Opioids are commonly prescribed postoperatively for pain control, especially in spine surgery. Not only does this pose concerns for potential abuse, but it also has been shown to worsen certain outcomes. Risk factors for increased use include preoperative opioid use, female sex, psychiatric diagnoses, and drug and alcohol use. Over the past few decades, there have been increasing efforts mostly spearheaded by governmental agencies to decrease postoperative opioid use via opioid prescription limitation laws regulating the number of days and amounts of analgesics prescribed and promotion of the use of enhanced recovery after surgery (ERAS) protocols, multimodal pain regimens, epidural catheters, and ultrasound-guided peripheral nerve blocks. These strategies collectively have been efficacious in decreasing overall opioid use and better controlling patients’ postoperative pain while simultaneously improving other outcomes such as postoperative nausea, vomiting, and length of stay. With an aging population undergoing an increasing number of spinal surgeries each year, it is now more important than ever to continue these efforts to improve the quality and safety of pain control methods after spinal surgery and limit the transition of acute management to the development of opioid dependence and addiction long-term.

INTRODUCTION

OPIOID EPIDEMIC AND SEQUELAE

Opioid misuse has reached epidemic status in the United States. In 2008, more Americans died from opioid overdose than from automobile accidents.1 Studies have placed the number of daily deaths from an opioid overdose at over 220 people per day. The crisis has become widely regarded as a public health emergency with over 81,000 deaths, according to the Centers for Disease Control in 2020 alone in the United States from opioid overdoses. These sobering facts have led to Congress passing an $8 billion SUPPORT for Patients and Communities Act to address the nation’s opioid overdose epidemic.2–4

In 2017, opioids made up nearly 70% of all drug overdoses, and most were from prescriptions.1,5 The rate of drug overdose mortality by 2017 was five times that of 1999.6 Unfortunately, accidental/non-intentional overdose is not uncommon.4 Most illegal opioid use starts from legal prescriptions, pointing to the critical responsibility that healthcare workers, in particular physicians and prescribers, may have in this crisis.5

Opioid misuse contributes not only to mortality via overdose. Still, it has also been shown to increase the risk of acute coronary syndrome.2 Between 2015 and 2020, infective endocarditis related to injection drug use also nearly doubled, most notably among younger patients without significant comorbidities.2 Following surgery, chronic opioid use is additionally associated with a greater likelihood of complications such as wound dehiscence and surgical site infection and postoperative constipation that is more resistant to traditional laxative therapies.7

OPIOID PRESCRIPTIONS AND SURGERY

In the United States, 98% of patients have been prescribed opioid medications following surgery.8 While many of these patients do not use opioid medicines before surgery, most are routinely prescribed them postoperatively.8 The majority of patients receiving postoperative opioid prescriptions receive an excess of pills, and 40% of these prescriptions are never properly disposed of, creating an opportunity for diversion.1 To illustrate the excess of opioids in circulation, one study found that 88% of total knee arthroplasty (TKA) patients were prescribed more opioid pills than they used or
required.9

Among surgical specialties, orthopedic and neurosurgery procedures tend to have the highest rates of opioid use, and interventional spinal procedures fall at the intersection of these specialties.10 Over the past three decades, the diagnoses and treatment of spinal pathologies, such as lumbar stenosis and spondylolisthesis, have increased as the United States experiences an aging population.11 Meanwhile, opioid use following common procedures such as spinal and/or lumbar fusion operations is strikingly high. For the most part, physicians prescribe regimens that vary in dosage and duration without a standard regimen in place.12

Orfield et al. compared chronic opioid prescriptions following 50 common orthopedic procedures and found that 8 of the 10 surgeries with the highest rates of long-term opioid prescription usage were spine surgeries, consistent with the invasive nature of spinal surgery.9 Opioid overuse in spine surgery has also been demonstrated by a trial which showed an increase in post-surgical opioid dependence from 0% to 47.8% of patients who underwent surgical fusion for degenerative scoliosis from 2001-2015.13

