Evidence Review Conducted for the Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery: Focus on Anesthesiology for Hip Fracture Surgery

Ellen M. Soffin, MD, PhD,*† Melinda M. Gibbons, MD, MSHS,‡ Elizabeth C. Wick, MD,§ Stephen L. Kates, MD,‖ Maxime Cannesson, MD, PhD,¶ Michael J. Scott, MBChB, FRCP, FRCA, FFICM,#** Michael C. Grant, MD,†† Samantha S. Ko,†† and Christopher L. Wu, MD*†

Enhanced recovery after surgery (ERAS) protocols represent patient-centered, evidence-based, multidisciplinary care of the surgical patient. Although these patterns have been validated in numerous surgical specialities, ERAS has not been widely described for patients undergoing hip fracture (HFx) repair. As part of the Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery, we have conducted a full evidence review of interventions that form the basis of the anesthesia components of the ERAS HFx pathway. A literature search was performed for each protocol component, and the highest levels of evidence available were selected for review. Anesthesiology components of care were identified and evaluated across the perioperative continuum. For the preoperative phase, the use of regional analgesia and nonopioid multimodal analgesic agents is suggested. For the intraoperative phase, a standardized anesthetic with postoperative nausea and vomiting prophylaxis is suggested. For the postoperative phase, a multimodal (primarily nonopioid) analgesic regimen is suggested. A summary of the best available evidence and recommendations for inclusion in ERAS protocols for HFx repair are provided. (Anesth Analg XXX;XXX:00–00)

Population trends predict that the annual number of hip fractures (HFxs) could reach 7.3–21.3 million worldwide by 2050.[1] HFx is associated with advancing age and comorbidity burden, making the perioperative care of these patients particularly challenging. As has been demonstrated in other surgical cohorts, patients with HFx may benefit from care standardization to optimize outcomes and minimize the length of hospital stay and associated cost of care.[2] Enhanced recovery after surgery (ERAS) is a leading example of pathway-based care, which minimizes variation in care, maximizes multidisciplinary evidence-based practice, and is associated with improved outcomes and fewer complications after surgery.[2]

The Agency for Healthcare Research and Quality, together with the American College of Surgeons and the Johns Hopkins Medicine Armstrong Institute for Patient Safety and Quality at Johns Hopkins University, created the Safety Program for Improving Surgical Care and Recovery (ISCR). The program relies on evidence-based pathways of care to improve outcomes and enhance perioperative care and patient safety. Orthopedic surgery service lines will include elective total hip and knee arthroplasty and HFx repair. The ISCR will be implemented in >750 hospitals nationwide over the next 5 years.

We have evaluated the evidence for the anesthetic components to be included in the HFx repair pathway. The surgical components will be reviewed and reported separately. The goals of this evidence review are to assess the current best evidence for anesthetic interventions leading to improved outcomes after HFx repair and determine the anesthetic elements of the HFx repair protocol.

METHODS

A review protocol was developed with input from participants (anesthesiologists and surgeons listed as the authors in this article). Two researchers (E.M.S., C.L.W.) reviewed current HFx fast-track pathways from several sources (eg, Kaiser Permanente, Virginia Commonwealth University, University of Rochester, clinical guideline for HFx from the National Institute for Health and Care Excellence [United Kingdom]), extracted data on items included in major HFx pathways, undertook a scoping literature review, and

From the *Department of Anesthesiology, The Hospital for Special Surgery, New York, New York; †Department of Anesthesiology, Weill Cornell Medicine, New York, New York; ‡Department of Surgery, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California; §Armstrong Institute for Patient Safety and Quality, Johns Hopkins University, Baltimore, Maryland; ‖Department of Orthopaedic Surgery, Virginia Commonwealth University School of Medicine, Richmond, Virginia; ¶Department of Anesthesiology, David Geffen School of Medicine, University of California Los Angeles, Los Angeles, California; #Department of Anesthesiology, Virginia Commonwealth University School of Medicine, Richmond, Virginia; **Department of Anesthesiology and Critical Care Medicine, University of Pennsylvania, Philadelphia, Pennsylvania; and ††Department of Anesthesiology and Critical Care Medicine, Johns Hopkins University, Baltimore, Maryland.

Accepted for publication September 19, 2018.

Funding: This project was funded under contract number HHSP233201500020I from the Agency for Healthcare Research and Quality, US Department of Health and Human Services.

Conflicts of Interest: See Disclosures at the end of the article.

The opinions expressed in this document are those of the authors and do not reflect the official position of the Agency for Healthcare Research and Quality or the US Department of Health and Human Services.

Reprints will not be available from the authors.

Address correspondence to Ellen M. Soffin, MD, PhD, Department of Anesthesiology, The Hospital for Special Surgery, 535 E 70th St, New York, NY 10021. Address e-mail to soffine@hss.edu.

DOI: 10.1213/ANE.0000000000003925

presented each item to the group (anesthesiologists and surgeons listed as the authors in this article) for consideration. Items were included for consideration if majority consensus (>50%) from the group was reached. The group sought expert feedback to identify individual components in each perioperative phase of care (Table 1).

