International Journal of Spine Surgery, Vol. 14, No. 4, 2020, pp. 623–640 https://doi.org/10.14444/7083 -International Society for the Advancement of Spine Surgery

# Enhanced Recovery After Surgery Trends in Adult Spine Surgery: A Systematic Review

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#### ABSTRACT

Background: Enhanced Recovery After Surgery (ERAS) is a multimodal, multidisciplinary approach to optimizing the postsurgical recovery process through preoperative, perioperative, and postoperative interventions. ERAS protocols are emerging quickly within orthopedic spine surgery, yet there is a lack of consensus on optimal ERAS practices.

**Objective:** The aim of this systematic review is to identify and discuss the trends in spine ERAS protocols and the associated outcomes.

Methods: A literature search on PubMed was conducted to identify clinical studies that implemented ERAS protocols for various spine procedures in the adult population. The search included English-language literature published through December 2019. Additional sources were retrieved from the reference lists of key studies. Studies that met inclusion criteria were identified manually. Data regarding the study population, study design, spine procedures, ERAS interventions, and associated outcome metrics were extracted from each study that met inclusion criteria.

Results: Of the 106 studies identified from the literature search, 22 studies met inclusion criteria. From the ERAS protocols in these studies, common preoperative elements include patient education and modified preoperative nutrition regimens. Perioperative elements include multimodal analgesia and minimally invasive surgery. Postoperative elements include multimodal pain management and early mobilization/rehabilitation/nutrition regimens. Outcomes from ERAS implementation include significant reductions in length of stay, cost, and opioid consumption. Although these trends were observed, there remained great variability among the ERAS protocols, as well as in the reported outcomes.

**Conclusions:** ERAS may improve cost-effectiveness to varying degrees for spinal procedures. Specifically, the use of multimodal analgesia may reduce overall opioid consumption. However, the benefits of ERAS likely will vary based on the specific procedure.

Clinical Relevance: This review contributes to the assessment of ERAS protocol implementation in the field of adult spine surgery.

Other and Special Categories

Keywords: Enhanced Recovery After Surgery, ERAS, fast-track surgery, rapid recovery program, spine surgery, orthopedics, multimodal analgesia

#### **INTRODUCTION**

Enhanced Recovery After Surgery (ERAS; also known as enhanced or rapid recovery program, fasttrack surgery, enhanced perioperative care/EPOC) refers to a multimodal care pathway to accelerate patient recovery after surgery. The goal of ERAS is to mitigate the surgical stress response while also enhancing the recovery of bodily functions, ultimately increasing cost-effectiveness without compromising the quality of care.<sup>1</sup> An ERAS protocol typically contains preoperative, perioperative, and/ or postoperative elements that are standardized across all patients undergoing a certain procedure.<sup>1</sup> The implementation of such a protocol is a multidisciplinary effort involving surgery, anesthesia, nursing, and other disciplines. This concept was first introduced by  $Kehlet<sup>1</sup>$  and adapted for colonic resection and colorectal procedures.<sup>2</sup> Since then, ERAS care pathways have been developed for a variety of other surgical specialties.<sup>3</sup> As evidence for and adoption of ERAS have grown, multiple societies also have been established (see the global society http://erassociety.org, the UK society http:// www.erasuk.net/, and the American society http://

enhancedrecovery.org/) to curate ERAS guidelines worldwide.

The stress response to surgical insult can be particularly devastating for a patient, resulting in a proinflammatory, procatabolic state that can drive metabolic changes and insulin resistance. $4-6$  Such changes in turn may significantly impact postoperative morbidity and mortality.5,6 Additionally, blood loss and fluid homeostasis are major factors that can affect surgical outcomes.<sup>2</sup>

To address these concerns, ERAS pathways are being implemented with increasing frequency. Compared with traditional care pathways, which are often unstandardized and according to surgeon preference, ERAS pathways have been associated with improved outcomes within various surgical fields<sup>2</sup>; for example, ERAS protocols developed for high-volume total knee and hip replacements have been associated with reductions in length of stay (LOS) and hospital costs, as well as in readmission, complication, and mortality rates to varying degrees. $7-11$ 

ERAS implementation may become a mainstay for orthopedic spine surgery. The volume of patients undergoing elective spine surgery is increasing, as is the population of aging patients who may become surgical candidates.<sup>3,12</sup> Moreover, some spine procedures are associated with significant postoperative pain, LOS, and complications.<sup>3</sup> Thus, there is room to grow in terms of optimizing clinical and economic outcomes.

Research on spine ERAS protocols is still in the early stages, but it has been gaining traction.<sup>12</sup> Recent reviews by Dietz et al,  $^{13}$  Elsarrag et al,  $^{14}$  and Corniola et  $al<sup>15</sup>$  highlight the various spine procedures for which ERAS pathways have been designed and implemented. However, there remains a lack of consensus on which specific ERAS elements may be relatively more effective. Indeed, there are no official ERAS guidelines for spine surgery, although many spine ERAS protocols contain elements that are present in the guidelines for other surgical specialties (see http://erassociety. org.loopiadns.com/guidelines/list-of-guidelines). Moreover, existing ERAS spine protocols vary significantly in their preoperative, perioperative, and postoperative elements, rendering it difficult to assess their individual effectiveness. Thus, the aim of this review is to discuss the trends in spine ERAS protocols—the commonly adopted interventions and prior evidence for their implementation in other

surgical specialties—as well as the associated outcome metrics.

