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INTRODUCTION

Enhanced recovery after surgery (ERAS) is an interdisciplinary, multimodal approach to improve postoperative outcomes by applying multiple evidenced-based interventions. These interventions are incorporated into preoperative, intraoperative, and postoperative protocols based on identified risk factors for high-risk patients and surgeries. These protocols have been shown to reduce complications, hospital stays by 30% to 50%, readmissions, and costs.1–3 ERAS has been effective in other specialties such as colorectal and orthopedic surgery, showing decreased postoperative complications and outcomes.1,3

ERAS has been recently adapted for spine surgery at multiple institutions in the United States. The Hospital for Special Surgery showed decreased length of stay, reduced complications, and no readmissions in their cohort study looking at 15 standardized ERAS elements.4 For lumbar spine fusions, there was decreased length of stay, decreased blood loss, and improved pain

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control in a retrospective cohort performed by Wang and colleagues. Other studies have identified decreased postoperative intensive care unit admissions, a shorter length of stay, reduced cost, and decreased opioid consumption throughout the duration of the hospital stay. In addition, some studies have shown improved mobilization and ambulation rates at the 1-month follow-up.\(^{6-8}\) Ali and colleagues\(^{7}\) identified additional postoperative benchmarks that were impacted positively by implementation of ERAS at University of Pennsylvania, including decreased urinary catheter use and decreased opioid consumption at the 1-month follow-up.

The recent opioid epidemic in the United States has seen drug overdoses triple from 1999 to 2014.\(^9\) Sixty-three percent of drug overdose-related deaths in 2015 involved use of an opioid medication.\(^9\) Narcotic-based postoperative protocols for pain management have contributed to the opioid epidemic with surgery being a key risk factor for chronic opioid use.\(^{10,11}\) Despite focusing on this postoperative issue, studies continue to show that the management of postoperative pain requires significant modifications.\(^{12,13}\) As a result, current practices in perioperative pain management must be addressed to reduce opioid use while improving pain control for patients. The Joint Commission recommends establishing protocols using “multi-modal adjuvant therapies,” including nonopioid analgesics to decrease the dose of opioids needed for optimal pain control. The National Action Plan to Prevent Adverse Drug Events states that federal agencies should use evidence-based strategies to optimize safe opioid prescribing including “multimodal, team-based care” and non-opioid pharmacologic therapies to “personalize pain management.” This multimodal approach is defined as 2 or more analgesic drugs that act via different mechanisms administered in conjunction\(^{14}\) (Fig. 1). The American Society of Anesthesiologists Task Force recommends that multimodal pain management be used whenever possible.\(^{14}\)

Improvements in pain management for spine surgery can play a significant role in decreasing opioid use and improving pain management. The potential impact of multimodal protocols to treat spine surgery pain is large, between 2001 to 2011 there was a 70% increase in the overall number of spine surgeries.\(^{10}\) A 2018 study showed that patients undergoing minimally invasive spine surgery consumed less than one-half the opioids they were prescribed postoperatively.\(^{15}\) These results highlight the need for continuous monitoring and evaluation of patient pain management needs to decrease unnecessary opioid prescriptions. This finding has positive implications for decreasing a patient’s risk of opioid dependence, as well as decreasing the possibility of opioid diversion.\(^{15}\) Implementation of protocols and reducing the quantity of opioids necessary for adequate pain control will only further reduce the quantity of opioids prescribed after hospital discharge.

Decreased opioid use is not only beneficial in decreasing drug-related adverse outcomes such as addiction, diversion, or death, but also advantageous for outcomes in spine surgery. Animal models have shown decreased rates of healing and fusion with opioid use.\(^{16}\) In spine surgery, higher opioid prescriptions are associated with an increased risk of deep venous thrombosis, postoperative infection, gastrointestinal and respiratory complications, increased hospital length of stay, and higher overall hospital costs.

The ERAS paradigm is an ideal framework in which to incorporate the needed changes in postoperative pain management for spine surgery. Using evidence-based and best practice principles, rational pain management protocols can and have been created. ERAS pain management protocols emphasize a multidisciplinary approach across the operative episode to improve pain control and minimize narcotic consumption. One such protocol has been developed at the Cleveland Clinic and can serve as an example of an evidence-based rational spine surgery pain management protocol.

