

# Evidence review conducted for the AHRQ Safety Program for Improving Surgical Care and Recovery: focus on anesthesiology for gynecologic surgery

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## ABSTRACT

Enhanced recovery after surgery (ERAS) protocols for gynecologic (GYN) surgery are increasingly being reported and may be associated with superior outcomes, reduced length of hospital stay, and cost savings. 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, which is a nationwide initiative to disseminate best practices in perioperative care to more than 750 hospitals across five major surgical service lines in a 5-year period. The program is designed to identify evidence-based process measures shown to prevent healthcare-associated conditions and hasten recovery after surgery, integrate those into a comprehensive service line-based pathway, and assist hospitals in program implementation. In conjunction with this effort, we have conducted an evidence review of the various anesthesia components which may influence outcomes and facilitate recovery after GYN surgery. A literature search was performed for each intervention, and the highest levels of available evidence were considered. Anesthesiology-related interventions for preoperative (carbohydrate loading/fasting, multimodal preanesthetic medications), intraoperative (standardized intraoperative pathway, regional anesthesia, protective ventilation strategies, fluid minimization) 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 GYN surgery.

## INTRODUCTION

Enhanced recovery after surgery (ERAS) pathways have grown in popularity as an innovative approach to deliver standardized, evidence-based care. ERAS programs have been associated with decreased length of hospital stay, reduction in surgical complication, as well as healthcare-associated infections and lower overall costs primarily after colorectal surgical procedures.<sup>1–3</sup> Although the implementation of ERAS pathways in gynecologic (GYN) surgery has lagged in comparison with colorectal surgery, the many similarities between the two surgical subspecialties would suggest that GYN ERAS would yield similar results.<sup>4</sup>

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, created the Safety Program for Improving Surgical Care and Recovery (ISCR), which represents a nationwide initiative to disseminate best practices in perioperative care to more than 750 hospitals across five major surgical service lines in a 5-year period. The program is designed to identify evidence-based process measures shown to prevent healthcare-associated conditions and hasten recovery after surgery, integrate those along with socioadaptive interventions into comprehensive service line-based pathways that improve surgical outcomes, heighten patient experience, and reinforce a culture of perioperative safety. The program relies on evidence-based pathways as foundational components of the implementation strategy.

In order to facilitate GYN ERAS pathway development, we have conducted a review of the available literature for relevant anesthesia components that might be included in the AHRQ Safety Program for ISCR in GYN surgery. The surgical components are reviewed and reported separately. The goals of this evidence review are to assess the current best evidence and to determine the appropriate anesthesia interventions to adopt in a comprehensive GYN surgery protocol.

## METHODS

A review protocol was developed with input from participants (anesthesiologists and surgeons listed as the authors in this manuscript). Two researchers (MCG, CLW) reviewed available GYN pathways, extracted data on items included in major GYN pathways, and presented each item to the group. Items were included for consideration if majority consensus (>50%) from the group was reached for each perioperative phase of care (preoperative, intraoperative, postoperative; **Box 1**).

This evidence review should not be considered as a systematic review but an attempt to distill and incorporate the latest evidence from the available literature. The protocol was developed based on guidelines from several professional associations/societies (**table 1**). In addition, literature reviews for each individual protocol component were performed in PubMed for English-language articles published before October 2018. Each search initially targeted GYN; if no GYN literature was

**Box 1 Improving Surgical Care and Recovery gynecologic surgery protocol components—anesthesia**

- ▶ Immediate preoperative.
  - Reduced fasting.
  - Carbohydrate loading.
  - Multimodal preanesthesia medication (ie, *acetaminophen, gabapentinoids, COX-2 inhibitors*).
- ▶ Intraoperative.
  - Standard intraoperative anesthesia pathway.
  - Lung protective ventilation.
  - Fluids/Goal-directed fluid therapy.
  - Postoperative nausea and vomiting prophylaxis.
- ▶ Postoperative.
  - Standard postoperative multimodal analgesic regimen (ie, *scheduled acetaminophen and NSAIDs, consider gabapentinoids, epidural analgesia for open procedures*).

COX-2, cyclo-oxygenase-2; NSAID, non-steroidal anti-inflammatory drugs.

