapentin, but both had significant opioid dose-sparing effects.[47]

Dolgun et al showed both gabapentin and pregabalin were effective in relieving neuropathic pain following lumbar discectomy with durable results at one year follow up, helping to prevent the progression from acute to chronic pain.[48] The benefits of perioperative gabapentinoids should be carefully weighed against the possible adverse effects. Dizziness and somnolence are the most commonly reported side effects of gabapentinoids. Serious, rare adverse effects include respiratory and central nervous system depression, which are potentiated with co-administration of opioids. Thus, gabapentinoids can potentially increase the risk of accidental opioid-related overdose mortality.[49] In a recent real-world, cohort study of five million surgical patients over a ten-year period, concomitant use of gabapentinoids with opioids was associated with an increased risk of opioid overdose and other opioid-related adverse events; however, the absolute risk of adverse events was low (number needed to treat for additional overdose to occur was more than 16,000 patients).[50] Other non-opioid medications with less established evidence base for post-operative pain management following spine surgery include antispasmodics, antidepressants,[51–53] melatonin,[54] vitamin C,[55] and cannabinoids.[56]

Physical and Behavioral Interventions

Many interventions have been studied in the non-pharmacologic management of post-operative pain following spine surgery. Rehabilitation programs, in the context of pre-habilitation[57] and early rehabilitation after spinal surgery[58–60] have shown differing, inconclusive results and have been limited to small studies without clear evidence for generalizability. Other studies have investigated the role of acupuncture and acupressure in post-operative pain management. Yeh conducted a placebo, sham-controlled study investigating the role of acupoint electrical stimulation (AES) to reduce postoperative pain and found that AES, compared to placebo and no intervention, reduced pain and reduced patient-controlled analgesia (PCA) morphine requirements at 4 hours and 24 hours after spine surgery.[61] A recent systematic review and meta-analysis found encouraging but limited evidence for the effectiveness of acupuncture treatment for acute postoperative pain after back surgery, with improvement of postoperative pain intensity without reduction of opioid use in the first 24 hours, when acupuncture was compared to sham treatment.[62] An RCT of auricular point acupressure vs sham in twenty-nine patients who underwent anterior cervical discectomy and fusion showed improvement in pain interference and decreased levels of plasma IL-1β, IL-6, and TNF-α after 4 weeks of treatment and at 1 month follow-up.[63] Two RCTs that investigated postoperative pain after lumbar fusion showed improvement in opioid requirements with transcutaneous electrical nerve stimulation administration (TENS)[64] and localized cold therapy.[64] A systematic review of RCTs evaluating the efficacy of psychotherapeutic approaches for postoperative pain found that cognitive behavioral therapy (CBT) and a CBT-physiotherapy variant were effective in improving pain intensity assessed at various time-points after surgery. Although early results are promising, more research is needed to characterize the efficacy of behavioral interventions to improve postoperative pain among patients undergoing spine surgery. Acceptance and commitment therapy (ACT) and other mindfulness-based psychotherapies may provide benefit.[65]

Multi-modal approaches to managing post-operative pain after spinal surgery that include behavioral interventions have shown great promise in helping to ameliorate postoperative pain and the transition to chronic postsurgical pain. Questions remain in defining the timing, duration, and efficacy of these interventions. Future well-controlled, rigorous studies will play a pivotal role in defining the extent to which these behavioral approaches are incorporated into structured, evidence-based recovery protocols after spine surgery.

Perioperative Ketamine Infusions

Ketamine is a dissociative anesthetic first synthesized in 1962 and marketed for human use in 1970.[66] The intravenous form is commonly used as an adjunct to general anesthesia due to its analgesic and sedative qualities with minimal impact on hemodynamic stability. Subanesthetic doses of ketamine have also been utilized to treat cancer pain,[67] chronic nonmalignant pain,[68,69] as well as acute and postsurgical pain.[70] Ketamine's profound analgesic effects are attributed to its reversible antagonism of the NMDA receptor;[71] this mechanism is also widely hypothesized to inhibit or reverse central sensitization of pain after surgery.[72,73] Ketamine also binds to several other receptors including opioid,[74,75] nicotinic,[76] muscarinic,[77] L-type calcium,[78] gamma-aminobutyric acid,[79,80] hyperpolarization-activated and cyclic nucleotide–gated,[81] dopamine[82] and serotonergic[82] receptors—any of which may also contribute to ketamine's analgesic mechanism of action.