This evidence review should not be considered as a systematic review (SR) but an attempt to incorporate the latest evidence. The protocol was developed based on guidelines from several professional associations/societies (Table 2). In addition, literature reviews for each individual protocol component were performed in PubMed for English-language articles published before December 2016. Each search initially targeted HFx; if no HFx literature was identified, then the search was broadened to surgical procedures in general. Given the volume of literature in this field, a hierarchical method of inclusion was used based on study design. If we identified a well-designed SR/meta-analysis (MA), then the study was included. We also included randomized controlled trials (RCTs) or observational studies published after the SR/MA. Results are described narratively.

Table 1. Improving Surgical Care and Recovery Hip Fracture Protocol Components: Anesthesia

Protocol Components
Immediate preoperative
Preoperative regional analgesia
Multimodal preanesthesia medication
Intraoperative
Standard intraoperative anesthesia pathway
Postoperative nausea/vomiting prophylaxis
Glycemic control
Postoperative
Standard postoperative multimodal analgesic regimen

Table 2. Summary of AHRQ Safety Program for Improving Surgical Care and Recovery Hip Fracture Protocol Components, Associated Outcomes, and Support From the Literature and/or Guidelines: Anesthesia

Intervention	Outcome(s)	Evidence	Guidelines[a]
Immediate preoperative			
Preoperative regional analgesia	↓ Pain, ↓ opioids, ↓ cardiac and pulmonary morbidity	[b]	95
Multimodal preanesthesia medication	↓ Pain, ↓ PONV, ↓ opioid use	[b]	93
Intraoperative			
Standard intraoperative anesthesia pathway	↓ Pain, ↓ PONV, ↓ opioid use	[b]	93
Multimodal PONV prophylaxis	↓ PONV	[b]	95
Glycemic control	↓ SSI	[b]	36
Postoperative			
Standard postoperative multimodal analgesic regimen	↓ Pain, ↓ PONV, ↓ opioid use	[b]	95

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; PONV, postoperative nausea and vomiting; SSI, surgical site infection.
[a]Designates a component where all guidelines supported a given practice.
[b]Designates a component where all evidence supported a given practice.

RESULTS

Preoperative

Use of Regional Anesthesia/Analgesia Before Surgery. *Rationale.* Use of regional analgesic (variations of femoral nerve blocks) techniques before surgery may reduce pain in patients with HFxs.[3–7]

Evidence. Four RCTs and 1 SR suggest that administering femoral nerve/fascia iliaca blocks before surgery reduces pain, decreases opioid use and opioid-related side effects, and minimizes cardiac and pulmonary morbidity.[3–7] There is some uncertainty in the available literature (relatively small number of subjects studied), and larger scale RCTs are needed.

Summary. When available, use of regional analgesic (femoral nerve/fascia iliaca blocks) techniques before surgery in patients with HFxs is recommended.

Immediate Preoperative

Carbohydrate Loading and Duration of Fasting Before Surgery. *Rationale.* The preoperative administration of oral carbohydrates may be associated with attenuation of the perioperative catabolic state, reduction in postoperative insulin resistance, and a decrease in protein breakdown. Although the American Society of Anesthesiologists allows clear liquids 2 hours and a light meal 6 hours before induction of anesthesia in healthy patients who are undergoing elective procedures,[8] HFx surgeries are usually not considered elective.

Evidence. There are 2 observational studies of fasting/gastric emptying after a carbohydrate-rich drink in elderly patients with acute HFx.[9,10] A study in elderly women noted no evidence of delayed gastric emptying after a 400-mL 12.6% carbohydrate-rich drink.[9] The second study examined 262 elderly patients with HFxs where preoperative fasting was restricted to 6 hours for solids and 2 hours for fluids, and surgery was performed in ≤24 hours of admission and no cases of pulmonary aspiration were noted.[10]

Summary. Although limited data suggest that gastric emptying time is not delayed in the presence of HFx, HFx surgeries are usually not considered elective, and the most conservative approach is to consider these patients as a "full stomach" who may be at higher risk for pulmonary aspiration compared to those undergoing elective surgery. The decision to use carbohydrate loading and minimize duration of fasting before surgery in a nonelective case should be made by the anesthesiologist in consultation with other perioperative health care providers and should be tailored to individual patient requirements.

Multimodal Preanesthetic Medication. *Rationale.* A standardized group of preanesthetic medications may be administered as part of a multimodal approach to analgesia and postoperative nausea/vomiting (PONV) prophylaxis. A multimodal approach to control perioperative pain focuses on the concurrent utilization of multiple nonopioid analgesics. Goals are to produce additive/synergistic

analgesia while minimizing opioid use/opioid-related side effects in patients with HFxs.[11] Control of PONV is important to facilitate patient oral intake/recovery.