There are varying degrees of invasiveness among procedures within spine surgery, subsequently impacting opioid prescriptions and usage. For example, the spinal fusion of four or more levels, compared to one to three, is associated with greater opioid use after surgery.5 In lumbar fusion, there is increasing evidence showing that minimally invasive surgery (MIS) may lead to earlier opioid independence at 2 vs. 4 weeks and decreased postoperative opioid use.14-16 Similarly, Schoenfeld et al. showed that less intensive discectomy and decompression procedures had a greater likelihood of patient opioid discontinuation than lumbar interbody arthrodesis.17 Thus, specific surgical characteristics are crucial to keep in mind when considering postoperative opioid use.

The etiology of the opioid endemic surrounding spine surgery may also be influenced by the multidisciplinary nature of the patient care process. Although surgeons accounted for 69% of opioid prescriptions in the first three months after surgery, they accounted for only 11% of opioid prescriptions at 9-12 months, whereas primary care physicians accounted for 55%.18 Postoperative gaps in communication between care teams can lead to lack of ownership of opioid management, potentially leading to excess refills or misinformation regarding intended course longevity.19

Opioid pharmacology and physiology understanding have evolved in recent decades since identifying the opioid receptor over four decades ago. Opioid prescriptions or any exogenous opioid will shut down endogenous opioid production, resulting in reduced levels of endorphins, enkephalins, and dynorphins. This process, which takes weeks and months, results in opioid dependence. In addition, without exogenous opioid delivery, patients will exhibit central nervous system hyperarousal states or what is commonly known as withdrawal symptoms. Thus, acute pain management can directly affect patients and their resultant development of opioid dependence and addiction. Further, it is the basis of why the government has established policies throughout the United States in all fifty states limiting opioids in the setting of acute pain manage-

ment to reduce transition to opioid dependence and addiction states.

IMPACTS ON OUTCOME AND STAY

The clinical significance of increased opioid utilization has been shown to impact outcomes, especially ongoing opioid use before surgery negatively. Increased 1-year reoperations evidence this, emergency department (ED) visits, epidural and facet joint injections, wound complications, infections, neurological complications, acute renal failure, and venous thromboembolism rates following cervical fusion in patients on chronic opioid therapy (COT) preoperatively.20 One animal model showed that opioid use before and after lumbar fusion led to the delayed remodeling of the fusion at 6 weeks – one potential explanation for higher rates of reoperation in patients on COT preoperatively.21,22 Patients who receive preoperative COT are also less likely to return to work after spine surgery, affecting their quality of life and further confounding postoperative outcomes.22,23 Additionally, multiple studies have shown COT patients to have an increased length of stay.24,25 Kha et al. demonstrated an increase of 1.1 days for every 100 morphine milligram equivalents (MME), which directly impacts healthcare utilization and the outcomes of the individual patients.25 Finally, another concerning outcome is the development of chronic opioid use following spinal procedures. Cook et al. found that the development of chronic opioid use following common spinal procedures to be 15-18% in opioid-naive individuals and 50-64% in chronic opioid users.26 This illustrates both the magnitude of opioid use following spinal procedures in general and also the risk that preoperative COT poses for long-term use.