**Table 1 Summary of AHRQ Safety Program for Improving Surgical Care and Recovery gynecologic protocol components, associated outcomes, and support from the literature and/or guidelines— anesthesia**

Intervention	Outcome(s)	Evidence	Guidelines
<b>Immediate preoperative</b>			
Carbohydrate loading	↓ Insulin resistance, ↓ protein catabolism, ↓ LOS, faster return of bowel function	*	† <sup>6,7</sup>
Reduced fasting	No adverse outcomes	*	† <sup>6-8</sup>
Multimodal preanesthesia medication	↓ Pain, ↓ PONV, ↓ opioid use	*	† <sup>6,7</sup>
<b>Intraoperative</b>			
Standard intraoperative anesthesia pathway	↓ Pain, ↓ PONV, ↓ opioid use	*	† <sup>6,7</sup>
Protective ventilation strategy	↓ Pulmonary complications	*	† <sup>6,7</sup>
Fluids/Goal-directed fluid therapy	↓ Morbidity, ↓ LOS	*	† <sup>6,7</sup>
Postoperative nausea and vomiting prophylaxis	↓ PONV	*	† <sup>6,7,17</sup>
<b>Postoperative</b>			
Standard postoperative multimodal analgesic regimen	↓ Pain, ↓ PONV, ↓ opioid use	*	† <sup>6,7</sup>

NA designates a component where the component is not currently addressed in the guidelines.

\*Designates a component where all evidence supported a given practice.

†Designates a component where all guidelines supported a given practice.

AHRQ, Agency for Healthcare Research and Quality; LOS, length of stay; PONV, postoperative nausea and vomiting.

**Table 2 Recommendation where AHRQ Safety Program for Improving Surgical Care and Recovery gynecologic protocol components are similar between colorectal and gynecologic surgeries**

Intervention	Recommendations
<b>Immediate preoperative</b>	
Reduced fasting and carbohydrate loading	Reduced preoperative fasting (solids until 6 hours prior to induction and clear liquids until 2 hours prior to induction) for elective procedures.
Multimodal preanesthesia medication	A preoperative multimodal strategy including acetaminophen, COX-2 inhibitors, and gabapentinoids is shown to decrease postoperative pain and opioid consumption.
<b>Intraoperative</b>	
Standard intraoperative anesthesia pathway	A standardized, evidence-based perioperative anesthetic pathway is essential for every surgical ERAS protocol, and the intraoperative anesthetic should be tailored to facilitating a rapid awakening after completion of the surgical procedure.
Protective ventilation strategy	An intraoperative protective ventilation strategy of lower tidal volumes and positive end-expiratory pressure is associated with improved clinical outcomes (respiratory failure, pulmonary infection) in a number of surrogate surgical procedures.
Fluids/Goal-directed fluid therapy	Intraoperative fluid management should aim to minimize fluid and obtain early postoperative euvoemia. When available, GDFT may be beneficial in high-risk patients or when there is significant intraoperative blood/fluid loss.
Postoperative nausea and vomiting prophylaxis	Use of a multimodal antiemetic regimen for the prevention and treatment of PONV is recommended in patients undergoing gynecologic surgery.
<b>Postoperative</b>	
Standard postoperative multimodal analgesic regimen	A multimodal analgesic approach with multiple non-opioid analgesics agents and techniques are used in an attempt to minimize the use of and side effects from opioids.

AHRQ, Agency for Healthcare Research and Quality; COX-2, cyclo-oxygenase-2; ERAS, enhanced recovery after surgery; GDFT, goal-directed fluid therapy; PONV, postoperative nausea and vomiting.

identified, the search was broadened to surgical procedures in general. Given the volume of literature in this field, a hierarchical method of inclusion was employed based on study design. If we identified a well-designed systematic review/meta-analysis (MA) and/or randomized controlled trial (RCT), the study was included. Although observational studies were also reviewed, their results were considered only when higher level evidence was unavailable on the topic. All results are described narratively.

Because of the similarities between GYN and previously published colorectal pathway,<sup>5</sup> we have highlighted the differences between the pathways and provide details of data specific to GYN surgery in the text. Where there are commonalities between the two pathways (table 2), we refer the reader to the previously published AHRQ Safety Program for ISCR in colorectal surgery pathway<sup>5</sup> for further details, although recommendations are still provided throughout this manuscript.

**RESULTS**

**Standardized, evidence-based perioperative anesthetic pathway**

**Summary and rationale**

A standardized, evidence-based perioperative anesthetic pathway is essential for every GYN surgical ERAS protocol in order to reduce interprovider variation in administered care.<sup>6,7</sup> Although not every ERAS pathway will be alike due in part to differences based on local resources and expertise, every ERAS pathway

should contain core components such as guidelines for the use of multimodal analgesia with minimization of opioid use and prevention of postoperative nausea and vomiting (PONV).

## PREOPERATIVE

### Carbohydrate loading and duration of fasting prior to surgery

#### Evidence

There are no data from prospective randomized trials specifically examining carbohydrate loading and duration of fasting prior to GYN surgery.

#### Summary and rationale

Despite a lack of evidence specific to GYN surgery, we recommend reduced preoperative fasting (solids until 6 hours prior to induction and clear liquids until 2 hours prior to induction) for elective GYN procedures assuming no contraindications (eg, gastroparesis, bowel obstruction), similar to the existing colorectal recommendations. This is consistent with the American Society of Anesthesiologists guidelines allowing clear liquids up to 2 hours and a light meal 6 hours before induction of anesthesia in healthy patients who are undergoing elective procedures.<sup>8</sup>

### Multimodal preanesthetic analgesic medication

#### Acetaminophen

#### Evidence

There are no prospective randomized studies specifically examining *preoperative* acetaminophen administration in patients undergoing GYN surgery.