Ketamine can be given intraoperatively, as an adjunct to other anesthetic agents, with the intention of reducing postoperative pain and opioid use.[83] Commonly reported dosing regimens include an intravenous bolus of ketamine 0.1 to 0.5 mg/kg followed by an infusion of 0.1 to 0.6 mg/kg/h.[83,84] Patient populations considered to benefit most from ketamine include opioid-tolerant patients and adults undergoing surgery associated with severe postoperative pain.[84] Neurologic surgery—particularly spine surgery—can see significant overlap of these two populations. A recent review[85] and meta-analysis[86] examining the effect of perioperative ketamine for spine surgery found that ketamine reduces pain intensity and opioid consumption within the first 24 to 72 hours postoperatively. Aggregate outcomes past 72 hours were not examined due to few studies reporting long-term outcomes. There is evidence, however, to suggest that intraoperative ketamine yields long-term reductions in pain and opioid use manifesting several weeks to months after surgery.

In a RCT conducted by Loftus et al[87],102 opioid-dependent patients undergoing major spine surgery received an intraoperative bolus (0.5 mg/kg) plus infusion (0.6 mg/kg/h) of ketamine or normal saline. Patients who received ketamine had significantly reduced opioid consumption at 48 hours and 6 weeks after surgery. Although there was no difference in 48-hour pain intensity between groups, at 6 weeks the patients who received ketamine reported significantly lower pain scores despite using less opioids. In another RCT by Nielsen et al[88],147 opioid-dependent patients undergoing lumbar spinal fusion surgery were randomized to intraoperative bolus (0.5 mg/kg) plus infusion (0.25 mg/kg/h) of S-ketamine or normal saline. Patients who received S-ketamine had significantly reduced back pain at 6 months after surgery, although opioid use was not assessed at this timepoint.

The benefit of intraoperative ketamine is less clear in opioid-naïve patients who undergo spine surgery. In a RCT by Brinck et al[89] which compared low and high dose of ketamine infusions to saline placebo, there was no between-groups difference in opioid consumption 48 hours after spine surgery, as well as pain scores 48 hours, 3 months, and 2 years after surgery. Maheshwari et al[90] also failed to detect a difference in Quality of Recovery scores when comparing a multimodal analgesic regimen which included an intraoperative ketamine infusion to an opioid-only regimen in a mixed population with nearly half opioid-naïve patients.

In the postoperative period, subanesthetic ketamine infusions ranging from 0.1 to 1 mg/kg/h can be administered to awake patients in inpatient settings, typically under the guidance of an acute pain service.[84] Ketamine infusions started intraoperatively may also be continued through the acute postoperative period. Subanesthetic doses of ketamine are well-tolerated by most patients, with the most common adverse effects being dizziness and hallucinations.[91] In a RCT involving 59 patients, Barreveld et al[92] studied the effects of a postoperative ketamine infusion versus saline in patients who had undergone various nononcologic surgeries, the majority of which (66%) were spine surgeries. Both groups received patient-controlled analgesia with hydromorphone. Those who received ketamine infusions reported significantly lower pain intensity 24 hours after surgery but no difference in opioid consumption. In another RCT by Abrishamkar et al,[93] 45 patients who had undergone lumbar fusion were randomized to a postoperative infusion of either morphine or ketamine for 24 hours. Patients who had received ketamine infusion reported lower pain scores and used fewer supplementary doses of opioids. Long-term follow-up data was not reported in these studies. For other types of neurologic surgery such as intracranial surgery, the evidence for ketamine is much more sparse, possibly due to ketamine's perceived negative effects on cerebral blood flow and intracranial pressure, although this is controversial.[94]

In summary, ketamine is a versatile anesthetic and analgesic agent which can be administered perioperatively to reduce postoperative pain and opioid use. For neurologic surgery, the clearest evidence for ketamine's efficacy has been observed in opioid-dependent patients undergoing spine surgery, using an intraoperative regimen consisting of a 0.5 mg/kg bolus followed by an infusion of 0.25 to 0.6 mg/kg/h.