RISK FACTORS FOR INCREASED OPIOID USE FOLLOWING SPINE SURGERY

PRE-OP USAGE AND POSTOPERATIVE USE/DURATION

Just as preoperative opioid use impacts specific outcomes, it also plays a role in postoperative consumption. However, the term "preoperative opioid use" has varying criteria; some studies define it as self-reported opioid use or prescription availability at the time of surgery, while others include date ranges up to 365 days before surgery.27 Given the variability of this term, preoperative opioid use ranges from 10.2% to 70% of patients undergoing spine surgery.27,28 Regardless, preoperative opioid use has been widely associated with greater postoperative opioid use following spine surgery.20,21,25,29-32 Across all major spine surgery, Dunn et al. showed that 52% of patients on COT preoperatively still used opioids 12 months postoperatively compared to 18.3% of opioid-naïve individuals.33 Following one and two-level posterior lumbar fusions, one study found 87.4% of patients on preoperative COT were still using opioids for at least 12 months.31 Following lumbar decompression without fusion, transforminal or posterior interbody fusion, anterior cervical discectomy and fusion, cervical disc arthroplasty, and posterior lumbar fusion spine procedures, only 63-68% of opioid naïve patients fill an opioid prescription, contrasting with the 91-95% of chronic pre-
operative users. Additionally, preoperative opioid users have shown to have a significantly higher opioid fill rate than those who did not use opioids before cervical arthrodesis (45.3% vs. 6.3%). Following spinal decompression, patients on preoperative COT, have shown to receive more opioids while also having a significantly longer postoperative opioid course (7 months) compared to opioid naïve individuals (2.6 months).

SEX DIFFERENCES

A study of opioid use following spinal surgery found that female sex was associated with higher rates of opioid dependence postoperatively, with a relative risk of 1.166. An additional, separate study of patients undergoing lumbar decompression and fusion also found female sex to be an independent risk factor for prolonged opioid use following surgery with an odds ratio of 1.14. Notably, there was no significant sex difference among preoperative opioid use in this study population. Women may be more likely to be prescribed and therefore use opioid analgesics by healthcare providers. Additionally, opioid overdose deaths are also more frequent among female patients. Postoperatively, female patients have reported higher pain levels and required higher doses of morphine as soon as their arrival in the post-anesthesia care unit (PACU). These findings could perhaps be attributed to chronic pain conditions being more typical among female patients, who may also have increased pain sensitivity.

PSYCHIATRIC CONSIDERATIONS

Psychiatric diagnoses have been associated with higher rates of both pre- and postoperative opioid use. Anxiety and depression are not only associated with worse surgical outcomes, but they also make a patient less likely to discontinue postoperative opioid use. Among patients who were not taking opioids before surgery, a diagnosis of post-traumatic stress disorder was associated with an increased likelihood of prolonged postoperative opioid use. Unfortunately, psychiatric comorbidities may be inadvertently treated with increased opioid refills, prolonging and exacerbating the problem. Self-confidence and "positive mood" were found to be "the most effective pain relievers," according to a 2017 editorial by the Journal of Bone and Joint Surgery. Thus, patients suffering from psychiatric disorders may already be predisposed to poor outcomes further impacted by postoperative opioid use and dependence. One study found that regardless of psychiatric diagnosis, preoperative administration of duloxetine, an SNRI antidepressant, led to decreased postoperative pain and improved functional outcomes, pointing to the interrelated nature of physical and psychiatric pain.

SMOKING/ALCOHOL/RECREATIONAL DRUG USE

Tobacco smoking has been shown to increase preoperative opioid use among female patients undergoing spinal surgery; however, this study did not examine used in the postoperative period. Alcohol and drug abuse are associated with increased odds of chronic opioid use following any surgery, with odds ratios 1.85 and 3.15, respectively. A separate study of patients undergoing spinal surgery concluded that tobacco, alcohol, and drug abuse were risk factors for opioid dependence but did not quantify how great the impact was.

OTHER

Higher rates of postoperative opioid use are also associated with younger patients and obesity. Furthermore, the likelihood of postoperative opioid use increases with higher dosages, measured in MME. In other words, prescribing a lower dose of postoperative opioids may help decrease overall postoperative opioid use. Finally, patients with Health Maintenance Organization insurance plans are less likely to receive opioid prescriptions from an in-office provider.

