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

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Successes using enhanced recovery after surgery (ERAS) protocols for total hip arthroplasty (THA) are increasingly being reported. As in other surgical subspecialties, ERAS for THA has been associated with superior outcomes, improved patient satisfaction, reduced length of hospital stay, and cost savings. Nonetheless, the adoption of ERAS to THA has not been universal. The Agency for Healthcare Research and Quality, in partnership with the American College of Surgeons and the Johns Hopkins Medicine Armstrong Institute for Patient Safety and Quality, has developed the Safety Program for Improving Surgical Care and Recovery. We have conducted an evidence review to select anesthetic interventions that positively influence outcomes and facilitate recovery after THA. A literature search was performed for each intervention, and the highest levels of available evidence were considered. Anesthesiology-related interventions for pre- (carbohydrate loading/fasting, multimodal preanesthetic medications), intra- (standardized intraoperative pathway, regional anesthesia, ventilation, tranexamic acid, fluid minimization, glycemic control), and postoperative (multimodal analgesia) phases of care are included. We have summarized the best available evidence to recommend the anesthetic components of care for ERAS for THA. There is evidence in the literature and from society guidelines to support the Agency for Healthcare Research and Quality Safety Program for Improving Surgical Care and Recovery goals for THA. (Anesth Analg XXX;XXX:00–00)

Current projections estimate that by 2030, >570,000 total hip arthroplasties (THA) will be performed annually in the United States at a cost of >$9 billion.[1] In response to these pressures, multidisciplinary care pathways are being adopted for patients with THA patients due to demonstrated benefits for both clinical quality and cost savings.[2]

Enhanced recovery after surgery (ERAS) programs optimize perioperative factors to minimize the physiological/psychological stress response to surgery.[3–5] ERAS protocols have been associated with better outcomes, fewer complications, shorter length of hospital stay, and lower cost of care.[6–9] Despite these gains, widespread adoption of ERAS for THA has been slow. The first meta-analysis (MA) of ERAS for hip/knee replacement was only published recently.[10]

The Agency for Healthcare Research and Quality (AHRQ), together with the American College of Surgeons and the Johns Hopkins Medicine Armstrong Institute for Patient Safety and Quality, has created the Safety Program for Improving Surgical Care and Recovery (ISCR). The program will create, coordinate, and implement evidence-based best practices in perioperative care to >750 hospitals and multiple surgical disciplines over the next 5 years.

We have evaluated the evidence to support anesthetic-based components of the AHRQ Safety Program for ISCR for THA. The surgical components will be reviewed and reported separately. The goals of this evidence review are to evaluate the best evidence relating to anesthetic components of THA pathways and develop the evidence-based THA 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 THA pathways from several US health systems, extracted data on items included in major THA pathways, and presented each item to the group (anesthesiologists and surgeons listed as the authors in this article) for

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

Immediate preoperative
Reduced fasting
Carbohydrate loading
Multimodal preanesthesia medication
Intraoperative
Standard intraoperative anesthesia pathway
Fluids/goal-directed fluid therapy
Normothermia
Tranexamic acid
Glycemic control
Postoperative
Standard postoperative multimodal analgesic regimen

consideration. Items were included for consideration if majority consensus (>50%) from the group was reached. The participants (anesthesiologists and surgeons listed as the authors in this article) identified 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. This article should be viewed as a companion to the AHRQ ISCR for THA pathway, and the categories listed accompany those described in the AHRQ pathway. 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 June 2017. Each search initially targeted THA; if no THA 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/MA, then the study was included. We also included randomized controlled trials (RCTs) or observational studies published after the SR/MA or not included in the SR/MA used. Results are described narratively.

RESULTS

A standardized, evidence-based anesthetic pathway is essential for every ERAS protocol as standardization is a fundamental strategy to improve patient outcomes. We will provide the evidence but allow each hospital to tailor its pathway by choosing from items that would be incorporated into its standardized pathway. Not every ERAS pathway will be identical; however, every ERAS pathway should contain the core intraoperative components of fluid management, multimodal analgesia/minimization of opioids, and prevention of postoperative nausea/vomiting (PONV).

PREOPERATIVE

Carbohydrate Loading and Duration of Fasting Before Surgery

Rationale. Preoperative oral carbohydrates (CHO) help avoid preoperative dehydration, may attenuate the perioperative catabolic state, and minimize postoperative insulin resistance/protein breakdown.[11]

Evidence. Two RCTs examining preoperative CHO administration in patients with THA found some benefits in the perioperative period from the administration of oral CHO solution, which may result in a decrease in insulin sensitivity, nausea, and pain postoperatively.[15,16]

The numerous SRs examining the role of preoperative CHO loading in non-THA surgical procedures associate preoperative CHO treatment with an attenuation in postoperative insulin resistance, reduction in length of hospital stay, and less loss of muscle mass.[17–19] There are no reported adverse effects of CHO loading. There is no consensus on the optimal preoperative CHO loading regimen for patients with diabetes mellitus (DM).