## **METHODS**

#### Electronic Literature Search

A literature review of PubMed was conducted as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>16</sup> Keywords were combined with Boolean operators to generate the following search term: [''ERAS''] OR [''enhanced recovery after surgery''] OR [''rapid recovery''] OR [''accelerated pathway''] OR [''fast-track surgery''] OR [''same-day discharge''] AND [''spine surgery''], in order to retrieve relevant English-language literature published through December 2019. The literature search was performed independently by 2 reviewers, and a consensus was reached for which articles met inclusion criteria. The last search was performed on December 30, 2019. Later, additional articles were identified from the reference lists of key articles.

#### Inclusion and Exclusion Criteria

Titles, abstracts, and full-text articles were screened by 2 independent reviewers. Inclusion criteria included: (1) adult patients undergoing (2) any type of elective spine surgery, and (3) randomized, nonrandomized, controlled, noncontrolled, retrospective, and prospective study designs. Exclusion criteria included: (1) pediatric patients, (2) articles not available in English, (3) hypothetical ERAS designs, (4) studies that introduced only a single ERAS element (eg, not in full protocol), and (5) review articles and case reports. Duplicate articles were accounted for. Data from the articles that fit our criteria were extracted and assessed. This review does not incorporate the pediatric population because of the variability in protocols, parameters, and discharge criteria that significantly differ from those for adult populations.

#### Data Extraction and Quality Assessment

Where available, the following data were extracted from each study that met criteria: sample size, study design, spine procedure(s), quantity and types of ERAS interventions per protocol, and all associated outcomes that were reported—which commonly included LOS, cost, method(s) of pain control, and complication and readmission rates. If

the number of ERAS interventions in a study was not itemized explicitly (eg, in a data table), the information was extracted from the article text. Assessment of quality and risk bias was performed according to the Centre for Evidence-Based Medicine guidelines for therapeutic studies, $17$  as well as the Newcastle-Ottawa Scale,<sup>18</sup> which is a 9-point scale designed to assess nonrandomized and casecontrol studies for sample selection, comparability, and outcome/exposure. A higher score on the scale indicates a higher-quality study.<sup>18</sup>

#### Data Analyses

There was great heterogeneity among the studies; for example, there was a wide range of study designs, and several studies did not provide a comparative analysis of pre- and post-ERAS data. A meta-analysis would have been limited by the nature of this source data. As such, data points of interest were reported when available in the literature, but statistical analyses were not performed for this review.

#### **RESULTS**

#### Study Selection

A total of 106 articles were identified from the initial literature search. The 85 nonduplicate articles underwent abstract and title review for inclusion, of which 36 were excluded based on our exclusion criteria and nonapplicability. A total of 49 articles underwent full-text review, and 27 of those articles were excluded because of a lack of evidence pertaining to ERAS protocols. The remaining 22 articles met inclusion criteria.19–40

Of the 22 ERAS studies that met criteria, 12 were controlled "before-and-after" studies,  $22,25-30,32-36$  8 were prospective noncontrolled trials,<sup>19,21,23,24,31,37,39,40</sup> 1 was a retrospective matched cohort study,<sup>38</sup> and 1 was a retrospective noncontrolled study.<sup>20</sup> Publication dates ranged from 2004 to 2019.

The literature search process is presented in the PRISMA flow diagram (Figure). Table 1 presents an overview of the 22 studies and their associated outcomes.

#### Assessment of Quality and Risk of Bias

As per the Centre for Evidence-Based Medicine guidelines for therapeutic studies,  $17$  the 12 controlled "before-and-after" studies $22,25-30,32-36$  and the retrospective controlled study<sup>38</sup> are graded as level of evidence  $2B$ .<sup>17</sup> The remaining noncontrolled retrospective study<sup>20</sup> is graded as level of evidence 4. The 8 prospective noncontrolled trials<sup>19,21,23,24,31,37,39,40</sup> are graded as level of evidence 4.

According to the Newcastle-Ottawa Scale,  $^{18}$  12 of the nonrandomized, controlled cohort studies<sup>22,25–30,32,34–36</sup> received 8 stars out of 9 (4 for selection, 1 for comparability, and 3 for outcome), and 1 study<sup>39</sup> received 9 stars out of 9.

#### Types of Spine Surgery

Associated spine procedures included minor, major, and complex spine surgeries, such as laminectomy/laminotomy, (micro)discectomy, open and minimally invasive posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), anterior lumbar interbody fusion (ALIF), anterior cervical discectomy and fusion (ACDF), anterior cervical disc arthroplasty (AC-DA), and metastatic tumor resection (Table 1). Most spine ERAS protocols were implemented for lumbar spine procedures. Because reporting of the type(s) of spine surgery was not standardized across the 22 studies, quantifying the prevalence of any single type of spine procedure among the ERAS protocols was difficult to perform.

#### Associated Outcomes

A total of 13 of the 22 studies<sup>22,25–30,32–36,38</sup> conducted controlled trials that compared ERAS versus traditional care pathways. The outcomes are variable and are summarized in Table 1. Common outcome metrics reported were LOS, cost, opioid consumption, postoperative pain, intraoperative time, patient satisfaction, complication rate, and readmission rate. The most commonly reported outcomes were reductions in LOS, cost, and opioid consumption. Importantly, no ERAS study was associated with worse patient outcomes compared with traditional pathways.

A total of 10 studies reported significantly reduced hospital and/or intensive care unit  $LOS^{22,26,28-30,32-35,38}$ ; however, some studies found no significant change in LOS compared with control.<sup>25,27,36</sup> Additionally, there was large variation in mean/median LOS, ranging from several hours to several days.