INTERVENTIONS TO REDUCE USAGE AND THEIR OUTCOMES

ENHANCED RECOVERY AFTER SURGERY PROTOCOL

The enhanced recovery after surgery (ERAS) protocol, designed in 1997, is a multimodal approach to surgical care designed to address preoperative, intraoperative, and postoperative stressors to reduce complications, morbidity, and patient pain. In this regard, most ERAS protocols are designed to have decreased opioid consumption postoperatively, and reduced hospital stays. Since its development, ERAS protocols have been utilized in various surgical specialties, including breast surgery, colorectal surgery, and hepatic surgery. There are designed to be executed by a multidisciplinary team ranging from anesthesiologists, surgeons, nutritionists, occupational therapists, nurses, case managers, and others and is individually tailored to the surgical subspecialty. By design, ERAS protocols that are accepted in practice have not only been shown to reduce the length of stay (LOS) and opioid consumption postoperatively but as well, demonstrate a reduction in complications, reduction in postoperative costs, and lower patient dissatisfaction rates across a wide variety of surgical subspecialties.

In recent years, the utility of ERAS with regard to spinal surgery has explicitly come into question as spinal surgeries are particularly invasive and continue to increase in the United States each year. Patients undergoing these surgeries often experience significant postoperative pain, long recovery times, and high rates of complications. ERAS is thus a potential solution to reduce LOS, improve patient outcomes, and reduce postoperative opioid use.

Regarding lumbar surgery specifically, the ERAS society, a group designed to provide expert consensus on ERAS protocol recommendations for specific surgical subspecialties, recently investigated available data and made numerous recommendations. In the preoperative period, recommendations are focused on preoperative counseling and education, nutrition assessment, cessation of smoking and alcohol, preoperative fasting to include clear fluids up to 2 hours and solid foods up to 6 hours before surgery, and management of preoperative anemia. Further, the use of...
sedatives for anxiolysis preoperatively is not recommended. In contrast to this, NSAIDs, neuropathic pain medicines, and acetaminophen have been shown in numerous randomized control trials and meta-analyses to reduce opioid use.54,56,57

Intraoperatively, the ERAS protocol focuses on antimicrobial skin preparation, intraoperative anesthetics with neuromuscular blockade, and neuraxial techniques such as epidural anesthetics and inhalational agents, the prevention of hypothermia, the use of local and regional anesthetics, and careful fluid and urinary volume management.54 Specifically, randomized control trials have shown that intrathecal morphine and epidural anesthetics such as bupivacaine directly reduce opioid use after spine surgery.58–60 Direct wound installations with local anesthetics such as ropivacaine and bupivacaine have also been demonstrated to decrease opioid use.61

Postoperatively, particular attention is given to nausea control, early mobilization, and postoperative management of drains.54 In addition, a multimodal approach is taken to postoperative prescription medication management. Among this approach, acetaminophen, NSAIDs, and neuropathic pain medications, including gabapentinoids, remain the cornerstone of treatment. When used in combination, these drugs dramatically reduce pain, improve patient satisfaction, and reduce opioid consumption and opioid-related complications.62–64 Finally, the ERAS protocol involves continual auditing and improvement based on gathered data to further advance outcomes.54 While recommendations are limited to lumbar surgery currently, further prospective research is underway to investigate the benefits and limitations of an ERAS protocol for thoracic and cervical spine surgery.

PRESCRIPTION MEDICATIONS AND MULTIMODAL PAIN REGIMENS

When used in excess, opioids can have significant adverse side effects, including increased rates of constipation, depression, respiratory disorders, drug overdoses, and others.65–67 As a result, multimodal prescription pain regimens have been developed to reduce opioid use and subsequent adverse effects. Current multimodal regimens typically include acetaminophen, NSAIDs, gabapentinoids, muscle relaxants, and potentially local anesthetics.

Acetaminophen is an analgesic and antipyretic drug that appears to work via inhibition of prostaglandin synthesis by reducing the conversion of PGG2 to PGH2 and, thus, the ultimate generation of arachidonic acid metabolites and has no known anti-inflammatory effect.68 NSAIDs, another cornerstone of multimodal therapy, demonstrate anti-inflammatory, antipyretic, and analgesic effects and rely on the inhibition of cyclooxygenase enzymes that result in the development of inflammatory and pain-inducing prostaglandins.69 Neuropathic medications such as pregabalin and gabapentin are also typically included and function through interactions with the alpha2-delta subunit of voltage-gated calcium channels located in neurons throughout the nervous system.70 These medications are amino acid drugs that reduce pain processing by reducing excitatory amino acids and neuropeptides released during pain signaling.70,71 Less consistently included are muscle relaxants such as methocarbamol or diazepam and local anesthetics such as transdermal lidocaine patches that function via prolonging the inactivation of sodium channels within the cell membrane of neurons.72