Intravenous (IV) Lidocaine Infusions

Lidocaine is an amide local anesthetic primarily modulating voltage gated sodium channels while also inhibiting calcium and potassium channels. Animal models show that IV administration of lidocaine decreases the inflammatory response to acute pain by suppressing multiple interleukins and tumor necrosis factor.[95–97] Systemic administration of lidocaine can thus be analgesic and it is commonly used perioperatively.[98,99]

There is a significant variability in timing of initiation, duration, and dose of IV lidocaine infusions.[100,101] Monitoring lidocaine plasma level is essential in exerting analgesia without exceeding a safe dose. During treatment,

plasma lidocaine concentrations of below 5 micrograms per milliliter of plasma are sufficient to attenuate sympathetic responses, decrease pain, and demonstrate volatile anesthetic and opioid-sparing effects.[101] Signs of systemic toxicity related to IV lidocaine include dizziness, convulsions, arrhythmias, prolonged hypotension, and other cardio-respiratory events.[102] Various protocols report IV lidocaine starting doses of 1–3 mg/kg/h with or without a loading bolus to achieve perioperative analgesia.[100,101,103] Intravenous lidocaine can be started preoperatively, intraoperatively or even postoperatively as a rescue analgesic. However, the majority of studies assess the efficacy of IV lidocaine administered during surgery (sometimes continued for one to 24 hours after the operation).[100,101,103–122] A recent Cochrane review in 2018 summarized the literature up to 2017 regarding IV lidocaine for patients undergoing surgery.[100] Compared to no treatment (or placebo), there is low quality data supporting the use of IV lidocaine in the early postoperative period, hours after surgery. Beyond 24 hours, IV lidocaine likely has no clinically relevant effect on reducing postoperative pain. Perioperative IV lidocaine does not appear to decrease opioid consumption either.[100] A more recent meta-analysis supports the same findings in colorectal surgery.[114] Interestingly, the same Cochrane review concludes that IV lidocaine is non-inferior to epidural analgesia in improving pain scores, gastro-intestinal recovery and nausea/vomiting in postoperative patients but the quality of data is much lower.[100] A more recent retrospective study compared efficacy of IV lidocaine to epidural analgesia in patients with traumatic rib fracture. Both modalities similarly improved pain scores and incentive spirometry volume.[111]

Similar trends are noted when examining the efficacy of perioperative IV lidocaine among patients undergoing spine surgery.[123] Farag et al report an RCT of 116 patients undergoing complex spine surgery (elective multilevel spine surgery with or without instrumentation, with general anesthesia) randomized to either perioperative IV lidocaine (2mg/kg/h) or placebo.[106] Patients randomized to IV lidocaine reported significantly reduced pain scores without a significant decrease in postoperative opioid consumption in the first 48 hours after surgery. Ibrahim et al reported an RCT of 40 patients undergoing single or double level spinal fusion surgery comparing a pre-induction 2mg/kg dosage of IV lidocaine, followed by 3mg/kg/h until the end of the operation to a comparable volume of 0.9% sodium chloride.[124] IV lidocaine significantly reduced VAS scores 48 hours surgery as well as up to 3 months post-operation. Morphine consumption was significantly reduced in the 1st 24 hours after surgery.[124] In a meta-analysis of 8 RCTS comprised of 349 patients receiving perioperative IV lidocaine, and 343 patients randomized to a control group for spine surgery, IV lidocaine administration was associated with significantly reduced pain scores at 2 hours, 4–6 hours, and 24 hours, but not 48 hours after surgery. Opioid consumption was decreased in the first 24 hours and 48 hours after surgery among those receiving IV lidocaine.[102] Given the limited number of studies to date,[125] more research is needed to confirm these findings, and to examine the remote effects of IV lidocaine months after spine surgery including the development of persistent postsurgical pain. Compared to placebo, elderly patients receiving IV lidocaine for spine surgery demonstrate significantly better cognitive function three days after surgery, and these findings warrant further investigation of IV lidocaine's neuroprotective effects.[126]

IV lidocaine remains an important component of multimodal analgesia among patients undergoing spine surgery despite limited evidence regarding pain outcomes after hospital discharge given the additional risk of IV lidocaine is relatively negligible.[100,101,103–122] An acute pain management service often monitors IV lidocaine administration on regular nursing floors. The infusion can be initiated at 1 mg/kg/h based on adjusted body weight with no bolus. Lidocaine plasma levels are assessed every 8–12 hours during the course of therapy. After each resulted level, dose adjustment can be considered based on the absolute plasma level and trajectory. Vital signs and clinical assessments for lidocaine toxicity typically occur every four hours. The infusion may be paused and the acute pain management service notified if the patient develops; (1) elevated lidocaine plasma levels; or (2) any signs or symptoms of lidocaine toxicity. Typically lidocaine infusions are administered for no more than a continuous 5-day period, and the goal is often to bridge the patient to an oral pain medication regimen in anticipation of hospital discharge.