Four studies reported a reduction in hospital costs.<sup>26,30,32,34</sup> Wang et al<sup>26</sup> calculated a mean acute care cost reduction of \$3,444 (15.2%) for ERAS





Abbreviations: ACDA, anterior cervical disc arthroplasty; ACDF, anterior cervical discectomy and fusion; ALIF, anterior lumbar interbody fusion; CDA, cervical disc<br>arthroplasty; ICU, intensive care unit; LOS, length of sta lumbar interbody fusion; XLIF, extreme lateral interbody fusion.

#### Table 1. Extended.





Figure. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for systematic review of Enhanced Recovery After Surgery (ERAS) protocols in adult spine surgery.

minimally invasive TLIF (MIS TLIF) procedures; Carr et al<sup>30</sup> reports a \$19,344 reduction in cost. Dagal et  $al^{32}$  calculated a mean cost reduction of \$62,429 (control) to \$53,355 (ERAS) for several types of major spine surgery; and Feng et  $al<sup>34</sup>$  found a mean cost decrease from \$71,426 to \$70,467, also for MIS TLIF. Although the study was not a controlled trial, Chakravarthy et  $al<sup>31</sup>$  also estimated a per-patient decrease of \$827 in hospital costs.

A reduction in intraoperative time has also been noted,<sup>26</sup> but conversely no change in intraoperative time has been reported as well.<sup>34,36</sup> Here, a decrease in LOS and/or intraoperative time may translate to decreased cost; in fact, Wang et  $al^{26}$  reported reductions in LOS and intraoperative time, as well as cost.

For postoperative opioid consumption, the bulk of evidence suggests a reduction in opioid use after ERAS implementation,  $25,27,29,36,38$  with no reports of increased opioid use. Interestingly, Soffin et  $al^{38}$ reported both reduced and no change in opioid consumption at different time points, with reduced perioperative opioid consumption but no difference in postoperative opioid consumption.

#### Common ERAS Elements

Preoperative ERAS elements are defined here as interventions that occur any time before the day of surgery (postoperative day 0 [POD0]). They are

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Abbreviations: ACDA, anterior cervical disc arthroplasty; ACDF, anterior cervical discectomy and fusion; ALIF, anterior lumbar interbody fusion; CDA, cervical disc arthroplasty; MIS, minimally invasive surgery; PCDF, posterior cervical discectomy and fusion; PLIF, posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion; XLIF, extreme lateral interbody fusion.

designed to optimize the patient's condition prior to surgery. The most common interventions were patient education (72.7% of studies), assessment of patient health and comorbidities (45.5%), carbohydrate loading (40.9%), and a modified preoperative fasting regimen (31.8%). Perioperative ERAS elements refer to interventions that occur from POD0 until patient extubation and transfer to the postanesthesia care unit (PACU). Common interventions were perioperative multimodal analgesia (MMA) (68.2%), infection prophylaxis (54.5%), ''preemptive'' analgesia (50%), catheter and surgical drain sparing (50%), and minimally invasive surgery (MIS; 40.9%). Postoperative ERAS elements are defined as interventions that occur during and after admission to the recovery area (eg, PACU). Common postoperative elements include postoperative MMA (81.8%), early mobilization/rehabilitation  $(77.3\%)$ , and early nutrition  $(54.5\%)$ .

The number of ERAS elements per protocol ranged from 3 to 40 items (Table 1); however, it is important to note that there was great variability across studies in how the ERAS elements were itemized and the degree of detail to which the protocols were presented.

Tables 2, 3, and 4 summarize the percentage prevalence of preoperative, perioperative, and postoperative ERAS elements that were common among the 22 studies, respectively. Table 5 details the postoperative discharge criteria reported by several spine ERAS protocols. Other studies did not report discharge criteria.

## **DISCUSSION**

The most commonly implemented preoperative, perioperative, and postoperative spine ERAS elements are discussed here, both with regard to how they were implemented in the ERAS studies and in the context of prior evidence from other surgical specialties or non-ERAS spine studies. ERAS elements that were not popular among the reviewed studies are not discussed.





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Abbreviations: ACDA, anterior cervical disc arthroplasty; ACDF, anterior cervical discectomy and fusion; ALIF, anterior lumbar interbody fusion; CDA, cervical disc arthroplasty; MIS, minimally invasive surgery; MMA, multimodal analgesia; PCDF, posterior cervical discectomy and fusion; PLIF, posterior lumbar interbody fusion; TLIF, transforaminal lumbar interbody fusion; XLIF, extreme lateral interbody fusion.

#### Preoperative ERAS Elements

## Patient Education

Educating the patient prior to surgery is a common component of the ERAS preoperative pathway. Although traditional care pathways may include patient education, they are less structured and standardized in implementation. ERAS patient education for spine surgery includes setting realistic goals and expectations for surgery and recovery,21–25,28,30,32–34,36,37,39,40 recommending preoperative nutrition and exercise regimens,25 educating about the ERAS components,  $2^{3,34,39}$  and educating about pain management (perioperative and postoperative MMA, how to grade pain, how pain scores translate to analgesia selection, etc.).<sup>25,33,34,37–39</sup> In addition to providing videos, handouts, and oral presentations to educate patients, some research groups also implemented a helpline and enlisted 24 hour on-call nurses to aid in preoperative patient education.23,28,33 Many of the ERAS patient education guidelines share similar features but differed in their degree of detail and implementation.

Despite the frequent inclusion of patient education in ERAS protocols, there is a lack of evidence regarding its impact on patient outcomes. Previously, patient education was not found to significantly improve surgical outcomes or reduce patient anxiety; in a review of preoperative education for hip and knee replacement procedures, McDonald et al<sup>41</sup> concluded that patient education may only benefit patients with preexisting depression, anxiety, or unrealistic expectations. It is thus unclear whether standardized patient education guidelines are necessary in most cases. However, some research groups<sup>34,39</sup> have based their rationale for including ERAS patient education on the McDonald et  $al<sup>41</sup>$ review article, claiming that educating patients can enhance postoperative and recovery outcomes.