While multimodal approaches have previously been used in orthopedic surgery and other surgical fields, recent research has investigated the use of multimodal approaches involving these drugs specifically in postoperative pain for spine surgery. A multimodal regimen consisting of scheduled doses of acetaminophen, NSAIDs, gabapentin, lidocaine patches, and one of two muscle relaxants was compared to a non-standardized provider-dependent regimen in one retrospective cohort after posterior lumbar surgery.73 Opioids were only reserved for breakthrough pain. Opioid use was significantly lower in the multimodal group (p < 0.02), while pain scores were also significantly lower (p < 0.001). Another series compared IV morphine to a similar multimodal approach and again found a reduction in opioid usage after lumbar surgery.74 Mathiesen et al. also found a multimodal approach to be associated with statistically significant lower rates of nausea, earlier rates of mobilization, shorter lengths of stay, and lower rates of sedation.75

Additionally, in 2016, Bohl et al. investigated a multimodal approach to pain management in cervical spine surgery with similar results. Their series of 239 patients again found decreased length of stay (p < 0.001), decreased narcotic use (p <0.001) and decreased nausea and vomiting (p < 0.001). Other series with cervical, thoracic, and lumbar spine surgery patient populations have also validated these findings.76 Although research largely supports multimodal approaches to postoperative prescribing. Further research is necessary to continue drug combination optimization.

EPIDURAL CATHETERS AND PERIPHERAL NERVE BLOCKS

Although often employed as a multimodal pain regimen that also includes oral and enteral medications, several local techniques have been utilized to reduce postoperative pain and opioid use after spinal surgery. One such technique includes continuous epidural analgesia in which a catheter is used to deploy medications such as bupivacaine or fentanyl into the epidural space.77 In one series of 615 patients undergoing scoliosis surgery, patients were randomized to either having an epidural catheter placed intraoperatively that could continually deploy medication or receiving patient-controlled anesthesia (PCA) via a pump that deployed opioid medications.78 Pain scores were significantly decreased in the epidural group at all measured time periods compared to the PCA group (p < 0.001). This was again shown in a series demonstrating that patients with epidural catheters that deployed bupivacaine and fentanyl required less opioid medication after lumbar surgery.79

Other spinal regimens include single-dose epidural medications and intrathecal medications.80 Single-dose regimens are applied preoperatively by advancing a needle into the epidural space or administered directly by the surgeon to exposed dura once decompression has been performed.81,82 Drugs used include bupivacaine, methylpred-

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An Update on Postoperative Opioid Use and Alternative Pain Control Following Spine Surgery

Orthopedic Reviews
nisolone, morphine, clonidine, and many others. Bourke et al. demonstrated that dural application of a single dose of 5 mg of morphine decreased postoperative pain scores compared to controls.85 However, a series of 150 patients comparing a single dose of epidural bupivacaine or methylprednisolone versus normal saline found no difference in postoperative pain or opioid use.81

Intrathecal administration is typically conducted via direct injection of medication into the dural sac once decompression has been completed.84 One of the more common medications used for this purpose, morphine, has been demonstrated to suppress the respiratory drive and cause hypoxia.85 Thus, it is essential to use the lowest dose possible and to monitor respiratory rate and oxygen saturation. However, in one series of 150 patients, 0.2 mg of intrathecal morphine was shown to reduce opioid usage (p < 0.03) and was not shown to increase the risk of respiratory depression.84 Chan et al. also used 15 micrograms of intrathecal fentanyl in a series of patients. It is absorbed more rapidly due to its lipophilic properties with a lower risk of respiratory compromise.86 Another series demonstrated that intrathecal neostigmine, an acetylcholinesterase inhibitor, was able to reduce postoperative opioid use.87