**PREOPERATIVE PAIN MANAGEMENT INTERVENTIONS**

Preemptive analgesia has been shown to reduce postoperative pain and narcotic consumption (Fig. 2). ERAS pain protocols therefore, should include preemptive analgesia on the day of surgery before initiation of the operation. A number of medications have been shown to be helpful preoperatively, including acetaminophen, gabapentin, and cyclooxygenase (COX)-2 inhibitors.

**Acetaminophen**

Multiple studies have demonstrated benefit of acetaminophen as part of a greater multimodal pain management protocol. The American Society of Anesthesiologists recommend administering scheduled acetaminophen with a maximum dose not to exceed 4 g/d to prevent the risk of hepatotoxicity.\(^ {14}\)

The benefits of acetaminophen include decreased opioid use, increased analgesic control, and more cost-effective care.\(^ {17}\) After lower extremity surgery, the addition of preoperative acetaminophen has been shown to decrease
opioid consumption and reduce the need for analgesic rescue.\textsuperscript{18} This low-cost analgesic medication provides effective pain relief after surgery, indicating a cheaper alternative.\textsuperscript{19} A systematic review of acetaminophen in combination with nonsteroidal anti-inflammatory drugs (NSAIDS) by Ong and colleagues\textsuperscript{20} demonstrates superior analgesia compared with either drug alone. Acetaminophen has few contraindications including severe liver disease, and few drug interactions. Current recommendations advise administering oral acetaminophen over intravenous (IV) administration with some studies showing little benefit of IV infusion.\textsuperscript{17,21} However, there is controversy in the literature, with studies indicating a clear benefit that has been corroborated by a Cochrane review of 75 studies presenting high-quality evidence.\textsuperscript{22–24}

**Gabapentin**

Gabapentin has been shown to decrease pain scores, decrease morphine use, and decrease rates of postoperative nausea, vomiting, and pruritus with minimal side effects.\textsuperscript{25–28} The significant decrease in postoperative nausea and vomiting provides additional justification for its use as a preemptive measure.\textsuperscript{29} Other studies have confirmed decreased rates of opioid consumption without additional side effects and decreased rates of

![Fig. 1. A representation of various levels of analgesia from the site of local tissue manipulation to the feedback loop in the central nervous system.](image-url)
the use of rescue pain medications.\textsuperscript{30,31} Hegarty and Shorten\textsuperscript{31} in a randomized placebo-controlled trial found that a single dose of pregabalin decreased postoperative morphine consumption, with an absolute difference of 42.3\%. Gabapentin not only prevents hyperalgesia, but also acts as an anxiolytic, addressing the association between preoperative anxiety and postsurgical pain.\textsuperscript{25} Based on these findings, The American Society of Anesthesiologists recommends that gabapentin be administered in the perioperative period.\textsuperscript{14}

Cyclooxygenase-2 Inhibitors

The use of COX-2 inhibitors has had a significant impact on postoperative pain control when administered before surgery.\textsuperscript{32} This is mediated by a decrease in prostaglandin synthesis, decreased tissue inflammation, and by preventing the sensitization of nociceptive receptors.\textsuperscript{25} Furthermore, these agents are preferred to nonselective COX inhibitors owing to the preservation of platelet function and decreased risk of gastric bleeding. COX-2 inhibitors were not shown to increase the risk of bleeding in the perioperative period and have a decreased incidence of gastrointestinal side effects compared with nonselective NSAIDs.\textsuperscript{33}

The American Society of Anesthesiologists Task Force recommends COX-2 inhibitors and nonselective NSAIDs to be added to the perioperative pain management regimen.\textsuperscript{14} Pain management protocols combining COX-2 inhibitors and gabapentin have been shown to have effective analgesic control, improved patient satisfaction, and decreased opioid use with fewer side effects when compared with gabapentin monotherapy as found by Vasigh and colleagues.\textsuperscript{34}

INTROOPERATIVE AND POSTOPERATIVE PAIN MANAGEMENT INTERVENTIONS

An effective intraoperative pain management protocol requires collaboration with anesthesiology to create a rational multimodal series of intraoperative interventions to improve postoperative pain control. This collaboration is an integral aspect of the multimodal ERAS protocol. Various intraoperative specifications were delineated to aid in the postoperative management of all patients undergoing elective spine surgery.