There is 1 SR in patients without THA exploring the duration of preoperative fasting and perioperative outcomes.[20] Preoperative permissive drinking resulted in significantly lower gastric volumes. Guidelines support clear liquids up to 2 hours and consuming a light meal 6 hours before induction of anesthesia in healthy patients undergoing elective procedures.[12,21]

Summary. CHO loading may be considered before THA; however, the ideal composition and volume/timing of administration have yet to be defined. The provision of CHO drinks may improve compliance of oral intake and reduce preoperative dehydration. There is a no consensus regarding CHO loading for patients with type 1 and type 2 DM. CHO loading is best avoided in type 1 DM, and if it is provided to patients with type 2 DM, ongoing blood glucose monitoring is recommended. Free intake of clear fluids up to 2 hours and solid food up to 6 hours before induction of anesthesia is recommended.[12]

Multimodal Preanesthetic Medication

Rationale. Assuming no contraindications, a standardized group of preanesthetic medications may be administered as part of a multimodal approach to analgesia and PONV prophylaxis. ERAS focuses on the concurrent utilization of multiple nonopioid analgesics to achieve additive/synergistic analgesia while minimizing opioid use/side effects. Control of PONV facilitates patient oral intake/recovery.

Acetaminophen

Evidence. There are no RCTs/SRs examining acetaminophen administration preoperatively in patients with THA. Data in non-THA procedures indicate that preoperative acetaminophen is associated with reduced postoperative pain scores, opioid consumption, and PONV.[22,23] Rectal administration of acetaminophen is discouraged due to the unreliable absorption/excessively high doses needed to achieve sustained therapeutic plasma concentrations.[24] The acetaminophen dose should be decreased/withheld in patients with liver disease.

Nonsteroidal Anti-inflammatory Drugs/COX-2 Inhibitors

Evidence. There are no large-scale RCTs/SRs of the analgesic efficacy of preoperative nonsteroidal anti-inflammatory drugs (NSAIDs) in patients with THA. We identified 2 MAs in patients without THA, suggesting a

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

Intervention	Outcome(s)	Evidence	Guidelines
Immediate preoperative			
Carbohydrate loading	↓ insulin resistance, ↓ protein catabolism, ↓ LOS, faster return of bowel function	+	√11
Reduced fasting	No adverse outcomes	+	√12
Multimodal preanesthesia medication	↓ pain, ↓ PONV, ↓ opioid use	+	√11
Intraoperative			
Standard intraoperative anesthesia pathway	↓ pain, ↓ PONV, ↓ opioid use	+	√11
Fluids/goal-directed fluid therapy	↓ morbidity, ↓ LOS	+	√13
Tranexamic acid	↓ blood loss	+	√[a]
Glycemic control	↓ SSI	+	√14
Postoperative			
Standard postoperative multimodal analgesic regimen	↓ pain, ↓ PONV, ↓ opioid use	+	√11

Abbreviations: AHRQ, Agency for Healthcare Research and Quality; LOS, length of stay; PONV, postoperative nausea and vomiting; SSI, surgical site infection.
[a]Management of Osteoarthritis of the Hip; Guidelines from the American Academy of Orthopaedic Surgeons (http://www.orthoguidelines.org/topic?id=1021; accessed January 22, 2018).
+A component where all evidence supported a given practice.
√A component where all guidelines supported a given practice.

benefit of preoperative celecoxib for reducing postoperative pain/opioid consumption and PONV.[25,26] COX-2 inhibitors may be preferred to traditional NSAIDs before surgery due to minimal effects on platelet function and no significant increase in the risk of perioperative blood loss.[27,28] A typical dose of preoperative celecoxib is 200–400 mg.[29]

Gabapentinoids

Evidence. We identified 4 RCTs that examined perioperative gabapentin for THA.[30–33] Three of the 4 RCTs failed to show a decrease in perioperative opioid consumption with gabapentinoids.[30–32] All 3 RCTs that assessed post-THA pain failed to demonstrate an analgesic benefit for gabapentinoids.[31–33]

We identified 2 additional MAs of gabapentin for THA analgesia.[34,35] Taken together, these studies suggest that gabapentinoids may not have opioid-sparing benefits, and the degree/duration of analgesic benefit was inconsistent.