Abbreviations: ACDF, anterior cervical discectomy and fusion; ALIF, anterior lumbar interbody fusion; CDA, cervical disc arthroplasty; f/u, follow-up; PACU, postanesthesia care unit; PLIF, posterior lumbar interbody fusion.

Comorbidity Assessment and Health Optimization Patients who undergo elective spine surgery often have other comorbidities, such as diabetes or cardiovascular disease, especially as the population of elderly patients desiring spine surgery continues to increase. Considering the physiologic stress placed on the body by surgery, several institutions opted to evaluate and address patient comorbidities as part of their preoperative ERAS protocol (Table 2). In this way, the patient's health may be optimized prior to surgery to reduce the risk of postoperative complications.<sup>40</sup>

Several ERAS spine protocols required screening for risk factors like diabetes, cardiovascular disease, obesity (body mass index), smoking status, narcotic/ alcohol use, anemia, nutritional status, and obstructive sleep apnea. The American Society of Anesthesiologists classification, which indicates the severity of a patient's comorbidities, was also calculated in some protocols.<sup>20,21,36,40</sup> For patients who presented with comorbidities or who did not meet the health criteria, one of several forms of intervention were taken. Some studies built in exclusion criteria for surgery, such as cutoff body mass index and American Society of Anesthesiologists classification values<sup>20,31</sup>; some delayed the procedure and/or offered counseling and medical services for diabetes, weight loss/nutrition, exercise, smoking cessation, obstructive sleep apnea, and narcotics/alcohol use21,22,28,31,37,40; and some developed their own "pre-habilitation" exercise regimens for patients to follow. $22,27$ 

Although it is unclear how health assessment and optimization independently contributed to patient outcomes, previous studies in other surgical specialties have shown a link between preoperative comorbidities and postoperative outcomes. In a study of geriatric patients undergoing noncardiac surgery, Leung and  $Dzankic^{42}$  showed that patients with neurologic or cardiovascular comorbidities were at higher risk of adverse postoperative events. Oresanya et  $al<sup>43</sup>$  similarly reported a correlation between cognitive impairment, malnutrition, and frailty with adverse outcomes in geriatric surgical patients.<sup>43</sup>

#### Modified Preoperative Fasting With Carbohydrate Loading

Traditionally, patients are instructed to begin fasting the night prior to surgery. But this practice not only lacks scientific backing but also can exacerbate the surgical stress response and the development of postsurgical insulin resistance.<sup>2</sup> As such, several spine ERAS protocols modified their preoperative fasting guidelines, instead permitting consumption of solid foods up to 6 to 12 hours prior to surgery and liquids up to 2 to 8 hours prior to surgery.<sup>24,25,33,34,37,39</sup> There is evidence that clear fluids are safe to ingest up to 2 hours prior to surgery, and so fasting guidelines have been changing accordingly since the mid-1990s. $<sup>2</sup>$ </sup>

Additionally, carbohydrate loading—which involves the oral (PO) or intravenous (IV) administration of a carbohydrate fluid (eg, Nutricia preOp)—usually 2 hours prior to surgery—was incorporated into many spine ERAS protocols (Table 2). The carbohydrate fluid was often but not always administered in conjunction with the shortened preoperative fasting regimen. Carbohydrate loading has become a staple practice in ERAS surgery protocols and is thought to help mitigate postsurgical insulin resistance.<sup> $44$ </sup> A review by Smith et al<sup>44</sup> of preoperative carbohydrate loading treatments from ERAS surgery protocols found an association with reduced LOS, but not with postoperative complications. Similarly, spine ERAS protocols that featured carbohydrate loading have not yielded significant changes in postoperative complication and/or readmission rates.25,27,30,32 However, some protocols that included carbohydrate loading did report reduced LOS,28,30,32,34 whereas others denied any significant change in outcomes<sup>25,27</sup>

#### Perioperative ERAS Elements

#### ''Preemptive'' Analgesia

The consumption of nonopioid analgesics prior to induction has been correlated independently with decreased pain levels and reduced opioid consumption (known as an opioid sparing effect) after spine surgery.<sup>45,46</sup> Notably, Kim et al<sup>46</sup> administered a cocktail of 200 mg of celecoxib, 75 mg of pregabalin, 500 mg of acetaminophen, and 10 mg of extended-release oxycodone—as opposed to conventional morphine for the control group—at least 1 hour prior to surgery. Patients who received this preemptive cocktail demonstrated lower visual analog scale (VAS) and Oswestry Disability Index values at nearly all POD time points measured. Furthermore, there were no significant differences in postoperative complication rates.<sup>46</sup>

For spine ERAS protocols, the combination of acetaminophen PO (usually 1000 mg) and gabapentin PO (usually 300 mg) was commonly administered to patients on the morning of surgery,<sup>25,30,32,36–39</sup> and also the night before surgery.<sup>30,32</sup> Other oral analgesics, like 200 mg of celecoxib<sup>34</sup> and 150 or 75 mg of pregabalin, $25,34$  were also administered. These analgesic options have been shown to effectively reduce pain<sup>45–47</sup> and opioid consumption<sup>45</sup> following spine surgery. For the acetaminophen and gabapentin combination specifically, Syal et  $al<sup>48</sup>$  previously reported improved postoperative pain scores in patients who underwent open cholecystectomy, which suggests that this combination of premedication may be effective for other types of surgeries.