Ketamine

The American Society of Anesthesiologists Task Force recommends the use of ketamine combined with IV morphine, which has demonstrated improved pain scores, decreased analgesic use, and improved nausea scores compared with IV morphine alone.\textsuperscript{14} Previous studies have shown ketamine infusions to be effective in spine surgery and other surgical specialties with improved pain control and decreased opioid use.\textsuperscript{35,36} A systematic review by Laskowski and colleagues\textsuperscript{36} found ketamine to be of particular benefit in painful procedures, including upper abdominal, thoracic, and major orthopedic procedures. Pendi and colleagues\textsuperscript{35} reviewed a total of 14 randomized controlled trials, finding supplemental perioperative ketamine to decrease postoperative opioid consumption up to 24 hours postoperatively in spine surgical patients.

The use of ketamine is recommended for patients with chronic pain owing to its opioid-sparing effect. Therefore, this therapy confers the greatest advantage in the patient population that is expected to require high doses of postoperative
opiods. Major side effects include neuropsychiatric symptoms and postoperative nausea and vomiting.

**Lidocaine**

Intraoperative IV lidocaine infusion has been shown to improve pain outcomes, decrease hospital length of stay, and has been associated with a decreased 30-day complication rate. The clinical effects of lidocaine, by attenuation of the proinflammatory system to decrease pain and ileus, may outlast the infusion by hours or days. This pain attenuation has an opioid-sparing effect and additionally reduces postoperative nausea and vomiting. These effects have been demonstrated in multilevel and major spine surgery where infusions resulted in decreased postoperative pain, decreased opioid consumption, and improved functional outcomes.

**Ketorolac**

Ketorolac is an IV NSAID that has demonstrated significant effectiveness in controlling postoperative pain and decreasing opioid consumption when administered perioperatively. It is typically given at the end of the case and continued into the postoperative period. For patients younger than 65 years of age, a 30-mg dose is given; patients 65 and older a 15-mg bolus is given. Contraindications for administration include a creatinine of more than 1.3 mg/dL, a bleeding disorder, or surgeon discretion based on intraoperative hemostasis.

The American Society of Anesthesiologists Task Force recommends NSAIDs to be administered around the clock, with improved pain scores when IV morphine is combined with ketorolac compared with IV morphine alone. A meta-analysis by Gobble and colleagues demonstrated that ketorolac was equivalent to opioids for pain control after surgery and should be administered in the perioperative period to decrease opioid use. In a randomized, double-blind trial by Cepeda and colleagues, adding 30 mg IV of ketorolac to an analgesic regimen for treating postoperative pain decreased morphine rescue dose requirements and opioid-related side effects in the early postoperative period.

**Ketorolac and spinal fusion**

For patients undergoing spinal fusion, there was no difference in long-term rates of spinal fusion found between groups provided with normal dose (<120 mg/d) NSAID therapy versus those without NSAID therapy. A meta-analysis showed that normal dose NSAID exposure for less than 2 weeks after spinal fusion does not have adverse effects on fusion rates; however, high doses (>120 mg/d) of ketorolac were associated with impaired spinal fusion rates. In animal models, NSAIDs have also been shown to significantly inhibit fracture healing process; however, these effects depend on their timing, dose, and duration, supporting the recommendation that they should only be administered for short periods.

**Ketorolac and hemostasis**

Interestingly, the only side effect that has been documented to occur with single-dose or short-term administration of ketorolac is increased operative site bleeding after surgical procedures with raw surface areas (eg, tonsillectomy, adenoidectomy, total joint replacements, and major plastic surgery). There are no controlled studies in the peer-reviewed literature demonstrating an increase in blood loss during or after surgery when standard doses of ketorolac were administered at the end of surgery or in the early postoperative period. It is our practice for the anesthesiologist to confirm with the surgeon before ketorolac administration and withhold the dose if there were any intraoperative concerns with hemostasis.