Postoperative Nausea and Vomiting Prophylaxis

Evidence. Preventing PONV facilitates patient oral intake/recovery. Several antiemetic agents may be administered intraoperatively to maximize their pharmacologic benefits. Although there are no relevant THA-specific data, we also found 1 comprehensive evidence-based guideline for the management of PONV for a generalized surgical population.[36]

Summary. A multimodal strategy preoperatively to optimize pain control/prevent PONV is recommended for THA. Specific agents include acetaminophen and NSAIDs. There is insufficient evidence to recommend routine perioperative use of gabapentinoids. A multimodal regimen for antiemetic prophylaxis is recommended for the prevention of PONV.

INTRAOPERATIVE

Standardized, Evidence-Based Intraoperative Anesthetic Pathway

Rationale. A standardized intraoperative anesthetic pathway is essential for every ERAS protocol. Standardization is a fundamental strategy to improve patient outcomes.[37] The anesthetic should be tailored to facilitate a rapid awakening after surgery.

Regional Anesthesia: Neuraxial/Peripheral Nerve Blocks

Rationale. Regional anesthesia and analgesia figure prominently in ERAS pathways because local anesthetic-based techniques improve outcomes, facilitate pain control, and minimize opioid consumption/opioid-related side effects. For THA, neuraxial (epidural and spinal) and/or peripheral nerve blocks (psoas compartment/lumbar plexus block and sciatic nerve block) are used for intraoperative anesthesia and as part of a postoperative multimodal analgesia strategy.[38] Sedation (midazolam) may improve patient satisfaction during regional anesthesia and increase the patient's acceptance of regional anesthesia.[39] Although pre-/intraoperative midazolam may reduce PONV,[40] doses generally should be limited to avoid potential residual sedative effects postoperatively. This is particularly important in the elderly, who have a higher risk of postoperative cognitive dysfunction.

Neuraxial (Epidural or Spinal) Anesthesia

Evidence. Six observational studies comparing neuraxial to general anesthesia for THA indicate that neuraxial anesthesia is associated with improved patient outcomes, including decreased major complications/mortality, length of stay, cost, surgical site infections (SSIs), pulmonary complications, and blood transfusion.[41–46] One additional SR[47] and 2 MAs[48,49] in THA suggested a lower incidence of deep venous thrombosis/pulmonary embolism and intraoperative blood loss/blood transfusion with neuraxial anesthesia.

Peripheral Nerve Blocks

Evidence. We identified 2 RCTs that examined peripheral nerve blocks as the primary anesthetic for THA.[50,51] Compared to spinal anesthesia, psoas compartment/iliac crest blocks were associated with significantly higher

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mean arterial blood pressure at the beginning of surgery through the 20th minute of surgery and offered equivalent anesthesia for THA.[50] Sciatic nerve and L1 paravertebral blocks provided equivalent anesthesia compared to unilateral spinal anesthesia.[51]

Summary. For patients without contraindications, and assuming local expertise and resources are available, neuraxial anesthesia may be preferred for THA. Neuraxial blocks/catheters should be placed with caution in any patient on anticoagulation therapy.[52] Caution should be exercised whenever multiple sources of local anesthetics are used, and doses should be reduced accordingly to minimize the risk of systemic toxicity.

Intrathecal Morphine for Postoperative Analgesia

Rationale. A single dose of intrathecal (IT) opioid may be administered during placement of spinal anesthesia before THA. IT opioid may decrease postoperative pain scores/opioid requirements after THA.

Evidence. We identified several RCTs[53,54] and 1 MA[55] investigating IT morphine in patients undergoing THA. There are 2 additional MAs investigating the use of IT morphine in mixed surgical cohorts, including orthopedic surgery.[56,57] These data suggest that IT morphine (0.05–0.2 mg) improves postoperative pain scores, decreases opioid requirements, and provides equivalent analgesia compared to other regional analgesic techniques.

There are significant side effects of IT opioids, including increased risk of PONV, urinary retention, and pruritus. Respiratory depression is associated with higher doses of IT morphine (>0.3 mg).[58]

Summary. When other neuraxial regional analgesic techniques are not used, a single dose of IT opioid may be considered before THA. The benefits of IT opioids must be balanced against the risks of respiratory depression, pruritus, urinary retention, and PONV. Guidelines for the prevention/detection/management of respiratory depression associated with neuraxial opioids have been published.[59] Likewise, the risks of IT/spinal techniques in patients on concurrent anticoagulant therapy should be considered with referral to the latest American Society of Regional Anesthesia guidelines.[52]

Ventilation and Oxygenation

Rationale. Optimal tissue-oxygen delivery may reduce SSIs. An intraoperative protective ventilation strategy may protect against pulmonary complications.