Indeed, some spine ERAS studies that implemented preemptive analgesia showed decreased use of postoperative patient-controlled analgesia (PCA) and/or opioid consumption, even as their associated surgical procedures varied greatly.<sup>25,27,36,38</sup> These studies did not indicate reduced pain scores, however.<sup>25,27</sup> In fact, Soffin et al<sup>38</sup> implemented the acetaminophen-gabapentin combination yet found neither reduced pain scores nor reduced opioid consumption postoperatively—even with the contribution of other ERAS elements. It seems that more research regarding the effects of preemptive analgesia on postoperative outcomes in spine surgery is required.

#### Intraoperative MMA

The use of intraoperative medications to minimize postoperative pain is another integral component of optimizing patient outcomes. A variety of intraoperative MMA regimens have been implemented in the spine ERAS protocols (Table 3). For example, for spinal metastatic tumor resection surgeries, Grasu et  $al^{25}$  implemented infusions of propofol, dexmedetomidine, ketamine, and lidocaine, along with a single upfront IV dose of methadone  $(0.1-0.2)$ mg/kg) in opioid-tolerant patients. In contrast, Ali et al<sup>27</sup> administrated intraoperative NSAIDs, dexamethasone, and local bupivacaine in addition to conventional opioids for various elective spine procedures.27 Other common analgesic medications were used intraoperatively, like acetaminophen $30,32$ and other local analgesics.<sup>24,31,34,39,40</sup> Particular attention was given to modulating the choice of anesthetics; several studies avoided using general anesthesia and long-acting agents. When general

anesthesia was used, propofol appeared to be preferred among the ERAS studies.<sup>25,30,32,38-40</sup>

Moreover, numerous non-ERAS studies have investigated whether a multimodal approach to pain management can limit postoperative pain and opioid use in spine surgery.<sup>49–52</sup> Loftus et al<sup>49</sup> studied the effect of intraoperative ketamine (initial bolus of 0.5 mg/kg, followed by infusion at 10  $\mu$ g/ kg/min). In this study, the treatment group received a loading dose of ketamine prior to induction and a continuous drip during surgery.<sup>49</sup> Patients in this treatment group required 24% less intraoperative opiate medication; these patients also consumed 37% less morphine in the 48 hours following surgery compared with the control group.<sup>49</sup> Moreover, at the 6-week follow-up, the treatment group patients reported the same reduction in pain despite a 71% reduction in opioid consumption. $49$  Tunali et al<sup>50</sup> similarly studied the efficacy of IV paracetamol (1 g) and dexketoprofen (50 mg) on postoperative pain and morphine consumption following lumbar disc surgery. Here, Tunali and colleagues<sup>50</sup> measured VAS scores and total morphine consumption in the first 24 hours after surgery, respectively. The authors reported that pain scores were significantly reduced with dexketoprofen administration but not with paracetamol.<sup>50</sup> However, there was no difference in morphine consumption with either medication when compared to placebo.<sup>50</sup> Later, in a randomized controlled study, Nielsen et  $al<sup>51</sup>$  investigated the administration of preoperative dexamethasone (16 mg) combined with intraoperative paracetamol, reporting that although pain scores were significantly reduced in the first 24 hours following surgery, this difference dissipated at the 3-month follow-up. Notably, there was a 6.5% incidence of postoperative infection in the dexamethasone treatment group, which limits the benefit that this medication can have on patients.<sup>51</sup> Finally, Garg et  $a1^{52}$  administered ketamine (bolus 0.25 mg/kg) followed by 10 mg/kg/hr infusion) or dexmedetomidine (0.5 mg/kg followed by 0.3 mg/kg/hr infusion) to patients during induction for various elective spine procedures.<sup>52</sup> The authors reported that patients who received ketamine and dexmedetomidine experienced greater pain-free periods during the first 48 hours after surgery, as well as reduced consumption of rescue pain medication, compared with the control group.<sup>52</sup>

#### Minimally Invasive Surgery

The MIS technique is being adopted rapidly in spine surgery and involves minimizing intraoperative soft tissue disruption and blood loss. $53$  The inclusion of MIS in ERAS pathways is aimed at improving cost-effectiveness and enhancing postoperative recovery. Prior research comparing MIS TLIF/PLIF with the traditional open approach suggests that MIS results in reduced hospital costs,<sup>26,53,54</sup> LOS,<sup>53,55,56</sup> and blood loss.<sup>53,56</sup> However, the benefits of MIS on overall clinical outcomes remain controversial,  $3,55$  with some studies achieving reduced short-term readmission and complication rates, $56$  and others finding no additional short- or long-term clinical benefits compared with the open surgical approach. $53-55$ From current evidence, it seems that MIS procedures are more cost-effective and yield comparable clinical outcomes.

The MIS approach was adopted by several ERAS protocols for lumbar fusion or decompression procedures (Table 3). Grasu et  $al^{25}$  also employed MIS technique for an ERAS metastatic tumor resection protocol. Brusko et  $al^{29}$  employed MIS technique for 1- to 3-level posterior-only lumbar fusion surgeries. Debono et  $al<sup>23</sup>$  and Soffin et  $al^{38}$  pursued a protocol for lumbar microdiscectomy.23,38 In ERAS studies, MIS technique involved a small incision, tubular working channels and endoscopy, percutaneous screw insertion, expandable cage implants,  $24,26,38-40$  and robotic and microscope guidance.<sup>38-40</sup>

Thus far, the use of MIS in spine ERAS studies has been associated with various positive outcomes, especially for MIS TLIF procedures (Table 1). For example, Wang et  $al^{26}$  reported reduced intraoperative time, LOS, complication rate, and acute care costs, and Feng et  $al<sup>34</sup>$  reported reduced LOS and mean costs but no difference in intraoperative time or complication and readmission rates. Interestingly, Wang et  $al^{26}$  were able to enhance the cost-effectiveness of MIS TLIF using only 6 perioperative ERAS interventions, 3 of which pertained to an MIS surgical approach (working channel endoscope, expandable cage, small-caliber percutaneous screws). Results by Wang and colleagues<sup>26</sup> suggest that the use of MIS may account significantly for the benefits of ERAS pathways.