#### Non-steroidal anti-inflammatory drugs

#### Evidence

The three RCTs examining the use of non-steroidal anti-inflammatory drugs (NSAIDs) (including cyclo-oxygenase [COX-2] inhibitors) given prior to GYN surgery suggest that preoperative COX-2 inhibitors (compared with placebo) provide significantly better pain control and opioid-sparing in both open and laparoscopic procedures.<sup>9–11</sup>

#### Gabapentinoids

#### Evidence

There are two MAs<sup>12–13</sup> and three RCTs<sup>14–16</sup> examining the *preoperative* administration of gabapentinoids in patients undergoing GYN surgery. The MAs suggest that preoperative gabapentinoids may result in a decrease in postoperative pain scores, opioid consumption, and PONV.<sup>12–13</sup> Two RCTs in laparoscopic GYN surgery also indicate that preoperative gabapentinoids may decrease postoperative pain scores and opioid consumption<sup>14–15</sup>; however, the analgesic benefits of preoperative gabapentinoids may not be as apparent in minor uterine procedures.<sup>16</sup>

#### Summary and rationale

For preventive analgesia, a multimodal approach to control perioperative pain focuses on the concurrent utilization of multiple non-opioid analgesics to ideally produce additive/synergistic analgesia while minimizing opioid use and opioid-related side effects in GYN surgical patients.<sup>4</sup> There is insufficient evidence to guide the optimal dose, selection, combination, and timing of the individual agents. However, a preoperative multimodal strategy including either COX-2 inhibitors and/or gabapentinoids has been shown to decrease postoperative pain and opioid consumption after open and laparoscopic GYN surgery. The use of gabapentinoids should be tailored to

individual patient requirements and avoided in high-risk patients (at risk for sedation and respiratory depression). Despite a lack of evidence that specifically evaluates its use in GYN surgery, acetaminophen can be reasonably administered as part of this medication bundle based on surrogate data from the colorectal population.<sup>5</sup> The acetaminophen dose should be decreased or withheld in those with evidence of severe liver disease (ie, cirrhosis) as acetaminophen toxicity/overdose may contribute to liver failure.

### PONV prophylaxis

#### Summary and rationale

Control of PONV is important to facilitate patient oral intake and recovery. GYN surgical patients are at higher risk for PONV due in part to both patient and surgical risk factors. A multimodal regimen for antiemetic prophylaxis, which may include preoperative measures such as the use of a scopolamine patch, is recommended for prevention based on a recent evidence-based guideline for the management of PONV.<sup>17</sup>

## INTRAOPERATIVE

### Standardized evidence-based intraoperative anesthetic pathway

#### Summary and rationale

Similar to a prior recommendation regarding the use of a perioperative anesthetic pathway, the intraoperative anesthetic should be both standardized to reduce interprovider variation in care and tailored to facilitate rapid awakening after completion of the surgical procedure. There are many anesthetic regimens that can be used to achieve these goals, with several key measures specifically evaluated in the context of GYN surgery.

### Intraoperative regional anesthesia

#### Evidence

Since 2007, there are 25 studies (17 truncal blocks including transversus abdominis plane [TAP] block, 7 neuraxial [epidural and spinal], and 1 mixed) specifically examining the use of various regional anesthetic techniques for GYN surgical procedures.

### Neuraxial (epidural, spinal)

#### Evidence

There are six RCTs examining neuraxial (primarily spinal) anesthesia for open GYN surgery.<sup>18–23</sup> Use of neuraxial anesthesia in GYN surgery is associated with improved analgesia and decreased systemic opioid use, and improvement in quality of recovery and sleep<sup>21</sup> in the postoperative period. One RCT performed in robotic laparoscopic GYN surgery reported a reduction in pain and analgesic use associated with a spinal technique.<sup>24</sup> As part of an established ERAS pathway, spinal anesthesia facilitated patient recovery in part by reducing postoperative opioid use and opioid-related side effects.<sup>22–23</sup>

### Truncal (TAP, rectus sheath, ilioinguinal-iliohypogastric) blocks

#### Evidence

There are 17 RCTs/MAs investigating various truncal (TAP, rectus sheath, ilioinguinal-iliohypogastric) blocks in both open and laparoscopic GYN surgery.<sup>25–41</sup> The majority of data suggest that the utilization of TAP blocks for GYN surgery is associated with decreased postoperative opioid consumption and improved quality of recovery, particularly for open approach surgery. The efficacy is less well established in laparoscopic surgery, with variable impact on postoperative opioid administration and pain scores. The one MA examining TAP blocks in hysterectomy

indicated evidence of short-term benefit (within 2–24 hours) through decreased pain and opioid consumption.<sup>25</sup> The efficacy of TAP blocks in the context of an ERAS pathway is uncertain, although at least one study did report reduced variability in dynamic postoperative pain when TAP was used in combination with acetaminophen and NSAIDs.<sup>27</sup>