Acetaminophen

Evidence. There are no studies specifically examining the preoperative acetaminophen administration in patients undergoing HFx surgery. There is 1 MA in patients undergoing non-HFx surgery that examines the administration of preoperative acetaminophen, which is associated with a reduction in postoperative pain scores, opioid consumption, and PONV.[12]

Summary. Data from non-HFx surgery indicate that preoperative acetaminophen is associated with a reduction in postoperative pain scores, opioid consumption, and PONV. The acetaminophen dose should be decreased or withheld in patients with concomitant liver disease. The maximum dose is 15 mg/kg per dose up to a maximum of 1 g. There are insufficient data to determine whether 1 route of administration (intravenous [IV] versus oral) is superior.

Nonsteroidal Anti-Inflammatory Agents

Evidence. There are no studies specifically examining the use of perioperative nonsteroidal anti-inflammatory agents (NSAIDs) for patients with HFxs, which may be due in part to the concern of delaying bone healing and nonunion. There are 3 observational studies[13–15] and 3 SRs[16–18] examining NSAIDs on bone healing after fractures.

The wide diversity and heterogeneity of available data with conflicting results[14] preclude any definitive conclusions on NSAIDs and bone healing after fracture. There are patient-related characteristics that may influence the development of fracture-healing complications.[14] Several SRs on the topic have found no increased risk of nonunion with NSAID exposure when only the highest quality studies were assessed and with short duration (<1 week) of NSAID use.[16,17] Nonetheless, the clinician may want to avoid NSAIDs after HFx in high-risk patients.[18]

Summary. The use of NSAIDs (including cyclo-oxygenase [COX]-2 inhibitors) should be tailored to individual patient requirements and should be avoided in high-risk (renal, bleeding comorbidities) patients. Limited data preclude any definitive conclusions on the use of NSAIDs (including COX-2 inhibitors) on bone healing in fractures. Traditional NSAIDs are associated with platelet dysfunction and gastrointestinal irritation/bleeding, and the dosage of NSAIDs should be decreased or withheld in patients with these comorbidities. If used, the dosage of NSAIDs should also be decreased in elderly patients.

Gabapentanoids

Evidence. There are no studies examining perioperative gabapentanoids in patients with HFxs. There are multiple MAs/SRs in patients without HFxs, suggesting that a single dose of preoperative gabapentin may be associated with decreased postoperative pain and opioid consumption. However, more recent studies suggest that the analgesic effects of gabapentin may have been overestimated and the potential harms have not been fully explored.[19,20]

Summary. Limited data preclude any definitive conclusions on the routine use of gabapentanoids in patients with HFxs. The use of gabapentanoids should be tailored to individual patient requirements and avoided in high-risk patients (those at risk for sedation and respiratory depression, the elderly, or patients with obstructive sleep apnea).

PONV Prophylaxis. *Rationale.* Control of PONV is important to facilitate patient oral intake and recovery.

Evidence. There are no studies specifically examining different antiemetic agents in patients with HFxs. A recent evidence-based guideline for the prevention of PONV has been published.[21] The general approach for the prevention of PONV is to formally perform a risk assessment for PONV, decrease baseline risk factors if possible, and administer PONV prophylaxis using appropriate interventions based on the PONV risk assessment.[21]

Summary. A multimodal regimen for antiemetic prophylaxis is recommended for the prevention of PONV. Certain anesthetic techniques (regional anesthesia/propofol-based total IV anesthesia) may be associated with a lower incidence of PONV. Choices of specific antiemetic agents must be made on an individual basis, balancing risks and benefits. Caution should be exercised in using anticholinergic and antihistamine agents in a largely geriatric population.

Intraoperative

Standardized Evidence-Based Intraoperative Anesthetic Pathway. *Rationale.* A standardized evidence-based perioperative anesthetic pathway is essential for every surgical ERAS protocol. Although not every ERAS pathway will be alike due in part to differences based on local resources/expertise, every ERAS pathway should contain the core components of fluid management, multimodal analgesia with minimization of opioid use, and prevention of PONV. The intraoperative anesthetic should be tailored to facilitate a rapid awakening after completion of the surgical procedure. Several anesthetic regimens can be used to achieve these goals.

Regional Anesthesia (Neuraxial and Peripheral Nerve Blocks). *Rationale.* The use of regional anesthetic/analgesic techniques (epidural or spinal anesthesia in most cases) is part of many ERAS pathways. Local anesthetic-based techniques are associated with superior patient recovery and analgesia and decreasing opioid consumption and opioid-related side effects.