## Maintaining Homeostasis (Blood Loss, Fluids, Temperature)

Managing body homeostasis during surgery helps to reduce postoperative complications and enhance the return of normal bodily functions.<sup>2</sup> In particular, the management of blood loss, normovolemia, and normothermia has emerged as a popular inclusion in ERAS pathways. Minimizing blood loss in turn can reduce the risk of hypotension, end-organ damage, and coagulopathy, as well as complications related to blood transfusions. Maintaining normovolemia for patients undergoing major spine surgery has been associated with reduced blood loss and transfusion, improved postoperative respiratory function, faster return of bowel function, and reduced LOS.<sup>57</sup> Conversely, overhydration and underhydration of the patient intraoperatively have been associated with increased complications.<sup>2</sup> Monitoring and maintaining body temperature during surgery is similarly important for postoperative recovery, because hypothermia increases the risk of wound infection after spine surgery.<sup>58</sup>

For blood loss management, tranexamic acid which has been reported to decrease bleeding and transfusions during spine surgery<sup>59</sup>—was administered intraoperatively in several spine ERAS pathways (Table 3). In the studies, tranexamic acid was given as an IV bolus before skin incision and as an infusion through the procedure. Bolus dosage varied  $(2 g, 20 mg/kg, 0.5 g/hr, or 1 g prior to incision and$ another 1 g over 8 hours)<sup>21,30,31</sup> because optimal dosing for surgery has not yet been determined. Other methods of minimizing blood loss include minimal use of blood transfusions and preoperative arterial embolization for high-risk bleeding tumors,25 making available autologous cell-salvage transfusions,40 and administering oral iron supplements or iron transfusions for anemic patients prior to surgery.<sup>34</sup> Consequently, Feng et  $a^{34}$  and Dagal et  $al^{32}$  were able to significantly reduce intraoperative blood loss for MIS TLIF and various major spine procedures, respectively. Chakravarthy et  $al<sup>31</sup>$ also reported decreased blood transfusions for ERAS patients undergoing major and complex spine surgeries. Other studies that administered tranexamic acid did not report a comparative blood loss measure.<sup>25</sup>

For maintaining normovolemia intraoperatively, a combination of hemodynamic monitoring and asneeded fluid replacement therapy was used (Table 3). This type of intervention is known as goaldirected fluid therapy  $(GDFT)$ .<sup>60</sup> According to the American Society for Enhanced Recovery, the goal of GDFT is to achieve a net ''zero-fluid balance'' (euvolemia) perioperatively in order to reduce postoperative complications and LOS.60 Thiele et  $a<sup>160</sup>$  recommend the use of isotonic IV crystalloids (salt solution with small molecules) for fluid replacement, which was employed by Chakravarthy et al.<sup>31</sup> Other ERAS protocols that implemented GDFT did not specify their method of fluid therapy. Ljungqvist<sup>2</sup> further recommends the use of a combination of colloids (which contain larger molecules) and crystalloids, and warns against the use of 0.9% saline, which can cause prolonged postoperative fluid retention. Of note, both Thiele et  $a^{60}$  and Ljungqvist<sup>2</sup> formulated their guidelines based on data from ERAS colorectal surgery. But there seems to be no consensus for optimal GDFT for spine surgery.<sup>2,60</sup>

Finally, normothermia was monitored and maintained intraoperatively in a number of studies (Table 3). Optimal body temperature was set between  $36^{\circ}$ C and  $37^{\circ}$ C and was monitored throughout the procedure. Various methods of body warming were used intraoperatively, like hot air blankets, fluid warmers, and a convective warming device.

## Deep Venous Thrombosis, Infection, and

Postoperative Nausea and Vomiting Prophylaxis Deep venous thrombosis, infection, and postoperative nausea and vomiting (PONV) are postoperative complications that can significantly hinder patient recovery. To avoid such complications, prophylactic measures have been incorporated into spine ERAS protocols (Table 3). For antithrombotic prophylaxis, compression stockings/devices and low–molecular weight heparin were used intraoperatively.<sup>24,35,40</sup> Postoperative thromboprophylaxis has been implemented as well, also in the form of compression devices, heparin, and early and frequent ambulation.<sup>31,35</sup> Notably, Sivaganesan et al<sup>35</sup> reserved the use of chemoprophylaxis for uncommon cases, namely for cases involving combined anterior and posterior approach, trauma, spinal cord injury, tumor, and hypercoagulable-state patients; only mechanical prophylaxis was used for common elective spine surgeries.

To reduce the risk of infection, several types of antimicrobial agents and routines have been documented in the literature. For example, Bradywood

et  $al^{22}$  required that patients take chlorhexidine showers or baths prior to surgery, given that preoperative bathing is believed to reduce bacterial load; Feng et al $^{34}$  administered 1.5 g cefuroxime close to time of incision<sup>34</sup>; and Smith et al<sup>36</sup> administered 2 to 3 g of Ancef, 900 mg of Clindamycin, or 15 mg/kg Vancomycin.<sup>36</sup> These interventions were mostly perioperative in nature, with the exception of the chlorhexidine baths.