In summary, moderate-quality evidence supports the efficacy of IV lidocaine in reducing immediate postoperative pain intensity and opioid consumption while reducing hospital length of stay among patients undergoing spine surgery.[102] Future research is needed to determine whether IV lidocaine prevents the development of persistent pain after spine surgery. Given the low incidence of adverse events, IV lidocaine is a reasonable addition to the perioperative pain management regimen for patients undergoing spine surgery.

Regional and Neuraxial Techniques

Perioperative pain management of patients undergoing spine surgery includes consideration of regional anesthetic techniques typically initiated in the intra-operative phase. Lower thoracic and lumbar spine surgery is still commonly performed under general anesthesia, yet regional anesthesia, spinal anesthesia, and epidural anesthesia (either alone or combined with spinal or general anesthesia) presents potential advantages of rapid onset of action; and reduction in intraoperative blood loss, thrombotic events, pulmonary complications, and postoperative cognitive dysfunction.[127] With advancement of spine surgery techniques including percutaneous and minimally invasive instrumentation systems, spinal fusions are now possible with use of these regional anesthetic techniques in lieu of general anesthesia. Common indications for outpatient spine surgery include canal stenosis, prolapsed intervertebral disk, or disk degeneration.[128] Enhanced recovery after surgery (ERAS) protocols apply a multidisciplinary approach to perioperative care to minimize the adverse effects of surgery.[129] ERAS protocols have been developed for lumbar decompression (eg microdiscectomy or lumbar laminotomy/laminectomy). Analgesic recommendations of such ERAS protocols include local anesthetic wound infiltration at the end of the operation.[129]

To extend the duration of local anesthetic wound infiltration, disposable, elastomeric pain pumps have been designed to deliver continuous infusions of local anesthetic into surgical wounds in the postoperative phase. The pumps deliver local anesthetic via a flow restrictor to a catheter lying in the surgical wound. A variety of pump volumes, flow rates, treatment durations, and catheter lengths can be selected. In a retrospective case-control study of 26 patients undergoing posterior lumbar spine fusion with or without a pump for local anesthetic wound infiltration of 0.5% bupivacaine, those receiving the pump used significantly less opioids in the first four postoperative days, but there were no differences in opioid use noted on the fifth and sixth days.[130] However, patients receiving the pump reported significantly reduced average pain intensity over the first five postoperative days. No complications were noted in this study.[130] Thus, elastomeric pain pumps present an option for acute incisional pain management.

The efficacy and safety of these continuous infusion local anesthetic pumps has been studied in higher-risk patients undergoing thoraco-pelvic fusion for the treatment of persistent spinal pain syndrome. In a retrospective study of 26 patients, 14 underwent pump placement and 0.5% bupivacaine administration into the wound at a rate of 2mL/hr. A catheter was placed on each side of the involved spinous processes in the subfascial plane and removed on the third postoperative day (POD).[131] There was no significant reductions in opioid usage during hospitalization or after hospital discharge up to 3 months after surgery, and continuous local anesthetic wound infiltration may be less effective for patients with pre-existing chronic pain and opioid use.[131] Larger prospective RCTs are warranted to examine the immediate and sustained effects of perioperative local anesthetic wound infiltration in patients undergoing spine surgery.