Evidence. There are numerous MAs in orthopedic/nonorthopedic procedures examining the effect of oxygenation on SSIs.[60–62] The evidence on the efficacy of perioperative supplemental (typically inspired fraction oxygen [F_{IO_2}] >0.8) oxygen therapy on SSI is inconsistent. A 2015 Cochrane review suggested that robust evidence was lacking for a beneficial effect of a fraction of inspired oxygen of >60% and insufficient to support the routine use of a high fraction of inspired oxygen.[61]

We identified 3 MAs[63–65] and 1 RCT[66] (none in orthopedic procedures) examining the effects of intraoperative protective ventilation on postoperative outcomes. Overall, the data link use of lower tidal volumes (6–8 vs 10–12 mL/kg) to improved clinical outcomes and reduced incidence of respiratory failure/pulmonary infections and length of hospital stay.[63–66]

Summary. There is insufficient evidence to recommend routine perioperative hyperoxia for THA. If positive pressure ventilation is used for general anesthesia, then protective ventilation with lower tidal volumes (6–8 mL/kg predicted body weight) and optimal positive end-expired pressure is recommended.

Perioperative Nausea and Vomiting Prophylaxis

Rationale. ERAS protocols emphasize multimodal strategies to prevent perioperative PONV, which may delay oral intake/patient recovery.

Evidence. We identified 1 large observational study of PONV in THA.[67] General anesthesia (versus spinal anesthesia) was strongly associated with higher PONV after THA.

A perioperative guideline for the management of PONV[36] recommended various pharmacologic classes of antiemetics for PONV prophylaxis, including 5-hydroxytryptamine receptor antagonists (ondansetron), corticosteroids (dexamethasone), butyrophenones, antihistamines, anticholinergics (transdermal scopolamine), and neurokinin-1 receptor antagonists. The number of antiemetic interventions should be based on the patient risk profile for PONV.[36] When general anesthesia is used, a propofol-based total intravenous anesthesia (TIVA) is recommended to further reduce the risk for PONV.

Summary. A multimodal antiemetic regimen for the PONV prevention is recommended for patients undergoing THA. Certain anesthetic techniques (regional anesthesia/propofol-based TIVA) 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.

Tranexamic Acid

Rationale. Tranexamic acid (TXA) is an antifibrinolytic drug that blocks the conversion of plasminogen to plasmin. TXA may reduce intraoperative blood loss and blood transfusion in some THA cases.

Summary of Evidence. We identified numerous RCTs/MAs[68–72] examining the use of TXA for THA. The data suggest that perioperative TXA in THA results in lower total blood loss/less frequent allogeneic blood transfusion without increasing the risk of thromboembolic complications.

Topical and IV TXA appear to be equally effective in reducing blood loss. Although the optimal topical dose and timing of TXA are uncertain, the most commonly reported regimens comprise a bolus of IV TXA (10–30 mg/kg) with/without infusion (1 mg/kg/h). Higher doses increase the risk of seizures.

TXA should be used with caution in patients with renal dysfunction, hypercoagulable states, hypersensitivity to

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TXA, coronary/vascular stent placement, thromboembolic disease, or cerebrovascular event within the prior 6 months. Many studies excluded these high-risk groups, and the efficacy/safety of TXA in these high-risk patients is uncertain.

Summary. TXA is recommended for THA for all patients without contraindication. The optimal dose, timing, and regimen of administration are undefined. Use of TXA in high-risk patients is uncertain and should be made on an individual basis.

Lidocaine IV

Rationale. The intraoperative administration of IV lidocaine bolus and/or infusion has become an important nonopioid, analgesic component of many ERAS pathways. Administration of IV lidocaine via bolus and/or infusions may provide analgesia via a nonopioid mechanism and decrease perioperative opioid consumption.

Evidence. We identified 1 RCT examining the use of IV lidocaine in patients undergoing THA.[73] Compared to saline, IV lidocaine bolus (1.5 mg/kg), followed by an infusion (1.5 mg/kg/h), did not offer any beneficial analgesic effects on postoperative pain scores.

Several MAs suggest that perioperative IV lidocaine infusions in mostly nonorthopedic procedures may be associated with decreased postoperative pain intensity/opioid consumption and earlier return of gastrointestinal function.[74–76]

Summary. There is insufficient evidence to recommend the routine use of IV lidocaine for THA analgesia. Caution should be exercised whenever multiple sources of local anesthetics are used, and doses should be reduced accordingly to minimize the risk of systemic toxicity.

Ketamine

Rationale. The administration of perioperative IV ketamine may provide analgesia via a nonopioid mechanism and decrease perioperative opioid consumption.