**Ketorolac and renal failure**

The transient decrease in renal function postoperatively is clinically insignificant for patients with normal renal function. There is no greater risk of acute renal failure when administered for short periods in the acute postoperative setting. However, patients with preexisting low creatinine clearance may be at greater risk for postoperative renal failure.

**Narcotic Analgesia**

Short-acting narcotic anesthetic agents such as remifentanil, fentanyl, or sufentanil are routinely given intraoperatively during surgery to provide intraoperative analgesia. Remifentanil has consistently been shown to induce hyperalgesia in the 24 hours after surgery. However, based on a randomized controlled trial by de Hoogd and colleagues in the cardiac surgery literature, it is suggested that intraoperative administration is associated with increased narcotic use for up to 3 months postoperatively. Using long-acting IV narcotics intraoperatively can provide analgesia that extends into the immediate postoperative period, thereby diminishing the need for rescue narcotic doses in the recovery room.

**Epidural Analgesia**

In a meta-analysis by Wu and colleagues, epidural analgesia provided a statistically and
clinically significant improvement in postoperative pain control compared with IV patient-controlled analgesia with opioids regardless of analgesic regimen, measured pain outcomes, type of epidural analgesia, or surgical site. Attempts at enhancing the analgesic potential of patient-controlled analgesia demonstrated that a combination solution (local anesthetic with opioid) compared with opioid alone resulted in improved pain scores but greater motor weakness. Patients who received infusions of opioid alone had greater amount of pruritus.\(^{14}\) Epidural analgesia (combination solution) provides more significant analgesia and higher patient satisfaction compared with IV patient-controlled analgesia after spinal fusion surgery.\(^{49}\) In addition, it has been found to decrease postoperative opioid consumption. Contraindications include occurrence of intraoperative durotomy and/or if the epidural space is deemed too small to advance an epidural catheter (eg, multiple revisions or fibrosis of epidural space). Analgesic infusion begins in the postanesthetic care unit once a stable neurologic examination has been obtained.

**Local Anesthetics**

The American Society of Anesthesiologists Task Force recommends regional blockade with local anesthetic.\(^{14}\) Meta-analysis of randomized controlled trials report improved pain scores and decreased analgesic use with preincisional infiltration of ropivacaine and bupivacaine.\(^{49}\)

Recently, liposomal bupivacaine (Exparel), an amide local anesthetic that targets the voltage gated sodium ion channels, has emerged as an extended release form that may last up to 72 hours after infiltration. Since its approval by the US Food and Drug Administration, it has been used in thoracic, orthopedic, and abdominal surgeries, demonstrating decreased pain, decreased opioid requirement, and improved patient satisfaction.\(^{49}\) In spine surgery liposomal bupivacaine was shown to decrease pain in the immediate postoperative period and decrease the total opioid consumption.\(^{2,49}\) The formulation used in the United States encapsulates the drug in liposomes made of biodegradable cholesterols that breakdown slowly over a desired time period.\(^{30,51}\) It is our practice to infiltrate the incision before skin closure with a combination of both liposomal bupivacaine and marcaine to provide both immediate and delayed pain relief.

**Nonpharmacologic Interventions for Pain Management**

Nonpharmacologic interventions that have been used to manage postoperative pain include preoperative counseling with cognitive–behavioral therapy, biofeedback visualization, and chiropractic manipulation (Fig. 3). A case series by Archer and colleagues\(^{51}\) reviewed 8 postoperative patients who suffered from a high fear of movement who underwent 6-session cognitive–behavioral–based physical therapy. This therapy addresses the fear of movement through behavior self-control and cognitive restructuring techniques aiming to increase physical activity. At the 6-month follow-up, 7 patients demonstrated a clinically significant decrease in pain and all 8 patients had significant reduction in disability. This was quantified by 5 patients demonstrating clinically significant improvement on the 10-m walk test. Nicholls and colleagues\(^{52}\) found 6 papers in their systematic review citing a decrease in postoperative pain disability and intensity in cognitive–behavioral therapy–based psychological interventions.