Spinal anesthesia presents several advantages compared to general anesthesia as patients can reposition themselves and reduce the risk of compression injuries such as pressure necrosis to the face or brachial plexus injuries. Overall, spinal anesthesia appears to decrease postoperative pain, nausea, and urinary retention. Spinal anesthesia is a form of regional anesthesia that has been used safely in lumbar surgery (eg microdiscectomy discectomy, laminectomy) for high-risk patients in whom general anesthesia is contraindicated with resulting excellent postoperative pain relief[127] The high prevalence of general anesthesia for lower thoracic and lumbar spinal surgery is primarily driven by surgeon preference as spinal anesthesia demonstrates comparable efficacy and favorable cost-effectiveness. Among patients undergoing lumbar discectomy, patients receiving spinal anesthesia report higher satisfaction, reduced blood loss, and reduced postoperative analgesic requirements compared to general anesthesia.[132] In patients undergoing lumbar laminectomy, those receiving spinal anesthesia demonstrated less postoperative nausea and vomiting, less hemodynamic instability, and reduced urinary retention compared to general anesthesia.[133] In a retrospective cohort of 34 patients undergoing lumbar spine surgery under spinal anesthesia, there was no appreciable learning curve for implementing spinal anesthesia in a surgical team familiar with minimally invasive discectomies and decompressive laminectomies and minimally invasive transforaminal lumbar interbody fusion. In this cohort, patients received L3-4 or L4-5 spinal anesthesia in the sitting position with 2.5mL of 0.5% bupivacaine, and then were placed prone. Light sedation consisted of intravenous dexmedetomidine and propofol precluding the need for general anesthesia.[134]

Spinal anesthesia is typically provided with a combination of bupivacaine and fentanyl with or without epinephrine. Typically isobaric bupivacaine results in higher levels of sensory block and fewer hemodynamic events compared with hyperbaric bupivacaine.[133] The disadvantages of hyperbaric bupivacaine include higher cephalic settling in the prone position with resulting intercostal paralysis and respiratory depression. Hyperbaric bupivacaine also results in less favorable early sensory and later motor reversal making isobaric bupivacaine a more favorable choice for spine surgery.[133]

Epidural anesthesia alone is a less favorable option for lumbar spine surgery compared to spinal anesthesia given inconsistencies in anesthetic distribution, unpredictable anesthetic depth, and obstruction of the operative site with the epidural catheter. When comparing lumbar laminectomy and discectomy outcomes for patients receiving combined epidural and general anesthesia or general anesthesia alone, patients demonstrate a lower incidence of postoperative nausea and vomiting, lower requirement for opioids, and reduced blood loss with the additional of epidural anesthesia.[135,136] When comparing spinal, epidural, and combined spinal-epidural anesthesia for patients undergoing lumbar laminectomy, efficacy was comparable, yet those receiving spinal anesthesia had higher morphine consumption over the first 24 hours and a higher rate postoperative nausea and vomiting.[137] Continued epidural analgesia in the postoperative phase presents distinct advantages for pain management. Postoperative epidural analgesia results in reduced postoperative opioid consumption. In an RCT of 85 patients undergoing major reconstructive spine surgery (eg anterior, posterior, or combined anterior and posterior spinal fusion of 2 or more levels) combined epidural and general anesthesia during surgery and postoperative epidural analgesia was compared to patients receiving general anesthesia and intravenous opioids for postoperative pain control. Those randomized to the epidural group received intraoperative epidural anesthesia with an infusion of ropivacaine, fentanyl, and epinephrine. After surgery, epidural analgesia was continued with infusion of 0.2% ropivacaine, 2 μg/mL fentanyl and 2 μg/mL epinephrine, at a rate of 2 to 8 mL/hr for 2 or 3 days. Epidural catheters were removed on the fourth POD. Patients randomized to receive epidural analgesia demonstrated significantly less pain, bleeding, nausea; earlier mobility; and higher satisfaction in the first 36 hours after surgery.[138] Future research examining the long-term effects of epidural analgesia are warranted to determine how perioperative pain management impacts persistent pain and opioid use after surgery.

Several regional anesthetic blocks have been described in management of patients undergoing spine surgery. The thoracolumbar interfascial plane block targets the dorsal rami of the lumbar spinal nerves. Under ultrasound guidance, local anesthetic is injecting into the fascial place between the multifidus and longissimus muscles at the level of L2-3 with a lateral to medial approach. A modified thoracolumbar interfascial plane block was subsequently developed to reduce the potential for inadvertent intrathecal injection with a lateral to medial needle orientation. The local anesthetic in the modified approach is targeted to the fascial plane between the iliocostalis and longissimus muscles with a medial to lateral approach. Typically, the modified thoracolumbar interfascial block is performed after induction of anesthesia and prone positioning. The spinous process of L2, and the fascial plane between the iliocostalis and longissimus muscles is identified under ultrasound guidance. Then, 20mL of dilute liposomal bupivacaine (consisting of 10mL of liposomal bupivacaine and 10mL of sterile saline) is injected and the block is repeated on the contralateral side.[139] In a retrospective review of 65 patients undergoing elective lumbar spinal fusion or lumbar laminectomy with or without an ERAS protocol incorporating the modified lumbar interfascial plane block,[139] there was a significant 51% mean reduction in opioid administration (42 MME) in patients undergoing laminectomy and a significant 38% mean reduction (60MME) in patients undergoing spinal fusion.[139] Addition of the modified thoracolumbar interfascial block to perioperative pain management for lumbar spine surgery represents a promising technique.