Evidence. We identified 1 RCT examining the role of ketamine in THA[77] and 1 RCT in a mixed group of patients undergoing general orthopedic surgery.[78] Ketamine significantly decreased morphine consumption at 24 hours after THA, facilitated rehabilitation at 1 month, and decreased postoperative chronic pain up to 6 months after surgery.[77] An RCT in orthopedic patients >60 years of age found no differences between ketamine and saline in the neurocognitive function tests on postoperative days 1 and 6.[78]

There is no consensus regarding the precise dose/timing of ketamine administration. Doses of RCTs included in MAs[79] suggest an intraoperative bolus of 0.25–1.0 mg/kg followed by an infusion of 0.1–0.25 mg/kg/h.

Summary. Intraoperative ketamine may be considered as part of a balanced intraoperative regimen for anesthesia/analgesia for THA. Ketamine may be particularly useful in opioid-tolerant patients and when attempting to minimize opioid administration.

Fluid Minimization and Goal-Directed Fluid Therapy

Rationale. Optimizing perioperative fluid management is a key component in ERAS pathways. Excessive administration of IV fluids is associated with delayed recovery due to gastrointestinal/cardiac/renal/pulmonary dysfunction. Perioperative goal-directed fluid therapy (GDFT) using devices to estimate cardiac output may potentially be associated with decreased postsurgical complications and reduced length of hospital stay.

Evidence. We identified 1 RCT examining outcomes using GDFT in primary THA performed under regional anesthesia.[80] Compared to control, GDFT was associated with significantly fewer postoperative complications, no effect on mortality/length of hospital stay, and surprisingly more intraoperative fluid/blood administration, which may have been related to the protocolized hemodynamic management where more fluid was given due to the relative hypovolemia and increased venous capacitance from the spinal anesthetic.[80]

The numerous MAs (in mostly nonorthopedic patients) on GDFT[81–84] suggest that a GDFT (versus liberal fluid) regimen is associated with a lower incidence of wound infection/complications, shorter hospital length of stay, faster time to oral intake, and less postoperative hypotension. Benefits of GDFT are most apparent in high-risk patients undergoing major surgery[80] and those not treated within an ERAS pathway.[83,84] The universal superiority of GDFT therapy versus a restrictive fluid strategy remains uncertain.[82]

Summary. The specific value of GDFT for THA is uncertain but may be useful in high-risk patients. Intraoperative fluid management should aim to minimize fluid and maintain euvolemia. Intraoperative fluid requirements can be generally met with an isotonic balanced crystalloid solution.[85] Hydroxyethyl starches should not be used due to an association with increased mortality.[86]

Glycemic Control

Rationale. Perioperative glycemic control has been hypothesized to be protective against SSIs.

Evidence. We identified 1 SR of risk factors for periprosthetic joint infection after total hip/knee arthroplasty.[87] Preoperative DM was among the most significant factors associated with postarthroplasty joint infection. We identified 1 guideline for the prevention of SSI where perioperative blood glucose levels <200 mg/dL in patients with and without DM were recommended.[14] It should be noted that although the Centers for Disease Control (CDC) recommended implementation of "perioperative glycemic control and use 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."[14] In addition, the CDC recommends maintaining perioperative normothermia (category IA: strong recommendation) as high-quality evidence suggested a benefit of patient warming over no warming.[14]

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Summary. During surgery, glycemic control should be strongly considered using blood glucose target levels <200 mg/dL in patients with and without DM.

POSTOPERATIVE

Standardized Evidence-Based Postoperative Multimodal Analgesic Regimen

Rationale. Control of post-THA pain facilitates patient mobility and recovery. A multimodal analgesic approach based on nonopioid pharmacologic agents is emphasized as part of ERAS pathways. The effectiveness of some analgesic interventions discussed in this section is listed in Table 3.

Acetaminophen

Rationale. Acetaminophen may be used with other nonopioid agents to produce additive/synergistic analgesia while minimizing opioid use/opioid-related side effects.

Evidence. We identified 1 study examining acetaminophen administration postoperatively in patients undergoing THA.[110] A single dose of IV acetaminophen was associated with reduced opioid use/pain intensity.

We found numerous MAs examining the use of acetaminophen for the treatment of postoperative pain in orthopedic/nonorthopedic patients.[22,88–90] These data suggest that postoperative acetaminophen is associated with superior analgesia and decreased opioid consumption.

Acetaminophen should be administered on a scheduled basis. If the patient is not yet tolerating oral intake, scheduled IV acetaminophen, if available, can be administered.[88–90] When the patient is tolerating oral intake/medications, an oral formulation of acetaminophen can be administered. Typical doses of acetaminophen for an average-sized adult are between 3 and 4 g/d. Doses >1 g are not associated with greater analgesic benefit.[111] When possible, acetaminophen should be concurrently administered with an NSAID (also on a scheduled basis): administration of both agents produce superior analgesic effects compared to either agent alone.[112]

Summary. Provided no contraindication, acetaminophen should be administered on a scheduled basis.