One RCT examining intermittent local anesthetic boluses through a rectus sheath catheter in patients undergoing midline laparotomy for GYN cancer surgery showed that rectus sheath analgesia resulted in decreased postoperative pain and opioid consumption.<sup>39</sup> The two RCTs examining ilioinguinal-iliohypogastric nerve block provided mixed results with regard to postoperative analgesia.<sup>40,41</sup>

### Summary and rationale

The use of regional anesthetic/analgesic techniques is central to ERAS pathways as these local anesthetic-based techniques are shown to facilitate patient recovery by providing superior analgesia while decreasing opioid consumption and opioid-related side effects. The use of regional anesthesia is encouraged for open GYN surgical procedures and should be tailored to individual patient requirements. Although results are more mixed in laparoscopic procedures, selection of spinal and TAP blocks in particular may reduce reliance on opioid analgesics. Additional prospective trials are necessary to evaluate the efficacy of regional analgesia in the setting of other multimodal analgesics (ie, standing preoperative and postoperative medications) as the majority of available data did not account for this practice. The concurrent use of anticoagulants on the presence of neuraxial blocks/catheters should be used with caution, and guidelines for such use have been published.<sup>42</sup>

### Intrathecal morphine for postoperative analgesia

#### Evidence

There are six studies (five RCTs, one observational) investigating the use of intrathecal morphine in open GYN surgery.<sup>43–48</sup> There are limited prospective data in laparoscopic surgery. Overall, the data suggest that the administration of intrathecal morphine for GYN surgical procedures is associated with improved postoperative analgesia and decreased postoperative systemic opioid consumption. There are several side effects from intrathecal opioids, including increased risk of nausea, vomiting, urinary retention, pruritus, and (uncommonly) respiratory depression. However, in one MA, there were no more episodes of respiratory depression for a dose <0.3 mg of morphine compared with placebo patients who received systemic opioid analgesia.<sup>49</sup>

#### Summary and rationale

Intrathecal morphine (typically administered prior to surgical incision) is a recommended technique for providing postoperative analgesia in open GYN surgery. Further prospective data are necessary to evaluate the role of intrathecal morphine in laparoscopic surgery. Given the potential side effect profile, its use is recommended in particular when other analgesic techniques cannot be administered. Guidelines for the prevention, detection, and management of respiratory depression associated with neuraxial opioid administration have been published.<sup>50</sup>

### Intraperitoneal local anesthetics

#### Evidence

There are 10 studies (8 RCTs, 2 observational) and 1 MA examining the intraperitoneal administration (nebulized, instillation) of local anesthetics in patients undergoing predominantly

laparoscopic or minimally invasive GYN surgery.<sup>51–60</sup> The majority of the data indicate that intraperitoneal administration of local anesthetics is associated with decreased postoperative pain. An MA of intraperitoneal instillation of local anesthetics after GYN laparoscopy noted a reduction in pain scores up to 6 hours postoperatively.<sup>61</sup>

### Summary and rationale

Intraperitoneal administration (ie, nebulized, instillation) of local anesthetics is recommended after laparoscopic or minimally invasive GYN surgery due to a short, but significant reduction in postoperative pain. The efficacy is not sufficiently evaluated in open procedures. Local volume and concentration should be modified in the context of use of other concomitant local administration (ie, wound infiltration, intravenous and continuous subcutaneous use).

### Local anesthetic wound infiltration

#### Evidence

There are seven RCTs examining the use of “single-shot” or continuous infusion of subcutaneous local anesthetics in open and laparoscopic GYN surgery.<sup>62–68</sup> Only two demonstrated analgesic benefit for local anesthetic infiltration during GYN surgery.<sup>65,67</sup> Two RCTs examined continuous local infusions.<sup>62,64</sup> The first RCT demonstrated that continuous infusion of the incisional wound did not confer additional analgesia over patient-controlled analgesia morphine after abdominal hysterectomy.<sup>62</sup> The other RCT showed that continuous local anesthetic wound infiltration (vs no infiltration) resulted in equivalent analgesia but less opioid analgesic requirements.<sup>64</sup>

#### Summary and rationale

Based on the best available evidence, local anesthetics administered via single-shot infiltration or continuous wound infusions are not routinely recommended after open or laparoscopic GYN surgery.