Evidence. There are 4 MAs/SRs[22–25] and multiple observational studies comparing regional to general anesthesia for patients with HFxs. Overall, whether the use of regional (versus general) anesthesia actually decreases perioperative mortality is uncertain,[22,26,27] but a nonrandomized study found improved survival and fewer pulmonary complications with neuraxial anesthesia in patients with intertrochanteric (but not femoral neck) fractures.[28] In addition, an SR of 20 retrospective observational and 3 prospective randomized controlled studies found a significant decrease in in-hospital mortality (odds ratio, 0.85; 95% confidence

interval, 0.76–0.95; P = .004) and length of hospital stay with neuraxial anesthesia, but there was no difference in the 30-day mortality.[25] A recent, large database analysis of 107,317 patients after HFx surgery found that survival independently improved as hospital-level neuraxial use increased, with most of the survival benefit realized with an increase in hospital-level neuraxial use >20%–25%.[27]

Some large-scale observational data indicate that regional anesthesia is associated with lower 30-day all-cause and surgical site infection, a decrease in deep venous thrombosis, and a shorter length of stay.[22,26,29] Large-scale RCTs examining regional to general anesthesia for Hfx are ongoing. The concurrent use of anticoagulants and neuraxial blocks/catheters should be approached with caution, and guidelines for such use have been published.[30]

Summary. Although the choice of anesthesia (general or regional) should be made by the patient in consultation with the anesthesiologist and other perioperative health care providers, the use of neuraxial anesthesia for HFx surgery is preferred.

Intrathecal Morphine for Postoperative Analgesia. *Rationale.* Intrathecal hydrophilic opioids (morphine) may provide prolonged postoperative analgesia.[31–33]

Evidence. There is 1 RCT investigating the use of intrathecal morphine (0.2 mg) in patients with HFxs. In this study, intrathecal morphine provided prolonged postoperative analgesia.[31] Two MAs in non-HFx suggest that intrathecal morphine (0.05–0.2 mg) decreases pain scores and opioid use.[32,33] It is not clear if intrathecal morphine provides superior analgesia or outcomes compared to other regional anesthesia techniques. Several side effects from intrathecal opioids may preclude use in the elderly patient with HFx, including PONV, urinary retention, and pruritus.[32] Respiratory depression remains a concern, and higher doses of intrathecal morphine (>0.3 mg) are generally associated with more episodes of respiratory depression.[34]

Summary. When other neuraxial regional analgesic techniques are not used, intrathecal morphine may be a useful technique for providing postoperative analgesia in patients with HFxs and may be particularly useful when other regional analgesic techniques are not available or cannot be used; however, caution is warranted in the elderly and frail populations due to concerns with oversedation.[35] Lower doses of intrathecal opioids (≤150 μg morphine) carry less risk of respiratory depression, but due to the unpredictability, all patients should have the same level of monitoring. Guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration have been published.[35]

Glycemic Control. *Rationale.* Perioperative control of glucose has been hypothesized to contribute to a reduction in surgical site infections.[36]

Evidence. There are no studies specifically examining perioperative glucose control and outcomes in patients with HFxs. The Centers for Disease Control (CDC) recently released a guideline for the prevention of surgical site infection (SSI), which recommended perioperative blood glucose target levels <200 mg/dL in patients with and without diabetes.[36] It should be noted that although the CDC recommended implementation of "perioperative glycemic control and use of blood glucose target levels <200 mg/dL in diabetic and nondiabetic patients and rated the evidence as category IA (strong recommendation), this recommendation was based on data from nonorthopedic patients and the CDC did not identify enough data to determine the optimal timing, duration, or delivery method of perioperative glycemic control for the prevention of SSI."[36] In addition, the CDC recommends maintaining perioperative normothermia (category IA: strong recommendation) as high-quality evidence, suggesting a benefit of patient warming over no warming.[36]

Summary. Perioperative glycemic control should be considered targeted with blood glucose levels <200 mg/dL in patients with and without diabetes.

Ventilation and Oxygenation. *Rationale.* Optimization of perioperative oxygenation may reduce surgical site infections.[37–40] Using an intraoperative protective lung ventilation strategy may reduce pulmonary complications.[37–40]

Evidence. There are no studies specifically examining the effect of an intraoperative protective ventilation strategy and pulmonary outcomes or the effect of oxygenation in patients with HFxs.

Multiple MAs, including orthopedic and nonorthopedic procedures, have provided mixed results on whether perioperative supplemental (fraction inspired oxygen, >0.8) oxygen therapy will result in a decrease in SSIs. The potential benefits of hyperoxia need to be balanced against its potential harms. The optimal level of oxygenation for patients with HFxs is uncertain.

With regard to intraoperative protective ventilation strategies, the data (in patients without HFxs) overall suggest that an intraoperative protective ventilation strategy of lower tidal volumes may result in improved clinical outcomes (respiratory failure and pulmonary infection) and reduced length of hospital stay.[37–40]

Summary. If positive-pressure ventilation will be used for intraoperative general anesthesia, then the use of a protective ventilation strategy (lower tidal volume of 6–8 mL/kg) in conjunction with optimal positive end-expiratory pressure and intermittent recruitment maneuvers may be used. Routine perioperative hyperoxia for patients undergoing HFx is not recommended.