Biofeedback therapy encourages relaxation and helps to alleviate various conditions associated with stress. In a case series of Taiwanese patients after total knee arthroplasty, Wang and colleagues\(^{53}\) found that the group receiving biofeedback training twice daily for 5 days demonstrated significantly less pain from continuous passive motion therapy compared with the control group. Although pain is a subjective measure, this modality may offer patients an additional option when seeking nonpharmacologic care.

In a European study of patients undergoing surgical correction of adolescent idiopathic scoliosis,

![Fig. 3. The nonpharmacologic interventions available to patients during the postoperative period to decrease the use of narcotic medications.](image-url)
a novel cooling brace was used postoperatively to minimize opioid consumption. The Game Ready device is connected to an external circuit with ice cold water cooled to 4°C. The brace is applied in the postanesthetic care unit and is kept on for 24 hours. Bellon and colleagues found that in their consecutive cohort of 22 patients, the cooling brace allowed for decreased opioid use after surgical correction in children.

**Early Mobilization**

All patients are mobilized by nursing staff within 8 hours of arriving to the regular nursing floor. If the patient is unable to mobilize an automatic physical therapy order is sent out. High-risk patients receive a physical therapy evaluation automatically to ensure maximal mobilization and recovery. It is encouraged to remove the urinary catheter early in the postoperative period (ie, postoperative day 1). Prolonged immobilization has deleterious effects on pulmonary function and decreases the integrity of muscles, the urinary tract, and the skin. Immobilization prolongs hospital stay and carries an increased risk of deep venous thrombosis, pulmonary embolism, pulmonary infection, and urinary tract infections. Early mobilization has been shown to decrease perioperative complications and decrease length of stay by 34%. Additionally, patients mobilized early were more likely to be discharged to home.
DISCUSSION

Enhanced recovery after spine surgery is an iterative, innovative systems-based care approach that has demonstrated effectiveness and statistically significant outcomes at different tiers of care (Fig. 4). The growing opioid epidemic has placed pressure on health care administrators and providers to find effective non-narcotic, pain management options for postoperative patients. Multi-modal analgesia has been shown in the literature across different health care disciplines to decrease opioid consumption and improve postoperative mobilization. As discussed, there are various pharmacologic and nonpharmacologic perioperative interventions available to patients (Table 1). Although previous studies have identified the need to overhaul the postoperative pain management regimen of patients undergoing surgery, few data have been published on the most effective strategy to do so. Various ERAS protocols have been published citing standardization as a common theme leading to improved outcomes.

Although the creation of a standardized, iterative protocol is possible, there are challenges to implementation and compliance. One such challenge to implementing this type of program is compliance owing to individual surgeon preference and a limited ability to monitor adherence to the program. Additionally, the implementation of multi-level reforms makes for difficult analysis for causation with the potential for a variety of confounding factors. The various components of the protocol may need to be introduced in different phases to improve compliance. Working across multiple disciplines is a potential barrier owing to different methods of charting and decreased inter-specialty communication. Pain is a subjective physical examination finding and the subjectivity is what drives the challenge to both study and effectively treat the entity.

The effectiveness of ERAS protocols at improving outcomes, efficiency, and patient satisfaction remains to be seen. Early studies of ERAS protocols have shown that implementation of a multitiered approach to improving patient outcomes is possible, and may be effective and beneficial to the surgical spine patient. Multidisciplinary collaboration has been found to improve patient and provider satisfaction with greater confidence that each aspect of the patient’s preoperative and postoperative care benchmarks has been met.

Future studies are needed to analyze efficiency, efficacy, and cost effectiveness. Emerging research and innovation will help to determine the optimal protocols to use the various pain management options available to the clinician today.

REFERENCES


### Table 1

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<th>Pain-specific ERAS protocol at the Cleveland Clinic</th>
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**Abbreviations:** PO, per os; q6h, every 6 hours.
Enhanced Recovery in Spine Surgery


26. Arumugam S, Lau CS, Chamberlain RS. Use of preoperative gabapentin significantly reduces