### Subcutaneous liposomal bupivacaine

#### Evidence

There are three trials (two RCTs, one retrospective cohort) examining subcutaneous liposomal bupivacaine injected in patients undergoing both open and laparoscopy GYN surgical procedures.<sup>69–71</sup> The two RCTs showed no difference in pain scores within the first 48 hours after surgery or opioid consumption.<sup>69,70</sup> The one retrospective cohort study compared liposomal bupivacaine with a historic reference group treated with bupivacaine hydrochloride and found no difference in pain scores, proportion of patients developing postoperative ileus, or frequency of vomiting despite a lower frequency of nausea and need for intravenous rescue opioids in the liposomal bupivacaine group.<sup>71</sup>

#### Summary and rationale

Local anesthetics formulated in liposomes are theorized to result in extended release of local anesthetic, which may provide prolonged analgesia. As noted in a recent Cochrane review and based on the available randomized trial evidence, the use of liposomal bupivacaine at the surgical site does appear to reduce postoperative pain compared with placebo regardless of the surgical approach, and the limited evidence does not demonstrate superiority to bupivacaine hydrochloride.<sup>72</sup> The routine use of subcutaneous liposomal bupivacaine for GYN surgery is therefore not recommended based on the best available evidence.

## Ventilation and oxygenation

### Evidence

There are no randomized data specifically examining protective ventilation strategies and/or oxygen delivery in GYN surgical patients.

### Summary and rationale

An intraoperative protective ventilation strategy, particularly the combination of low tidal volumes (6–8 mL/kg vs 10–12 mL/kg predicted body weight) and positive end-expiratory pressure (2–5 cm H<sub>2</sub>O), is recommended. Despite the lack of data specific to GYN surgery, this strategy has been evaluated in numerous surgical subtypes, including open abdominal and cardiac surgery, and shown to lead to improved clinical outcomes (respiratory failure, pulmonary infection) and reduced length of hospital stay.<sup>73–76</sup> The role for protective ventilation is less well established in laparoscopic procedures and therefore requires additional prospective evaluation. We are unable to comment on the optimal oxygen delivery (ie, fraction of inspired oxygen) strategy due to the lack of available data.

## Postoperative nausea and vomiting

### Evidence

PONV is common after GYN surgery—particularly laparoscopic GYN surgery—with a reported incidence of nearly 70% within the first postoperative 24 hours.<sup>77</sup> There are 12 RCTs and 2 MAs examining multiple pharmacologic and non-pharmacologic (ie, acupoint stimulation) interventions to decrease PONV after GYN surgical patients.<sup>77–91</sup> A recent comprehensive evidence-based guideline for the management of PONV in all types of surgical patients has been published.<sup>17</sup> In this guideline, the number of antiemetic interventions should be based on the patient risk profile for PONV, and the recommended pharmacologic classes of antiemetics for PONV prophylaxis include the 5-hydroxytryptamine receptor antagonists (ie, ondansetron), corticosteroids (ie, dexamethasone), butyrophenones (ie, droperidol and haloperidol), antihistamine, anticholinergics (ie, transdermal scopolamine), and neurokinin-1 receptor antagonists.<sup>17</sup> In addition for intraoperative anesthesia, the use of propofol as part of total intravenous anesthesia may reduce baseline risk for PONV after GYN surgery.<sup>17 77</sup>

### Summary and rationale

Use of a multimodal antiemetic regimen tailored to known surgical and patient risk factors is recommended for the prevention and treatment of PONV in patients undergoing GYN surgery. Medications should be selected based on their respective risk profiles and local practice formularies.

## Intravenous lidocaine

### Evidence

There are two RCTs examining the use of intravenous lidocaine specifically in GYN surgical patients.<sup>92 93</sup> In the first, patients undergoing laparoscopic surgery received an intravenous lidocaine bolus of 1 mg/kg on induction of anesthesia followed by a continuous lidocaine infusion of 2 mg/kg/hour until skin closure (the control group received a placebo infusion). Patients randomized to receive lidocaine infusion had an earlier return of first flatus, although the analgesic and opioid consumption benefits for lidocaine infusion were not consistently demonstrated.<sup>92</sup> A similar RCT in patients undergoing open transabdominal hysterectomy also noted that intravenous lidocaine starting 20 min before surgery (vs saline infusion) improves immediate

postoperative pain management.<sup>93</sup> These results are consistent with previous research suggesting that intraoperative lidocaine infusion may shorten the time to return of bowel function and may provide some analgesic benefits.

### Summary and rationale

Similar to colorectal surgery, the use of intravenous lidocaine for open and laparoscopic GYN surgical procedures when no other concurrent sources of local anesthetics are used may facilitate return of gastrointestinal function and provide analgesia via a non-opioid mechanism.<sup>5</sup> Caution should be exercised whenever multiple sources of local anesthetics are used, and doses should be reduced accordingly to minimize risk of systemic toxicity.