Postoperative Nausea/Vomiting. *Rationale.* Control of PONV is an important anesthesiology component of any ERAS pathway because the presence of PONV will delay oral intake/patient recovery.[21]

Evidence. There are no studies examining PONV as a primary outcome in patients with HFxs. A comprehensive evidence-based guideline for the management of PONV has been published.[21] The recommended pharmacological

classes of antiemetics for PONV prophylaxis in adults include the 5-hydroxytryptamine receptor antagonists, corticosteroids (dexamethasone), butyrophenones, antihistamines, anticholinergics, and neurokinin-1 receptor antagonists.[21] In general, a multimodal approach using multiple classes of antiemetic agents for PONV prophylaxis is preferable to using a single drug alone. ERAS pathways often incorporate multimodal-preventive PONV strategies.[21]

Summary. Use of a multimodal antiemetic regimen for the prevention of PONV is recommended in patients with HFx. Certain anesthetic techniques (regional anesthesia/propofol-based total IV anesthesia) may be associated with a lower incidence of PONV. Choices of specific antiemetic agents must be made on an individual basis, balancing the risks and benefits. Caution should be exercised in using anticholinergic and antihistamine agents in a largely geriatric population to reduce the risk of delirium.

Tranexamic Acid. *Rationale.* Tranexamic acid (TXA) is an antifibrinolytic drug that inhibits fibrinolysis but blocks the conversion of plasminogen to plasmin, which breaks down fibrin in preformed blood clots.

Evidence. There are 3 RCTs,[41–43] 1 observational trial,[44] and 1 MA/SR[45] examining TXA in patients with HFx. Data suggest that the perioperative administration of TXA can significantly reduce the perioperative blood loss and requirement for blood transfusion.[45] The available studies are limited, and there are insufficient data to determine whether TXA in patients with HFxs will be associated with an increased incidence of thrombotic events.

Summary. Limited data preclude any definitive conclusions on the routine use of TXA in patients with HFxs. The use of TXA should be tailored to individual patient requirements and avoided in high-risk patients (renal dysfunction, hypercoagulable states, hypersensitivity to TXA, and coronary/vascular stent placement, thromboembolic disease, or cerebrovascular event within the previous 6 months).

IV Lidocaine

Rationale. Perioperative IV lidocaine bolus/infusions may provide analgesia via a nonopioid receptor mechanism and decrease perioperative opioid consumption.[46–48]

Evidence. There are no studies specifically examining IV lidocaine in patients with HFxs. However, there are several MAs examining perioperative IV lidocaine infusions in (primarily) nonorthopedic surgical procedures.[46–48] These studies suggest that lidocaine infusion may be associated with decreased postoperative pain and opioid consumption and earlier return of bowel function.[46–48] The benefits for the routine use of perioperative IV lidocaine for patients with HFxs are uncertain, but there may be instances where IV lidocaine may be considered, particularly when the use of other regional/local anesthetic-based techniques is not feasible.

Summary. The choice of whether to use IV lidocaine for HFx surgery should be made by the anesthesiologist in consultation with other perioperative health care providers and should be tailored to individual patient requirements.

Ketamine. *Rationale.* The administration of perioperative IV ketamine bolus/infusions may provide analgesia via a nonopioid mechanism and decrease perioperative opioid consumption.[49]

Evidence. There are no studies specifically examining intraoperative ketamine in patients with HFxs. There is no consensus as to the precise dosing/timing of ketamine administration. A recently published large RCT in older adults after major surgery examined 2 doses of intraoperative ketamine (0.5 or 1 mg/kg) to placebo and found no difference in adverse events (cardiovascular, renal, infectious, gastrointestinal, and bleeding) or delirium, but there were more postoperative hallucinations and nightmares with increasing ketamine doses compared with placebo.[49] Doses of ketamine from a variety of studies suggest a range of an intraoperative bolus of 0.25–1 mg/kg followed by an infusion of 0.1–0.25 mg/kg/h.

Summary. Ketamine may be a useful intraoperative anesthetic/analgesic agent, especially in opioid-tolerant patients and as part of a strategy to minimize opioid administration. The choice of whether to use ketamine for HFx surgery should be made by the anesthesiologist in consultation with other perioperative health care providers and should be tailored to individual patient requirements.

Fluid Minimization and Goal-Directed Fluid Therapy.

Rationale. Optimizing perioperative fluid management is a key component in every ERAS pathway. Excessive perioperative fluid administration is associated with cardiac and renal dysfunction, ileus, and delayed recovery.[50]

Evidence. There are 2 RCTs specifically examining the goal-directed fluid therapy (GDFT) in patients with HFxs.[51,52] GDFT therapy in patients with HFxs does not result in a significant reduction in length of stay or postoperative complications.[51] Fewer patients responded to GDFT than anticipated.[52] An SR found no evidence that fluid optimization strategies improve outcomes for participants undergoing surgery for HFx.[53]

Summary. The value of GDFT for patients with HFxs is uncertain, and there is insufficient evidence for its routine use in these patients.

Postoperative

Standardized Evidence-Based Postoperative Multimodal Analgesic Regimen. *Rationale.* Control of postoperative pain is an important component of any ERAS HFx pathway. Superior pain control facilitates patient mobility and recovery. A multimodal analgesic approach based on nonopioid analgesic agents and techniques are used to minimize the use and side effects of opioids.