Aside from neuraxial anesthesia, peripheral nerve blocks have been utilized in combination with other pain regimens to decrease intraoperative and postoperative pain. One novel technique is the erector spinae plane (ESP) block. Developed in 2016, the ESP block is an interfascial block that targets the dorsal and ventral rami of the spinal nerves as they exit the spinal cord with a local anesthetic.88 It is performed at the spinal level (s) undergoing surgery and is guided via ultrasound. Elyazed et al. found that only 13.3% of patients required intraoperative fentanyl with bilateral ESP blocks vs. 90% in the control group (p < 0.001).

Further, postoperative pain scores were reduced up to 12 hours after surgery.89 Outcomes were similar in another retrospective study.90 Side effects are rare but include infection, pleural injury, vascular injury, pneumothorax, and failure. While other prospective trials are currently underway, further research is warranted to continue outlining the benefits and limitations of ESP blocks. Other local blocks include continuous wound infiltration, targeted nerve root blocks, and local analgesic administered intraoperatively to the skin and subcutaneous tissues.

**PRESCRIBING LIMITATIONS**

In the past two decades, opioid use and prescribing have become the focus of state and national legislation. The number of opioid overdose deaths has quadrupled since 1999 and included over 500,000 people.91 Legislation targeting prescribing limitations has been enacted in over 35 states since 2016 to regulate the daily and total MMEs of narcotic medications that providers can prescribe.92 These laws are of particular interest in spine surgery, as patients facing chronic neck and back pain who undergo surgery are among the heaviest opioid users both preoperatively and postoperatively.93 Questions have subsequently been raised about the effectiveness of these laws and the potential for suboptimal pain control that could result in discomfort and complications such as decreased mobility after surgery.

While the evidence evaluating the efficacy and results of these prescribing limitations after spine surgery is limited, several studies have attempted to elucidate information. For example, in 2019, Reid et al. performed a retrospective review of 211 patients undergoing anterior cervical disectomy and fusion surgeries and compared patients who had surgery before the prescribing limitation to those who had surgery after.94 Interestingly, patients who had surgery post-law received fewer postoperative MMEs and fewer 30-day postoperative MMEs with no subsequent increase in ED visits or readmissions. Although not specifically investigated, this suggests there was no significant reduction in pain control.

Another retrospective review investigated this question in lumbar spine surgery. It again demonstrated a reduction in postoperative MMEs and 30-day postoperative MMEs with no increase in ED visits or readmissions after prescribing limitation laws.95 A recent study comparing nearly 25,000 patients undergoing spine surgery in Michigan also found a 9% decrease (p < 0.001) in preoperative opioid use after prescribing laws were enacted.96 Finally, Lovecchio et al. investigated a cohort of patients undergoing lumbar surgery before and after an educational conference, and institutional guidelines on postoperative opioid prescribing were instituted.97 These interventions significantly reduced the MMEs prescribed at discharge. While current work is underway to illustrate further the effects of prescribing limitation laws on patients undergoing spine surgery specifically, further prospective research that simultaneously investigates patient comfort, pain scores, and recovery after surgery is warranted.

**CONCLUSION**

As spinal conditions and procedures tend to be quite invasive and painful, physicians are tasked with a challenging and delicate balancing act between providing patients adequate pain control and curtailing excessive opioid use. Over the past few decades, the repercussions of excessive opioid use have been detrimental for health systems, communities, and individual patients. Furthermore, with an aging population, spine treatments will almost certainly continue to increase, which places a large responsibility on medical providers to deliver the best pain control possible to their patients without worsening the existing opioid epidemic. While there is undoubtedly room for improvement, the issue has continued to get well-deserved attention resulting in many efforts that have decreased not only opioid consumption but also improved certain patient outcomes. Therefore, further prospective research is warranted to continue implementing best practices by clinicians to continue improving the quality and safety of pain control methods following spine surgery.

**DISCLOSURES**

No relevant disclosures.
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