Nonsteroidal Anti-inflammatory Drugs

Rationale. As part of a comprehensive, multimodal approach to control perioperative pain, NSAIDs (including COX-2 inhibitors) may be used with other nonopioid agents to produce additive/synergistic analgesia while minimizing opioid use/opioid-related side effects.

Evidence. We identified 1 SR of NSAIDs for the treatment of pain after THA.[55] NSAIDs were associated with significant reductions in pain scores/opioid requirements.

We identified numerous MAs/SRs of perioperative use of NSAIDs (in orthopedic/nonorthopedic surgical patients), all of which demonstrate a significant reduction in pain scores/opioid consumption.[25,26,29,91] NSAIDs are preferably administered on a scheduled basis within most ERAS pathways. If the patient is not yet tolerating oral intake, then scheduled IV NSAIDs can be provided and subsequently converted to an oral formulation when appropriate.

Typical doses and choices of NSAIDs for an average-sized adult without contraindications include ketorolac 15–30 mg IV every 6 hours and ibuprofen 400–600 mg orally per OS every 6 hours (when the patient is tolerating oral intake). Assuming no contraindications, administration of a COX-2 inhibitor in place of ibuprofen would also be appropriate. NSAIDs are associated with several undesirable side effects, including platelet dysfunction, gastrointestinal irritation/bleeding, and renal dysfunction. NSAIDs should be decreased/withheld in patients with these comorbidities and in elderly patients. A brief perioperative course of NSAIDs (3 days) does not appear to be associated with increased risk for myocardial infarction after total hip/knee replacement.[113]

Summary. NSAIDs (including COX-2 inhibitors) are recommended as a routine part of post-THA multimodal analgesia. NSAIDs should be scheduled and can be administered IV and orally. NSAIDs should be decreased/withheld in patients with certain comorbidities (eg, renal dysfunction) and in elderly patients.

Dextromethorphan

Rationale. Dextromethorphan is commonly used as an antitussive agent and an antagonist at the *N*-methyl-D-aspartate receptor.

Evidence. There are no studies examining dextromethorphan specifically in patients undergoing THA.

We identified 1 SR[98] and 1 MA[99] on dextromethorphan for postoperative pain in orthopedic/nonorthopedic patients. The findings are inconsistent between these studies, with the more recent MA[99] supporting the use of dextromethorphan to reduce opioid consumption/pain scores. The earlier SR[98] failed to quantitatively combine the data into a pooled estimate.

The optimal dose, timing, and duration of dextromethorphan are uncertain. Dextromethorphan may be associated with nausea, vomiting, dizziness, lightheadedness, and sedation.[99]

Summary. There is limited evidence to guide the routine use of dextromethorphan for analgesia after THA. As part of an overall strategy of opioid-sparing analgesia, dextromethorphan may be useful, but it should only be considered on an individual basis.

Table 3. Postoperative Analgesic Treatments

	References
Proven effectiveness	
Acetaminophen	22, 88–90
Nonsteroidal anti-inflammatory agents	25, 26, 29, 55, 91
Local anesthetic infiltration by surgeon	55, 92–94
Regional analgesia	55, 95–97
Probable effectiveness	
Dextromethorphan	98, 99
Gabapentinoids	31, 78, 100–104
Tramadol	105
No proven benefits	
Continuous wound infusions of local anesthetics	106–109

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Gabapentinoids

Rationale. Gabapentin/pregabalin is an anticonvulsant agent used for the prevention and treatment of acute and chronic pain.

Evidence. We identified 1 RCT examining the analgesic efficacy of gabapentin as part of a multimodal analgesic regimen for THA.[31] There were no clinically important reductions in postoperative morphine consumption, pain scores, opioid-related side effects, or functional improvements in patients receiving gabapentin compared to standard multimodal analgesia.

Numerous MAs/SRs examining the analgesic efficacy of a single dose of preoperative gabapentin in orthopedic/nonorthopedic cohorts suggest that preoperative gabapentin may be associated with decreased postoperative pain and opioid consumption, PONV, and anxiety.[80,100–104] There are scant data regarding the postoperative and postdischarge administration of gabapentinoids. There are little systematic data to guide the postoperative dosing of these agents; however, 1 MA suggested that the lowest effective dose of pregabalin was 225–300 mg/d.[114] The dose of gabapentinoids should be decreased/withheld in patients with renal dysfunction and the elderly.