Acetaminophen. *Rationale.* Acetaminophen may be used with other nonopioid analgesics to produce additive/

synergistic analgesia while minimizing opioid use and opioid-related side effects.

Evidence. There are 2 observational studies examining perioperative acetaminophen administration in patients with HFxs.[54,55] Scheduled acetaminophen as part of a standardized pain management protocol for these patients is associated with shorter length of hospital stay, decreased pain scores and opioid use, fewer missed physical therapy sessions, higher functional performance on discharge, and higher rate of discharge to home.[54,55]

The 3 MAs[56–58] examining acetaminophen for the treatment of postoperative pain in orthopedic and nonorthopedic patients suggest that postoperative acetaminophen provides superior analgesia (versus placebo) and decreases opioid consumption. When possible, acetaminophen should be concurrently administered with an NSAIDs (both on a scheduled basis) because administration of both agents produces greater analgesic effects than either agent administered alone.[59] Doses >1 g are not associated with greater reduction in pain outcomes.[60] Caveats to the use of NSAIDs in patients with HFxs are addressed previously and must be considered in the overall context of patient care and surgical goals.

Summary. Acetaminophen should be administered on a scheduled basis. Typical doses of acetaminophen for a normal-sized adult are between 3 and 4 g maximum per day. The optimal dosage of acetaminophen after hospital discharge is uncertain, although it may be appropriate to decrease the maximum dose of acetaminophen to 3 g daily.

Nonsteroidal Anti-Inflammatory Agents. *Rationale.* NSAIDs may be used with other nonopioid analgesics to produce additive/synergistic analgesia while minimizing opioid use and opioid-related side effects.

Evidence. There are no studies specifically examining the use of NSAIDs for perioperative analgesia for patients with HFxs. However, 3 MAs/SRs of perioperative NSAIDs (including COX-2 inhibitors) in patients without HFx suggest that NSAIDs after orthopedic/nonorthopedic procedures result in a significant reduction in pain scores/opioid use.[61–63]

Summary. Perioperative health care providers may consider the short-term use of NSAIDs after HFx. Limited data preclude any definitive conclusions on the use of NSAIDs on bone healing in fractures. The use of NSAIDs should be tailored to individual patient requirements and avoided in high-risk patients. Caveats to using NSAIDs and fracture healing are considered earlier. NSAIDs are important as part of multimodal analgesic strategies, but their use in acute surgery and the elderly may be more limited due to the increased incidence of dehydration, presence of comorbidities, and reduced renal reserve in this age group.

Dextromethorphan. *Rationale.* Dextromethorphan is commonly used as an antitussive agent. At doses above those used for an antitussive effect, dextromethorphan is an N-methyl-D-aspartate receptor, which plays a critical role in the development of chronic pain and possibly opioid tolerance.[64,65]

Evidence. There are no studies specifically examining dextromethorphan in patients with HFxs. There are 2 SRs/MAs[64,65] of dextromethorphan for postoperative pain in orthopedic/nonorthopedic surgical patients. Perioperative dextromethorphan reduces the postoperative opioid consumption and pain scores after surgery.[64] The optimal dosing of dextromethorphan is uncertain, although typical doses used range from 30 to 60 mg per os preoperatively and twice or thrice a day postoperatively.[61] Dextromethorphan may be associated with nausea, vomiting, dizziness, lightheadedness, and sedation.[65]

Summary. Dextromethorphan may provide additional nonopioid analgesia. The choice of whether to use dextromethorphan for HFx surgery should be made by the anesthesiologist in consultation with other perioperative health care providers and should be tailored to individual patient requirements.

Gabapentanoids. *Rationale.* Gabapentanoids are anticonvulsants that have been used for the treatment of both acute and chronic pain and may be valuable nonopioid analgesic adjuvants.[19,20]

Evidence. There are no studies examining the use of perioperative gabapentanoids in patients with HFxs.

Summary. Limited data preclude any definitive conclusions on the use of gabapentanoids for postoperative in patients with HFxs. The use of gabapentanoids should be tailored to individual patient requirements and avoided in high-risk patients (at risk for sedation and respiratory depression).

Local Anesthetics Wound Infiltration and Infusions (Subcutaneous). *Rationale.* Local anesthetics may be delivered as single-administration infiltration or continuous wound infusions to provide nonopioid analgesia at the incision site.

Evidence. There are no studies examining the use of a continuous infusion of subcutaneous local anesthetics for patients with HFxs. The 1 RCT[66] investigating a local anesthetic wound infiltration in patients with HFxs showed no significant reduction in pain or opioid consumption associated with the use of local anesthetic wound infiltration. There are 3 SRs of the use of continuous wound infusions for postoperative analgesia in patients without HFx.[67–69] Taken together, the SRs suggest that the analgesic efficacy of the technique is uncertain due to multiple methodological issues in the available (underlying) studies.