For PONV prophylaxis, Soffin and colleagues $^{37-39}$  employed both perioperative prophylaxis and postoperative treatments in a series of spine ERAS protocols. Perioperatively, patients at high risk for PONV were given a scopolamine patch  $(1.5 \text{ g transdermal})$  in the surgical holding area,  $37,39$ as well as 4 to 8 mg of dexamethasone on induction and 4 to 8 mg of ondansetron 30 minutes prior to emergence from anesthesia.<sup>38</sup> Postoperatively, PONV was treated with IV metoclopramide (10 mg) or ondansetron (4 mg), plus a scopolamine patch (1.5 mg transdermal) if PONV was refractory.<sup>38,39</sup> Carr et al<sup>30</sup> also administered IV ondansetron intra-operatively as prophylaxis. Bednar<sup>21</sup> administered IV/PO dexamethasone 4 mg every 6 hours postoperatively until discharge.

## Catheter and Surgical Drain Sparing

Several spine ERAS protocols emphasized sparing the use of Foley catheters and surgical site drains either avoiding use or performing early removal (Table 3). The use of Foley catheters and surgical drains has been associated with postsurgical infection of the urinary tract and wound site, respectively. To minimize such complications and to facilitate patient mobility, Ali et  $al^{27}$  reported significantly decreased Foley catheter placements intraoperatively, as well as postoperatively for patients without bed restrictions; however, there was no significant difference in complication rate (which included infection rate) in pre-ERAS intervention versus post-ERAS intervention patients in this study. Staartjes et  $al^{40}$  used surgical drains only for patients who underwent mini-open decompression or MIS PLIF procedures; the authors also stressed the removal of catheters and drains as soon as possible postoperatively. Likewise, Debono et  $al^{23}$ and Sivaganesan et  $al^{35}$  reported no drain use for lumbar microdiscectomy and various elective spine surgery procedures, respectively; Debono et  $al^{33}$ described a drastic reduction in drain use for ACDF, ALIF, and PLIF procedures; Soffin et  $al<sup>37</sup>$ 

omitted the use of catheters or drains for ACDF and cervical disc arthroplasty  $(CDA)$  surgeries.<sup>37</sup> Wang et  $al^{24}$  avoided the use of a Foley catheter altogether. In studies that did not emphasize catheter or wound drain sparing, most documented removal on POD1<sup>31,36</sup> or POD2/3<sup>22,30,32</sup> in order to facilitation mobilization.

## Postoperative ERAS Elements

## Postoperative Pain Modulation

In addition to perioperative medication regimens for patients undergoing spine surgery (see the ''Preemptive Analgesia'' and ''Intraoperative MMA'' sections), postoperative MMA measures have been implemented. A variety of MMA combinations have been administered to supplement PCA opioid consumption. Common elements of a postoperative MMA cocktail include gabapentin/ pregabalin, 22,24,25,32,34–36,38,39 acetaminophen,<sup>22,24,25,27,30,32,37–39</sup> and celecoxib and other NSAIDs.<sup>22,25,27,33–40</sup> Other nonopioid options include dexamethasone,<sup>27</sup> paracetamol,<sup>40</sup> and ketamine.<sup>28</sup> To maximize opioid sparing, some studies also avoided the use of long-acting opioids<sup>24,40</sup> and implemented early discontinuation of PCA.22 For various types of lumbar decompression surgeries, Soffin et  $al^{38}$  stratified postoperative MMA and opioid use based on numeric rating scale pain scores: patients with numeric rating scale scores of 4 or less only received nonopioid interventions (acetaminophen, ketorolac, gabapentin); patients with scores 5 to 7 could receive 50 mg of tramadol; and patients with scores 8 to 10 received 5 mg of oxycodone.38 Interestingly, Soffin and colleagues found decreased perioperative opioid consumption, but no significant changes in postoperative pain scores or opioid consumption compared with the pre-ERAS control group. For 1- or 2-level lumbar fusion procedures, Smith et  $al^{36}$  administered a postoperative cocktail of 200 mg of celecoxib PO, 300 mg of gabapentin PO, and 975 mg of acetaminophen PO; the authors reported a decrease from 7% to 0% in PCA use and a decrease from 14% to 5.2% in the use of long-acting opioids.

Importantly, several research groups have investigated the effects of postoperative MMA for non-ERAS spine surgery, which yielded varied outcomes. $45,47,61,62$  In a randomized controlled trial, Korkmaz et al<sup>61</sup> studied the effect of either IV 1 g of metamizol, 1 g of paracetamol, or 8 mg of lornoxicam supplementation after wound closure

for lumbar disc surgery. These analgesics were administered in tandem with conventional postoperative PCA of morphine. $61$  The authors reported decreased VAS pain scores in the first 24 hours after surgery for patients who received metamizol and paracetamol, but not lornoxicam; PCA use in the paracetamol group also significantly decreased over time.<sup>61</sup> Other studies demonstrated the postoperative use of MMA pain management with nonsteroidal anti-inflammatories (NSAIDs) and GABAacting drugs. Mathiesen et  $al<sup>45</sup>$  compared the administration of a cocktail of acetaminophen, NSAIDs, gabapentin, S-ketamine, and dexamethasone versus PCA morphine in patients undergoing spinal fusion surgery. Results suggest that patients who received the MMA cocktail required less opioid consumption and could mobilize earlier with physical therapy compared with control patients who only depended on PCA morphine.<sup>45</sup> Likewise, Garcia et  $al^{62}$  studied the effect of giving celecoxib, pregabalin, and extended-release oxycodone supplementation for PCA morphine compared with the IV morphine infusion alone. Total morphine consumption and VAS scores were lower in patients receiving the MMA regimen compared with control.<sup>62</sup> Finally, a meta-analysis by Yu et  $al<sup>47</sup>$  analyzing the use of pregabalin and gabapentin in the postoperative period demonstrated that gabapentin PO was efficacious in the management of postoperative pain at all time points on POD1, and thus may significantly reduce total opioid consumption without increasing the incidence of adverse effects. Pregabalin also was found to be efficacious in the management of postoperative pain, but more trials were needed to further evaluate its effectiveness.<sup>47</sup>

