



Enhanced recovery after surgery (ERAS®) society guidelines for gynecologic oncology: Addressing implementation challenges - 2023 update

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HIGHLIGHTS

- Despite best efforts, many of the ERAS recommendations remain poorly adhered to and barriers to ERAS implementation persist.
- This guideline update summarizes evidence investigating ERAS implementation challenges highlighted by stakeholder groups.
- Overcoming implementation barriers will increase ERAS uptake and improve clinical outcomes for patients.

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ABSTRACT

Background. Despite evidence supporting its use, many Enhanced Recovery After Surgery (ERAS) recommendations remain poorly adhered to and barriers to ERAS implementation persist. In this second updated ERAS® Society guideline, a consensus for optimal perioperative care in gynecologic oncology surgery is presented, with a specific emphasis on implementation challenges.

Methods. Based on the gaps identified by clinician stakeholder groups, nine implementation challenge topics were prioritized for review. A database search of publications using Embase and PubMed was performed (2018–2023). Studies on each topic were selected with emphasis on meta-analyses, randomized controlled trials, and large prospective cohort studies. These studies were then reviewed and graded by an international panel according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system.

Results. All recommendations on ERAS implementation challenge topics are based on best available evidence. The level of evidence for each item is presented accordingly.

Conclusions. The updated evidence base and recommendations for stakeholder derived ERAS implementation challenges in gynecologic oncology are presented by the ERAS® Society in this consensus review.

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1. Introduction

Following publication of the original Enhanced Recovery After Surgery (ERAS®) Society Guidelines for gynecologic oncology in 2016 [1,2] and the first update in 2019 [3], a recent meta-analysis concluded that ERAS in gynecologic oncology was associated with a decrease in hospital length of stay (LOS) of 1.6 days, 32% reduction in complications, 20% reduction in readmission, no change in 30-day postoperative mortality, and mean cost savings of \$2129 USD per patient [4]. A dose-response relationship was also found to exist whereby higher compliance with ERAS gynecologic oncology guidelines was associated with greater impact on LOS and complication reductions [5]. Based on this evidence, ERAS should now be firmly established as standard of care within our discipline. However, there are several recent publications which have surveyed ERAS uptake in gynecologic oncology globally [6,7]. The results indicate that despite best efforts, many ERAS recommendations remain poorly adhered to and barriers to ERAS implementation persist. Furthermore, survey findings from a recent perioperative course held at the Annual Meeting of the Society of Gynecologic Oncology (SGO) in Phoenix, AZ (2022) point to specific gaps in understanding of many of the core tenets of ERAS. The rationale for this second update to the ERAS® Society Guidelines for gynecologic oncology is to summarize and update the evidence investigating specific implementation challenges identified by clinician stakeholders, with the goal of increasing ERAS uptake and improving clinical outcomes for patients.

2. Methods

2.1. Implementation challenges

Based on the gaps identified in the recent international ERAS surveys [6,7] and the SGO perioperative course, the following implementation challenges were prioritized for review:

- Is perioperative oral intake safe and how can I convince my anesthesiologist?
- Preoperative medications - which are the most important?
- How do I manage patients with penicillin allergies?
- What is the best approach to intraoperative analgesia?
- How should I manage urinary drainage?
- What is appropriate venous thromboembolism prophylaxis?

- What constitutes appropriate postoperative opioid prescribing?
- How do I create a successful same day discharge program?
- How can I overcome barriers to ERAS implementation?

Components of the ERAS® Society Guidelines for gynecologic oncology not addressed in this update are described in detail in the previous versions [1–3].

2.2. Literature search

Standard ERAS® Society Guideline methodology was adhered to [8] and the guideline proposal was approved by the ERAS® Society Guidelines Committee. International authors with expertise in gynecologic oncology enhanced recovery care were invited to participate in the guideline update. The literature search (2018–2023) used Embase and PubMed to search medical subject headings including “gynecology”, “gynecologic oncology”, and topics specific to each of the 9 ERAS implementation challenges chosen for review. Studies on each topic were selected with emphasis on meta-analyses, randomized controlled trials, and large prospective cohort studies. Reference lists of all articles were crosschecked for other relevant studies. The quality of evidence for each item was reviewed and verified by the senior editorial team (GN, AA, SB, PTR, and SCD).

2.3. Quality assessment

As in previous ERAS® Society guidelines, the quality of evidence and recommendations were evaluated according to the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) system [9] whereby recommendations are given as follows:

Strong recommendations: The panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects.