The erector spinae plane block is another regional anesthetic technique used during spine surgery. This paraspinal interfascial plane block results in a diffuse region of analgesia targeting ventral and dorsal rami of spinal nerves[140] Further diffusion of local anesthetic to paravertebral tissues extends the analgesia of this technique. For this block, patients are placed prone after induction of anesthesia. A curvilinear ultrasound probe is longitudinally placed over the sacrum and moved cranially to the target surgical level. The probe is then displaced in a longitudinal parasagittal orientation 3 to 4 cm lateral to the midline to visualize the transverse process. A needle is then inserted to contact the transverse process and 20mL of 0.25% bupivacaine is administered.[141] Correct local anesthetic placement is confirmed with linear spread local anesthetic separating the erector spinae muscle from the transverse process. In a double-blinded

RCT of 100 patients undergoing single level lumbar interbody fusion comparing ultrasound-guided erector spinae plane block to conventional opioid-based multimodal analgesia for postoperative analgesia,[141] patients receiving the block demonstrated significantly reduced opioid consumption in the first 24 hours following induction, reduced total muscle relaxant use during surgery, reduced intraoperative blood loss, reduced pain intensity in the first 48 hours, and higher satisfaction scores.[141] Beyond these regional blocks, case series have described the use of ultrasound-guided paraspinal interfascial plane blocks targeting the cervical multifidus plane and the cervical semispinalis plane in conjunction with neurophysiologic monitoring for postoperative analgesia following posterior cervical laminectomy.[142]

Many regional anesthetic techniques may be considered for perioperative pain management in patients undergoing spine surgery. These options include the use of local anesthetic wound infiltration or catheter placement, spinal anesthesia, epidural anesthesia, and combined spinal-epidural anesthesia. Several interfascial plane blocks have been developed to improve perioperative pain management. Characterization of long-term postoperative pain outcomes with implementation of regional anesthetic techniques for spine surgery is warranted. The efficacy of these regional anesthetic techniques is likely to further expand with continued advancements in minimally invasive spine surgery.

Future Techniques

Future techniques in the care of the spine surgery patient include identifying pain phenotypes and patient characteristics that are more likely to lead to decreased analgesic benefit from surgery and increased opioid use. Excellent work has been done by many groups that have identified that a significant contributing factor in determining the analgesic trajectory of a patient's post-surgical experience is the presence of alterations in the pain processing circuitry of the central nervous system. This includes the amplification of peripheral nociceptive input an addition to dampening of supraspinal descending pain inhibitory pathways. Research has shown that there may be common measurable phenotypic and physiologic characteristics at the individual level that are associated with poor analgesic outcomes after surgical procedures performed for the relief of pain. These phenotypic characteristics and physiologic states can be assessed using a variety of methods including patient-reported outcomes (PROs), quantitative sensory testing (QST), and neuroimaging. Current studies are underway to examine these constructs and how they impact pain trajectories and analgesic relief from spine surgery. The goal of such work is to identify baseline pre-operative characteristics that are most correlated with poor analgesic surgical trajectories and inform precision medicine techniques aimed at these characteristics that may improve outcomes for at-risk patients.

Conclusion

Optimizing the perioperative care of patients undergoing spine surgery is of great public health importance as there are millions of individuals who each year undergo spine surgery for an existing and refractory chronic pain condition. The present review has focused on the currently available pharmacologic and non-pharmacologic interventions that can be utilized pre-, intra-, and postoperatively to provide multimodal pain management of the patient undergoing spine surgery. The evidence-base highlights that comprehensive care is optimal for these patients. Phenotypic profiling of patients prior to surgery may play a future role in identifying pain- and patient-specific features that are more likely to lead to poor surgical outcomes with inadequate pain relief and increased opioid use. Choice of pharmacologic agents utilized should mechanistically target multiple physiologic pathways known to participate in pain processing. Lastly, it is paramount to provide patients pain education, increase self-efficacy, and promote physical rehabilitation.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Disclosure

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