## Early Mobilization and Physical Rehabilitation

Early mobilization of the patient is a critical prerequisite for achieving early discharge, which is one of the goals of ERAS. Here, early mobilization is defined as getting the patient out of bed on POD0 or POD1,63 which may involve physical therapy, occupational therapy, or other exercises. In a review of the effects of early mobilization after various types of surgeries,  $E$ pstein $63$  described correlations with reduced morbidity and LOS. However, research on mobilization/rehabilitation following spine surgery remains scarce. Nielsen et  $al<sup>64</sup>$ implemented a pre-habilitation (6- to 8-week exercise regimen and smoking/drinking cessation) and early rehabilitation program for patients undergoing surgery for degenerative lumbar disease; the authors reported reduced LOS and improved patient satisfaction for patients who received this intervention, although postoperative complication rate and pain did not significantly change.

Although only 1 ERAS protocol included a ''pre-habilitation'' regimen,<sup>28</sup> many other protocols encourage early mobilization and provided physical rehabilitation services (Table 4). In the ERAS protocols, patient mobilization started as early as less than 90 minutes after arrival at the PACU following a laminectomy/laminotomy/microdiscectomy procedure.<sup>38</sup> Early mobilization goals included independence in performing  $\log$  roll,<sup>22</sup> movement out of bed and to chair 3 times per day,25,39 working with physical therapy/occupational therapy,  $25,31,36-39$  or even being discharged after surgery.<sup>20</sup> Most protocols did not provide much detail beyond when early mobilization began and whether physical therapy/occupational therapy was offered; even then, there was considerable variety in early mobilization requirements. Because of the paucity of research on this topic, there seems to be no consensus on which features of early mobilization and physical rehabilitation are most beneficial to patients.

## Early Nutrition

Early commencement of postoperative enteral nutrition is an established ERAS intervention in other surgical specialties. For instance, in the ERAS guidelines for colonic resection<sup>2</sup> and rectal/pelvic surgery,  $65$  early oral intake of liquids, solids, or nutritional supplements is recommended.<sup>2</sup> Indeed, early postoperative enteral nutrition may decrease postsurgical infection rates, reduce LOS and hospital cost, and reduce postoperative ileus when compared to late enteral or parenteral feeding. $66-70$ 

Early nutrition was commonly advised for spine surgery patients treated under ERAS guidelines (Table 4). In the spine ERAS protocols, a subset of studies initiated a clear liquid diet at POD0 or POD1 that advanced to a regular diet as tolerated, $22,25,34,40$  whereas others permitted a regular diet of solids and liquids on POD0 or POD1.30,32,36,38–40 Some protocols initiated oral intake as soon as the patient recovered from anesthesia.<sup>34,37–39</sup> These early nutrition guidelines were similar across the different ERAS protocols, regardless of whether the patients had undergone major or minor surgery.

#### Early Discharge Criteria

Currently, there does not seem to be a consensus on the criteria for early discharge in spine surgery (Table 5). This diversity may be due in part to the different spine procedures for which the protocols were developed. Nevertheless, current ERAS discharge criteria include physical therapy clearance, pain control, mobility, tolerating diet, and scoring systems such as the  $\overrightarrow{\text{Aldrete}}^3$  and Chung postanesthetic discharge scoring system.23,33,71

## **CONCLUSIONS**

Research on ERAS protocols for spine surgery is still in the nascent stages. Although there are commonalities between existing spine ERAS protocols, there is also much diversity. Notably, studies included in this review varied in their methodology, the number of ERAS interventions per protocol, the types of spine surgery, and the degree to which their data were analyzed and reported. In turn, this review was limited in its ability to assess the efficacy of ERAS protocols.

Overall, ERAS protocols seem to improve costeffectiveness without compromising the quality of patient care. MMA administration as an ERAS intervention may be linked directly to decreased opioid consumption, which was reported in several studies included in this review. Moreover, MMA administration has been associated independently with decreased opioid consumption in a non-ERAS setting. Study outcomes suggest that improved costeffectiveness may be achievable through ERAS, in particular via reductions in LOS, cost, and opioid consumption.

Currently, it is difficult to isolate the effect of any one ERAS element on patient outcome; it is also difficult to determine whether ERAS would be more successful for particular spine surgeries. Different spine procedures vary in their expected surgical stress levels and recovery rates, and the age and comorbidity status of patients vary as well; different ERAS interventions may then disproportionately benefit certain patient populations compared with others. However, these distinctions have not been made yet in the literature; in fact, in most studies, the same ERAS protocol was implemented across a number of different spine procedures.

From a review of the relevant studies, it is clear that much investigation is still needed to determine the ideal ERAS elements that are more effective for particular patient populations, spine surgeries, and pathology—such as deformity, tumor resection, and degenerative spine. Focused studies in these areas may allow for more accurate analyses of the effectiveness of particular ERAS elements. As research on spine ERAS pathways grows, greater consensus and protocol standardization may be achieved to benefit patient care.

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**Disclosures and COI:** The authors received no funding for this study and report no conflicts of interest.

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#### Published 28 August 2020

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