Weak recommendations: The desirable effects of adherence to a recommendation probably outweigh the undesirable effects, but the panel is less confident.

Recommendations are based on both quality of evidence (high, moderate, low), the balance between desirable and undesirable effects on holistic clinical outcomes, and on values and preferences of

practitioners. Thus, strong recommendations may be reached from low-quality data and vice versa.

3. Results

The evidence base and recommendation for each individual ERAS implementation challenge is detailed below. Table 1 summarizes each ERAS implementation challenge along with corresponding recommendation, evidence level and recommendation strength.

3.1. Is perioperative oral intake safe and how can I convince my anesthesiologist?

The American Society of Anesthesiologists (ASA) Committee guidelines recommend solid meals until 8 h before elective surgery and unlimited clear fluids up to 2 h before surgery [10]. Consumption of fluids prior to surgery is associated with reduced preoperative anxiety, thirst, and hunger [11]. Furthermore, dehydration prior to surgery is associated with increased risk of acute kidney injury and myocardial infarction and more than doubles the risk of all-cause mortality [12].

Data regarding the benefits or harms of fasting with respect to gynecologic or gynecologic oncology procedures are limited. Most evidence is extrapolated from studies of elective abdominal surgery or colorectal procedures. The ERAS® Society recommends oral carbohydrate loading

2–3 h prior to surgery with an isotonic complex carbohydrate solution. A 2020 meta-analysis of 1921 elective surgery patients enrolled among 20 randomized controlled trials concluded that carbohydrate loading decreased postoperative length of stay by 0.4 days compared to strict fasting, but no difference compared to water or placebo clear liquids [13]. A 2022 meta-analysis of phase II/III randomized controlled trials specifically in elective abdominal surgery examined 2306 randomized patients [14]. Approximately half of patients underwent cholecystectomy, while the remainder underwent major abdominal procedures. Strict fasting was inferior to any clear liquid prior to surgery in terms of overall morbidity and post-operative nausea and vomiting (PONV), but evidence for the superiority of carbohydrate loading over water alone was limited. When length of stay was considered an endpoint, carbohydrate loading was the superior approach, but due to sample size this finding was less robust.

Carbohydrate loading may reduce perioperative insulin resistance [15]. A double-blinded multicenter trial randomized 240 patients undergoing elective gastrectomy, colorectal resection, or pancreatoduodenectomy to either carbohydrate loading or water [16]. Carbohydrate loading was associated with lower insulin resistance, fasting insulin, anxiety, hunger, and thirst, but length of stay was similar. A trial randomizing 200 gynecological laparoscopic patients to either carbohydrate loading or fasting [17] demonstrated reduced hunger and thirst, less insulin resistance, and more rapid correction of metabolic

Table 1

Enhanced Recovery after Surgery (ERAS®) Society guidelines for gynecologic oncology: addressing implementation challenges.