Summary. Local anesthetics administered via single-administration infiltration or continuous wound infusions are not recommended for routine use in patients with HFxs.

Tramadol. *Rationale.* Tramadol is a weak μ-opioid receptor agonist and inhibitor of serotonin and norepinephrine reuptake. Tramadol may be used with other nonopioid

agents to produce additive/synergistic analgesia while minimizing opioid use and opioid-related side effects.[70–72]

Evidence. There were no studies specifically examining oral tramadol in patients with HFx. There are 3 MAs of tramadol for the treatment of postoperative pain in orthopedic/non-orthopedic surgical patients.[70–72] These studies suggest that tramadol has a weak–moderate analgesic effect, which is significantly improved when combined with acetaminophen. Tramadol should not be used (or used cautiously) in patients already taking selective serotonin receptor inhibitors/serotonin and norepinephrine reuptake inhibitors/monoamine oxidase inhibitors, with renal insufficiency, or with a history of seizures.

Summary. Although the analgesic efficacy of tramadol for patients with HFxs is uncertain, tramadol has less μ-receptor (opioid) activity than morphine. Tramadol's weak–moderate analgesic effect is significantly improved when combined with acetaminophen.

Postoperative Peripheral Nerve Blocks. *Rationale.* The use of peripheral nerve blocks (PNBs) for postoperative analgesia may reduce pain from HFx surgery, facilitate patient recovery, and minimize opioid requirements and related side effects.

Evidence. There are 3 MAs/SRs,[73–75] 6 RCTs,[76–81] and 2 observational trials[82,83] examining the use of PNBs for postoperative analgesia in patients with HFxs. Overall, moderate evidence suggests that PNBs are effective for decreasing postoperative pain, decreasing opioid consumption, and possibly reducing delirium.[73–75] However, not all PNBs are equally effective in improving outcomes after HFx, although there are insufficient data to definitively determine the most optimal PNB for HFx.[73–75]

Summary. Use of PNBs is recommended for postoperative analgesia in patients with HFxs when local resources and expertise are available. The concurrent use of anticoagulants and the safety of placing PNBs and catheters should be considered on an individual basis. Guidelines for such use have been published elsewhere.[30]

Opioids. Almost every ERAS pathway will include strategies to limit opioid use. Opioid monotherapy is associated with significant side effects that may delay patient recovery. Nonetheless, opioids still have a role in ERAS pathways. Although it is not clear what percentage of total hip arthroplasty patients can be done "opioid-free," ERAS pathways typically strive to minimize opioid utilization, and opioids feature less prominently and are typically administered as a "rescue" (pro re nata) when all other nonopioid analgesic agents have failed to adequately control pain. One caveat for opioid use in ERAS pathways relates to the opioid-tolerant patient. These patients will likely require continuation of their baseline opioids to prevent symptoms of opioid withdrawal. Opioids generally should not be withheld in these patients.

DISCUSSION

ERAS programs are rapidly gaining in popularity across the United States in major part because ERAS protocols have been associated with superior outcomes and shorter length of hospital stay. Successes linking ERAS and improved outcomes after orthopedic surgery have been described, particularly for elective joint replacement.[84–89] However, the application of ERAS principles to repair of HFx has been more restricted. In a retrospective study, an ERAS protocol for HFx repair was associated with significant reduction in postoperative complications but had no effect on length of stay or 30-day mortality.[90] Two additional studies using before-and-after trial designs[91,92] demonstrated that ERAS produced significant reductions in post-HFx repair complications (including confusion, pneumonia, and urinary tract infection), shorter length of hospital stay, higher rates of home discharge,[92] and lower mortality in community-dwelling patients.[91] It should be noted that these pathways contained many of the same elements (use of regional anesthesia, fluid management, multimodal analgesia) listed in our pathway.

Our recommendations for the anesthetic components of an ERAS pathway for HFx are based on the best available evidence of benefit. However, it should be noted that not all of the evidence is specific HFx, and some had to be extrapolated from other surgical procedures. Evidence that is specific to surgery for HFx is included where feasible and derived from a preponderance of evidence in other surgeries where lacking.[93,94] Many of our recommendations (preoperative regional analgesia and postoperative multimodal analgesia) are similar to those advocated by the guidelines for management of HFxs published by the American Academy of Orthopaedic Surgeons (Table 2).

A comprehensive anesthetic approach to the preoperative phase should include regional analgesia. Peripheral nerves blocks reduce opioid administration, improve postoperative pain scores, and reduce cardiopulmonary comorbidity.[3–6] In addition, providers should consider the administration of a combination of preoperative oral acetaminophen and NSAIDs,[59] taking into account patient- and surgery-specific risk factors. Despite the proposed controversy regarding the impact of NSAIDs on adequate bone healing, the results of this review do not suggest such an association, and this may be less important depending on the type of surgical intervention. Finally, patients in a non-HFx ERAS pathway generally benefit from oral carbohydrate administration up to 2 hours before the start of surgery to prevent protein catabolism in elective surgery. However, in contrast to elective surgery, the urgent or emergent nature of HFx repair may prevent the uniform application of this process measure. Further high-quality studies in this area are necessary to provide additional evidence regarding the safety and relative benefits in the population with HFxs.