## Ketamine

### Evidence

There are two RCTs specifically examining the use of intraoperative ketamine in patients undergoing GYN surgery.<sup>94 95</sup> In both RCTs, an intraoperative bolus of ketamine (0.15 or 0.5 mg/kg) was followed by an infusion. The analgesic benefits of ketamine were inconsistent, with one study among open surgical participants showing a lack of analgesic benefit with the addition of a low dose of ketamine,<sup>94</sup> while the other study in laparoscopic surgery demonstrated lower pain scores and morphine consumption in patients who received intraoperative infusions or postoperative administration of ketamine.<sup>95</sup>

### Summary and rationale

Although the benefits of ketamine for GYN surgery were inconsistent, the agent is likely a useful intraoperative anesthetic/analgesic especially in opioid-tolerant patients and when attempting to minimize opioid administration. There is no consensus as to the precise dosing or timing of ketamine administration, and further prospective trials are necessary to establish efficacy in the setting of other multimodal analgesics and in laparoscopic surgery.

## Magnesium

### Evidence

There are four RCTs examining the use of an intraoperative magnesium bolus followed by an infusion in both open and laparoscopic GYN surgery.<sup>96–99</sup> As in other surgical procedures, the intraoperative use of magnesium (vs placebo) resulted in improved postoperative pain control and decreased opioid consumption.<sup>96–99</sup>

### Summary and rationale

Intraoperative magnesium for GYN surgery is associated with improved postoperative analgesia and decreased opioid use regardless of the surgical approach. Although the clinical manifestations of magnesium toxicity in typical therapeutic doses are unlikely, clinicians should be aware of the potential for prolonged neuromuscular block in cases of hypermagnesemia.

## Goal-directed fluid therapy/intraoperative fluid management

### Evidence

There are no studies specifically examining goal-directed fluid therapy (GDFT) in patients undergoing GYN surgery.

### Summary

Intraoperative fluid management should aim to minimize excessive fluid administration and obtain early postoperative euvolemia.<sup>5</sup> Although GDFT may play a more significant role in high-risk

patients (ie, presence of significant comorbidities such as congestive heart failure) or high-risk procedures (ie, blood loss >10 mL/kg), we are unable to provide recommendations regarding specific fluid administration algorithms or monitoring devices.

## POSTOPERATIVE

### Standardized, evidence-based postoperative multimodal analgesic regimen

#### Summary and rationale

Control of postoperative pain is an important component of any GYN ERAS pathway as superior pain control facilitates early patient mobility and hastened rates of recovery. A multimodal analgesic approach with several non-opioid analgesic medications and techniques is used in an attempt to minimize the use of and side effects from opioids.

### Epidural analgesia

#### Evidence

There are 13 studies (8 RCTs and 5 observational) examining the use of primarily thoracic epidural in GYN surgical procedures.<sup>100–112</sup> The vast majority of the findings are in the context of open abdominal incisions. In general, use of a local anesthetic-based epidural regimen was associated with improved pain control, although two studies did not show this benefit.<sup>102 111</sup> Older studies suggest that use of epidural analgesia with a local anesthetic-based solution may facilitate return of gastrointestinal function.<sup>104 105 109 112</sup>

#### Summary and rationale

Continuation of epidural into the postoperative period is theorized to provide superior analgesia especially when a local anesthetic-based solution is used. The use of a thoracic epidural is appropriate and recommended for open GYN surgical procedures and may facilitate early recovery of gastrointestinal function. Due to the lack of available evidence, we cannot comment on the role for epidural in laparoscopic GYN surgery or within an ERAS pathway. The concurrent administration of anticoagulants and epidural analgesia should be used with caution, and guidelines for this combination have been published.<sup>42</sup>

### Lidocaine (transdermal)

#### Evidence

There is one RCT investigating the use of transdermal lidocaine in patients undergoing laparoscopic GYN surgery.<sup>113</sup> Patients who were randomized to receive transdermal lidocaine patches (vs placebo patches) had significantly lower pain scores up to 12–24 hours after surgery.<sup>113</sup>

#### Summary and rationale

Based on the evidence of a single trial, transdermal lidocaine patch may be considered for GYN patients undergoing laparoscopic procedures, although its efficacy is unclear in the setting of open procedures or in the context of other analgesics.

### Acetaminophen

#### Evidence

There are three studies (two RCTs, one observational) examining the postoperative acetaminophen administration in patients undergoing GYN surgery.<sup>114–116</sup> Like that seen in other surgical procedures, the use of scheduled acetaminophen as part of a standardized pain management protocol for GYN surgery patients is associated with improved postoperative analgesia and reduced opioid

consumption in the immediate postoperative period.<sup>114–116</sup> When possible, acetaminophen should be concurrently administered with non-steroidal anti-inflammatory agents (both on a scheduled basis) as administration of both agents will result in a superior analgesic effect compared with either agent alone.<sup>117</sup>

#### Summary and rationale

Acetaminophen should be administered on a scheduled rather than “as needed” (pro re nata [PRN]) basis. It is recommended that acetaminophen be dosed in a manner not to exceed 3–4 g maximum per day. A reasonable schedule for acetaminophen would be 1 g every 6–8 hours while the patient is hospitalized. The optimal dosage and duration of acetaminophen after hospital discharge is uncertain. Acetaminophen dose should be decreased or not given in those with significant liver disease (ie, cirrhosis) as acetaminophen toxicity/overdose may contribute to liver failure.