Summary. Gabapentinoids are analgesic and opioid-sparing; however, the analgesic efficacy of gabapentinoids after THA is uncertain, especially when multiple nonopioid analgesics are administered together.[32] The use of gabapentinoids should be considered on an individual basis after THA.

Local Anesthetics (Subcutaneous)

Rationale. Local anesthetics may be administered via continuous wound infusions to provide nonopioid analgesia at the incision site.

Evidence. There are no studies investigating continuous wound infusions of local anesthetics for patients undergoing THA. We identified 4 SRs of continuous wound infusions for postoperative analgesia in orthopedic/nonorthopedic surgical patients.[106–109] The analgesic efficacy of this technique is uncertain due to the presence of multiple methodologic issues.

Summary. There is insufficient evidence to support the routine use of continuous wound infusions for post-THA analgesia. Caution should be exercised whenever multiple sources of local anesthetics are used, and doses should be reduced accordingly to minimize the risk of systemic toxicity.

Local Infiltration Analgesia

Rationale. Surgeon-administered infiltration of local anesthetics (with/without adjuvants) into the tissues in the surgical field may provide analgesia and promote early mobilization and hospital discharge.

Evidence. We identified 4 SRs,[55,92–94] examining the use of local infiltration analgesia (LIA) in patients undergoing THA. The data suggest that LIA in THA reduces postoperative pain scores/opioid consumption. The optimal choices of local anesthetic/adjuvants/doses/location of injection are unknown at this time.

Summary. Surgeon-administered LIA is recommended as part of a multimodal approach to pain control after THA, particularly where other regional anesthesia/analgesia resources and expertise are not available. Caution should be exercised whenever multiple sources of local anesthetics are used, and doses should be reduced accordingly to minimize the risk of systemic toxicity.

Peripheral Nerve Blocks: Lumbar Plexus

Rationale. Sensory afferents from the hip joint arise from several branches of the lumbar plexus. A lumbar plexus block and/or catheter may reduce pain and minimize opioid use and related side effects after THA.

Evidence. We identified 1 MA[55] and several RCTs[95–97] examining the use of lumbar plexus block/catheters for post-THA analgesia. The data indicate that use of a lumbar plexus block/catheter is associated with statistically significant reductions in postoperative pain scores and opioid consumption. The optimal choices of local anesthetic, dose/regimen for lumbar plexus block/catheters for THA are unknown at this time. The risk of falls caused by a lumbar plexus block is also uncertain but should be considered in high-risk patients.[115]

Summary. Where local resources and expertise permit, and provided no patient contraindication, the use of a lumbar plexus block can be considered as part of a multimodal approach to post-THA analgesia. Patients should be monitored for motor block and risk of falls. The concurrent use of anticoagulants on the presence of peripheral nerve blocks/catheters should be used with caution, and guidelines for such use have been published.[52]

Tramadol

Rationale. Tramadol is a weak μ-opioid receptor agonist that inhibits the reuptake of serotonin and norepinephrine.

Evidence. We identified 1 RCT examining the analgesic efficacy of 50 and 100 mg oral tramadol versus 1000 mg paracetamol + 60 mg codeine and placebo in patients undergoing THA.[105] Tramadol at both doses was not superior to placebo and was significantly inferior to paracetamol + codeine for pain scores.

Three MAs of tramadol in orthopedic/nonorthopedic surgical patients indicate that tramadol has a weak-moderate analgesic effect, which is significantly improved when combined with acetaminophen.[116–118] Tramadol should not be used or used with caution in patients taking selective serotonin receptor inhibitors, with renal insufficiency, or with a history of seizures.

Summary. The analgesic efficacy of tramadol monotherapy for patients undergoing THA surgery is not supported. However, as part of a multimodal regimen, tramadol may be considered, provided there is no contraindication.

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Opioids

Rationale. Traditionally, opioids form the basis for postoperative analgesia. ERAS pathways attempt to limit opioid use, limiting opioid-related side effects that can delay patient recovery. Although it is not clear what percentage of patients undergoing THA can be "opioid-free," ERAS pathways typically include opioids as a "rescue" (pro re nata [PRN]) when all other nonopioid analgesic agents have failed to control the patient's pain. One caveat for opioid use in ERAS pathways relates to opioid-tolerant patients. These patients will require continuation of their baseline opioid requirements to prevent withdrawal.