During the intraoperative phase, it remains unclear whether general or regional anesthesia contributes to better outcomes. The decision to use one over the other should incorporate local expertise and patient comorbidity. Large observational trials suggest that regional/neuraxial anesthesia may be associated with improved survival, fewer pulmonary complications, reduction in surgical site infections, and shorter lengths of stay.[22–29] However, prospective trials on this topic are notably lacking. When general anesthesia is selected, patients benefit from the application of

a "lung-protective" mechanical ventilation strategy, where low tidal volumes (6–8 mL/kg predicted body weight) should be emphasized. Any concerted anesthesia protocol should promote the routine use of antiemetics as directed by previously established PONV guidelines.[21] The use of several agents targeting multiple antiemetic pathways is recommended. Routine intraoperative glucose management is encouraged in accordance with the CDC guidelines.[36] No formal recommendation can be made regarding the optimal strategy for fluid administration in HFx surgery due to the conflicting nature of results in this area of research.

Similar to ERAS anesthetic guidelines for other procedures, the primary emphasis in HFx surgery during the postoperative phase is effective multimodal analgesia.[11] There is sufficient evidence to support the scheduled administration of acetaminophen—both to reduce pain scores and minimize reliance on opioid-based analgesia.[12,54–58,60] A similar recommendation is not supported, however, for the routine use of dextromethorphan or gabapentinoid medications.[64,65] The perioperative health care provider may consider the short-term use of NSAIDs after a fracture with the caveat that it remains unclear how the use of NSAIDs may impact bone healing in fractures. Where feasible, PNBs are recommended for the treatment of postoperative pain in HFx surgery.[73–83] Several high-quality studies support this conclusion provided that local expertise can facilitate these efforts. However, local wound infiltration is not encouraged because intertrial variability limits the quality of the evidence and concomitant analgesia may limit the effectiveness of this strategy.[66–69]

We have described the evidence associated with specific process measures associated with traditional ERAS pathways. However, individual providers and hospitals will need to utilize and adapt local resources and expertise to successfully implement these recommendations. When developing the local pathway, priority should be given to developing consensus and identifying components that are realistic and meaningful for the patient and provider populations. The Agency for Healthcare Research and Quality Safety Program for ISCR protocol components span all perioperative phases of care and will require interdisciplinary collaboration among surgeons, anesthesiology providers, nurses, hospital leadership, and patients.

DISCLOSURES

Name: Ellen M. Soffin, MD, PhD.
Contribution: This author helped with conception and design, analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content.
Conflicts of Interest: None.
Name: Melinda M. Gibbons, MD, MSHS.
Contribution: This author helped with conception and design, analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content.
Conflicts of Interest: M. M. Gibbons receives a consultant fee through a contract with the Agency for Healthcare Research and Quality (AHRQ) (HHSP233201500020I).
Name: Elizabeth C. Wick, MD.
Contribution: This author helped with conception and design, analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content.
Conflicts of Interest: E. C. Wick receives salary support through a contract with the AHRQ (HHSP233201500020I).
Name: Stephen L. Kates, MD.
Contribution: This author helped analyze and interpret the data, draft the manuscript, and critically revise the manuscript for important intellectual content.
Conflicts of Interest: None.
Name: Maxime Cannesson, MD, PhD.
Contribution: This author helped analyze and interpret the data, draft the manuscript, and critically revise the manuscript for important intellectual content.
Conflicts of Interest: M. Cannesson is a consultant for Edwards Lifesciences, Masimo Corp, and Medtronic, and he is the founder of Sironis. He receives research support from Edwards Lifesciences, Masimo Corp, and the National Institutes of Health (R01 GM117622, R01 NR013912).
Name: Michael J. Scott, MBChB, FRCP, FRCA, FFICM.
Contribution: This author helped analyze and interpret the data, draft the manuscript, and critically revise the manuscript for important intellectual content.
Conflicts of Interest: M. J. Scott received lecture and travel expenses from Cheetah Medical, Deltex Medical, and Merck.
Name: Michael C. Grant, MD.
Contribution: This author helped analyze and interpret the data, draft the manuscript, and critically revise the manuscript for important intellectual content.
Conflicts of Interest: None.
Name: Samantha S. Ko.
Contribution: This author helped draft the manuscript and critically revise the manuscript for important intellectual content.
Conflicts of Interest: None.
Name: Christopher L. Wu, MD.
Contribution: This author helped with conception and design, analysis and interpretation of data, drafting of the manuscript, and critical revision of the manuscript for important intellectual content.
Conflicts of Interest: C. L. Wu receives salary support through a contract with the AHRQ (HHSP233201500020I).
This manuscript was handled by: Tong J. Gan, MD.

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