### Non-steroidal anti-inflammatory agents (NSAIDs)

#### Evidence

There are five RCTs specifically examining the postoperative use of NSAIDs for GYN surgical patients.<sup>118–122</sup> Like that seen in other surgical procedures, the use of scheduled NSAIDs for the treatment of pain after GYN surgical procedures resulted in a significant reduction in pain scores and opioid consumption.<sup>118–122</sup>

#### Summary and rationale

The use of NSAIDs should be administered on a scheduled rather than PRN basis in GYN surgical patients without contraindications. The dose of NSAIDs should be decreased/withheld in patients with certain comorbidities (ie, kidney injury) and in elderly patients.

### Gabapentinoids

#### Evidence

There are no studies specifically examining the use of postoperative gabapentinoids in GYN surgery.

#### Summary

Limited data preclude any definitive conclusions on the use of gabapentinoids for postoperative in GYN surgical patients. If administered, doses should be reduced or avoided in high-risk patients (ie, kidney injury, excessive postoperative sedation, and/or respiratory depression).

### Tramadol

#### Evidence

There were no studies specifically examining the use of oral tramadol in GYN surgical patients.

#### Summary and rationale

Based on the available evidence, we cannot formally recommend the use of tramadol in GYN surgery. Additional investigation is necessary to establish its role in this patient population. Although the analgesic efficacy of tramadol for GYN surgical patients is uncertain, tramadol has less mu-receptor (opioid) activity than morphine and may be a useful analgesic adjunct as it demonstrates a weak-moderate analgesic effect which is significantly improved when combined with acetaminophen. Tramadol should not be used or used cautiously in patients receiving selective serotonin receptor inhibitors/serotonin and norepinephrine reuptake inhibitors/monoamine oxidase inhibitors (ie, possible

serotonin syndrome), exhibiting renal insufficiency, or having a history of seizures.<sup>5</sup>

## Dextromethorphan

### Evidence

There are no studies specifically examining the use of dextromethorphan in GYN surgical patients.

### Summary and rationale

Dextromethorphan cannot be formally recommended as an analgesic after GYN surgery. If administered, it should be noted that the optimal dosing of dextromethorphan is uncertain, and its use may be associated with side effects that consist primarily of nausea, vomiting, dizziness, light-headedness, and sedation, although it is unclear if these side effects occur more frequently versus that seen with opioids.<sup>123</sup>

## Opioids

### Evidence

Opioids have been studied in GYN surgery and across a broad range of other surgical procedures and approaches, the full extent of which is beyond the scope of this review. Opioid-based analgesia, in both oral and intravenous forms, is shown to both prevent and treat perioperative pain. However, its administration is associated with a number of well-documented side effects, including PONV, pruritus, gastrointestinal ileus, sedation, and respiratory depression, which likely delay postoperative recovery when compared with other available agents and techniques.

### Summary and rationale

Although almost every ERAS pathway will attempt to limit the amount of opioids administered as opioid-related side effects may delay patient recovery, opioids still play a potentially vital role. Rather than being the central component in pain management, opioids are recommended principally as “rescue” medications when all other non-opioid analgesic agents have failed to adequately control the patient’s pain. One caveat for opioid use in ERAS pathways relates to the opioid-tolerant patient. Although there are no prospective trials involving opioid-tolerant patients and ERAS pathways, these patients are likely to require continuation of their baseline opioid requirements to adequately address pain symptoms and prevent withdrawal. As a result, opioids should not be withheld in these patients.

## DISCUSSION

Although ERAS for GYN surgery is less well established than colorectal programs, similarities between the surgical procedures and available outcomes data suggest that many of the overarching principles may be transferrable. This review provides a summary of the available evidence for selected anesthesia process measures, the majority of which is derived from literature specific to GYN surgery. As a result, we have identified and provided recommendation for the various anesthesia components that should underline a comprehensive ERAS for GYN surgery program (tables 1 and 2). These components will be incorporated into the AHRQ Safety Program for ISCR GYN protocol, and hospitals participating in the program will be supported in developing and implementing these protocols in their service lines.