DISCUSSION

The demand for THA is escalating worldwide.[1] As the volume of procedures increases, it is important to also increase quality, control health care costs, and minimize the risk of patient harm. These needs have led to the adoption of ERAS in multiple surgical subspecialties as a framework for providing evidence-based best practice and improving patient outcomes.[119] We have provided a comprehensive evidence review of anesthetic interventions associated with improved outcomes after THA; however, it should be noted that other aspects of THA (preoperative risk assessment, venous thromboembolism prophylaxis, rehabilitation) are discussed in a separate surgical article,[120] and not all of the evidence is specific to THA and had to be extrapolated from other surgical procedures. For instance, the evidence benefits for CHO loading and GDFT are mostly described in the colorectal literature, and relatively little evidence was specific to THA. As such, the recommendations for THA are worded accordingly to reflect the uncertain nature of the evidence specific to THA ("CHO loading may be considered…" and "The specific value of GDFT for THA is uncertain…").

The evidence review provides several recommendations for pre-THA care. Consistent with ERAS recommendations in other elective surgical subtypes, patients should receive oral CHO up to 2 hours before induction of anesthesia for THA. The optimal CHO-containing solution (simple [eg, glucose] versus complex [eg, maltodextrin]) is unclear. The preoperative fasting duration can likewise be safely limited to 6 hours for solid food intake and 2 hours for clear beverages. Optimal perioperative analgesia and PONV prophylaxis start preoperatively, with evidence supporting an orally administered bundle, including acetaminophen and an NSAID.

The primary goals of intraoperative ERAS care for THA focus on a standardized anesthetic regimen and transition to effective postoperative analgesia, enabling early enteral intake and effective mobilization. There is a range of recommended techniques, and we recognize that some practice settings may be limited in the resources and expertise required to provide some of these techniques. Where possible, the evidence suggests, and we recommend, a primary neuraxial anesthetic for THA. Where patient contraindication or practice settings limit the use of neuraxial anesthesia, a general anesthetic that includes a protective lung ventilation strategy should be provided. TIVA-based general anesthesia or inhaled anesthetics without nitrous oxide may be associated with more rapid recovery after THA,[121] less PONV,[122] and improved pulmonary outcomes.[123]

It is also appropriate to consider postoperative analgesia during the intraoperative phase of care. We recommend the use of opioid-sparing regional analgesic techniques wherever patient conditions and local resources permit. Other components of intraoperative care include the prevention of PONV and SSI, glycemic control, and blood and fluid management. We recommend that TXA should be given to all patients, assuming no contraindication. PONV prophylaxis should be provided based on patient risk factors.

The evidence basis to guide the optimal IV fluid regimen and associated volume-status monitoring in THA are limited; however, the available literature supports the judicious use of fluids to achieve euvolemia. That being said, patients with significant comorbidities or significant blood loss may benefit from more intense hemodynamic monitoring.[124]

Effective, multimodal analgesia forms the cornerstone of post-THA care. Opioid monotherapy should be avoided. Multimodal analgesia may be achieved by a combination of analgesic modalities, including regional analgesia. Continuation of multimodal IV agents is recommended until the patient is tolerating an oral diet. Specific choices recommended include NSAIDs and acetaminophen. It must be noted that recent publications have questioned the analgesic benefits of gabapentinoids.[125,126] Although the goal of ERAS pathways is opioid minimization, some patients may require opioids, and if escalation to opioid therapy is needed, we feel that tramadol (assuming no contraindications) represents a reasonable first choice before using other stronger μ-receptor opioids, provided other nonopioid analgesics are simultaneously provided.

A few points should be noted about the use of regional anesthesia in THA. The data on the benefits of regional anesthesia are generally not in the context of an ERAS pathway, so the actual benefits of regional anesthesia in the presence of a multimodal analgesia regimen and ERAS pathway are not clear. Our recommendation that neuraxial anesthesia may be preferred for THA is based on the large-scale observational studies indicating that neuraxial anesthesia is associated with improved patient outcomes[41–46] as the MAs/SRs,[47–49] suggesting a lower incidence of deep venous thrombosis/pulmonary embolism with neuraxial anesthesia may be somewhat outdated. Based on the literature found, we also felt obligated to list the evidence for IT opioid alone (no local anesthetic) and lumbar plexus block although realistically; these techniques are probably much less commonly used clinically than neuraxial (local anesthetic–based epidural and spinal anesthesia).

The evidence-based recommendations provided can be used as a framework for creating anesthetic components of a full ERAS THA pathway. Although ERAS is an effective strategy and has been shown to significantly reduce the length of stay and incidence of complications,[10] protocol implementation requires collaboration between disciplines, together with support from hospital administrators and policymakers. The evidence provided regarding many of the enhanced recovery pathways elements is in flux and new evidence continues to be published. The recommendations provided on this document have been based on the best evidence available at the time of our literature searches—the development of recommendations is a dynamic process such that protocols should be modified when new evidence

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is made available. Ultimately, we hope these initiatives will allow hospitals to not only meet the increasing demand for THA but also to improve quality of recovery and patient safety while hopefully decreasing costs of medical care.

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