Based on these results, a comprehensive approach in the preoperative phase of care would involve adherence to the updated American Society of Anesthesiology (ASA) fasting guidelines, which allow for the consumption of clear liquids up to 2 hours

and a light meal up to 6 hours prior to surgery. Although not expressly evaluated in the setting of GYN surgery, it is reasonable to consider the use of carbohydrate loading to reduce symptoms of thirst and hunger, as well as prevent protein catabolism and attenuate insulin resistance associated with preoperative fasting. The optimal solution or carbohydrate regimen remains a topic of debate. In addition, it is recommended that patients receive multimodal preanesthetic medications in the form of acetaminophen, a COX-2 inhibitor, and a gabapentinoid in order to minimize perioperative opioid utilization and opioid-related side effects. Both COX-2 inhibitors and gabapentinoids have been evaluated in the context of GYN surgery and shown to decrease postoperative pain and opioid administration.

During the intraoperative phase, it is recommended that providers adopt a standardized evidence-based anesthetic pathway generally geared toward short-acting anesthetics, utilization of multimodal analgesia, lung protective ventilation, and comprehensive prevention of PONV to facilitate early awakening and rapid recovery from anesthesia.

Regional techniques involving the use of local anesthetic, including neuraxial (spinal/epidural) and/or “single shot” truncal nerve blocks, are most well studied in this patient population. Conversely, intraperitoneal and wound infiltration of local anesthesia as well as use of subcutaneous liposomal bupivacaine are not routinely recommended, particularly for open procedures, given inconsistent results, short duration of effect, or lack of general efficacy in the available literature. Given the association between GYN surgery and high incidence of PONV, anesthetic protocols should closely adhere to the established guidelines for quantification and prevention of nausea and vomiting. A multimodal PONV regimen may include a combination of serotonin antagonists, corticosteroids, butyrophenones, antihistamines, and anticholinergics, among others. As with the application of any medication bundle, careful consideration should be provided to relevant medication side effects, patient-specific contraindications, and potential drug–drug interactions.

The principal consideration in the postoperative phase is in regard to the use of a multimodal analgesic regimen. The routine use of a local anesthetic-based thoracic epidural for open procedures is encouraged based on the results of numerous high-quality studies. The benefits of epidural analgesia in laparoscopic cases are unclear. Further, neuraxial analgesia should be used with caution when coadministered with anticoagulation (ie, deep vein thrombosis chemoprophylaxis). Routine use of scheduled postoperative acetaminophen and NSAIDs is recommended. The specific dose and schedule should be sensitive to the route of administration (ie, nil per os status) and potential patient-specific contraindications (ie, liver or kidney impairment). Given there are no relevant studies, the literature would benefit from additional prospective data involving the use of gabapentinoids and/or tramadol in GYN surgery.

Importantly, despite the desire to limit (and even eliminate) the perioperative use of opioids, they remain an alternative when other non-opioid options are unable to provide adequate postoperative analgesia. The aforementioned emphasis on the use of multimodal pain medications should not be employed at the expense of adequately addressing pain. Therefore, after successfully using other available non-opioid options, the use of opioids is recommended in the lowest effective dose for the shortest duration possible to achieve optimal pain control and reduce opioid-related side effects. Further, we are unable to comment on the appropriate strategy for managing the perioperative administration of opioids in the opioid-exposed or opioid-tolerant patient.

There are several important limitations to this review. Recommendations are derived from a hierarchical approach to the available evidence that employed a literature search strategy that was not systematic in nature. While we are confident these recommendations reflect the evidence available, it is possible that certain individual trials were not captured. In addition, it should be noted that MAs in perioperative medicine should be interpreted with caution, particularly those that involve the pooled analysis of small trials, due to the fact that they might overestimate the frequency of statistically significant treatment effects of certain interventions.<sup>124</sup> The importance of establishing appropriate power to examine a chosen endpoint is therefore paramount. In the case of this review, the results of MAs tended to coincide with those of RCTs for a given intervention and endpoint. While we include the results of several observational trials, this is done so to reinforce intervention feasibility and hypothesis generation, and recommendations were not based expressly on their findings. Finally, we are unable to comment on the combination of interventions to maximize both efficacy and patient safety. Further investigation is necessary to establish an optimal approach for both open and laparoscopic GYN procedures.

Similar to prior evidence reviews, it should be noted that our recommendations may necessitate adaptation based on local technical expertise, medication formularies, hospital policy, and other relevant systems considerations. When designing the pathway, priority should be provided to establishing consensus and identifying components that are realistic, pragmatic, and value-added. This remains a fundamental aspect of reducing interprovider variation in care, reducing unintended patient harm, and optimizing perioperative outcomes. Further, it is recognized that all patient care decisions should be made in the context of an overarching multidisciplinary discussion and tailored to specific patient care requirements. The AHRQ Safety Program ISCR GYN protocol outlines anesthesia components that span all of the phases of perioperative care. In order to implement this program, transdisciplinary teams, including leadership from anesthesiology, surgery, nursing, administration, and the patients themselves, must engage in the effort to improve the value of clinical care.

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