Implementation challenge	Recommendation	Evidence level	Recommendation grade
Is perioperative oral intake safe and how can I convince my anesthesiologist?	In alignment with anesthesiology society guidelines, patients should be encouraged to consume clear liquids until 2 h prior to surgery. Preoperative carbohydrate loading prior to surgery improves patient satisfaction and comfort.	Clear fluids until 2 h: High Carbohydrate loading: High	Strong Strong
Preoperative medications - which are the most important?	Medications including NSAIDs, acetaminophen and gabapentinoids can be administered preoperatively, especially in the context of a multimodal opioid sparing protocol. Gabapentinoid use should be extremely limited in elderly patients.	Acetaminophen: Low NSAIDs: High Limit Gabapentin: High	Strong Strong Strong
How do I manage patients with penicillin allergies?	Patients with a reported penicillin allergy should receive the standard surgical antibiotic prophylaxis including cefazolin or ertapenem when indicated.	High	Strong
What is the best approach to intraoperative analgesia?	Techniques such as wound infiltration with local anesthetic and TAP block are preferred over TEA given the potential for complications and side effects.	Moderate	Strong
How should I manage urinary drainage?	Indwelling bladder catheters should be removed as early as possible in the postoperative period (on the day of surgery for MIS, and no later than POD1 for laparotomy) unless contraindications exist.	Moderate	Strong
What is appropriate venous thromboembolism (VTE) prophylaxis?	Patients at increased risk of VTE should receive dual prophylaxis with mechanical compression and chemoprophylaxis, initiated preoperatively. Extended chemoprophylaxis should be prescribed to patients who meet high-risk criteria or undergo laparotomy for gynecologic malignancy. Extended prophylaxis with LMWH or DOAC are equally effective and safe. Extended prophylaxis is of limited value in MIS patients.	Stockings, pneumatic compression devices, LMWH: High Preoperative administration: Moderate Postoperative extended prophylaxis with LMWH: Moderate Postoperative extended prophylaxis with DOACs: Moderate Limit postoperative extended prophylaxis in MIS: Moderate	Perioperative DVT prophylaxis: Strong Extended (28-day) prophylaxis in high-risk patients: Strong DOAC prophylaxis: Strong Limit MIS extended prophylaxis: Strong
What constitutes appropriate postoperative opioid prescribing?	Multimodal opioid-reduction strategies for postoperative pain control are critical to employ in the inpatient and outpatient settings. Decreased post-discharge opioid prescribing is feasible with a team approach and does not affect pain control or patient satisfaction. PCA is rarely required and should be used as a last resort for patients requiring repeated treatment with IV opioids.	Use of multimodal analgesia: Moderate Use of a post-discharge tiered opioid prescribing guideline: Moderate Limit use of PCA: Moderate	Strong Strong Strong
How do I create a successful same day discharge (SDD) program?	Multidisciplinary SDD programs should be considered for minimally invasive gynecologic oncology procedures. Implementation requires multidisciplinary collaboration, education, patient and case selection, and ERAS perioperative principles.	Moderate	Strong
How can I overcome barriers to ERAS implementation?	Barriers to successful implementation can be overcome with adherence to change management principles and education. Communication of the economic benefits of ERAS to healthcare administrators may be a strong incentive to garner support for implementation.	Moderate	Strong

Abbreviations: NSAIDs (non-steroidal anti-inflammatory drugs); TAP (transversus abdominis plane); TEA (thoracic epidural analgesia); MIS (minimally invasive surgery); POD (postoperative day); LMWH (low molecular weight heparin); DOAC (direct oral anticoagulant); PCA (patient-controlled analgesia); IV (intravenous).

abnormalities in the carbohydrate loading arm, while length of stay and PONV were similar.

Regarding clear liquids prior to surgery, consumption of 200–250 ml does not appear to increase risk of aspiration [18]. In a 2022 meta-analysis, aspiration was documented in one of 1647 non-fasting patients [14]. Ultrasonography has been used to monitor gastric residual volumes among fasting versus non-fasting patients. In one study of 60 patients, consumption of 200 ml of water prior to surgery was associated with lower residual gastric fluid volume and higher mean pH at the time of surgery compared to fasting, suggesting reduced risk of aspiration [18]. A randomized controlled trial found similar gastric volumes among patients consuming 200 ml of water or a 200 ml carbohydrate load at 2-h post-consumption but observed less hunger in the carbohydrate group [19].

Recommendation: In alignment with anesthesiology society guidelines, patients should be encouraged to consume clear liquids until 2 h prior to surgery. Preoperative carbohydrate loading prior to surgery improves patient satisfaction and comfort.

3.2. Preoperative medications - which are the most important?

Medications can be given before major gynecologic oncology surgery with the goal to alleviate specific symptoms including anxiety and pain. Short acting oral anxiolytics may be used to address severe preoperative anxiety in selected cases; however, routine administration of long-acting sedatives within 12 h of surgery should be avoided due to detrimental effects on postoperative recovery, such as delayed emergence from anesthesia [1]. Randomized controlled trials have demonstrated benefit with the administration of non-steroidal anti-inflammatory drugs (NSAIDs) prior to gynecologic surgery, specifically showing improved pain control and reduction in opioid requirements. Similarly, meta-analyses have shown that the preoperative administration of gabapentinoids is associated with a decrease in post operative pain, nausea/vomiting, and opioids [20]. Gabapentinoids, however, may cause sedation, and caution should be undertaken when these drugs are used in the elderly given recent evidence of increased risk of delirium, new antipsychotic use, and pneumonia among older patients after major surgery [21]. Although there is limited high level evidence for the use of oral acetaminophen preoperatively in major gynecologic oncology surgery it is reasonable to include it as part of an ERAS pre-medication bundle if one extrapolates from evidence in the colorectal surgery literature [20].

Recommendation: Medications including NSAIDs, acetaminophen and gabapentinoids can be administered preoperatively, especially in the context of a multimodal opioid sparing protocol. Gabapentinoid use should be extremely limited in elderly patients.

3.3. How do I manage patients with penicillin allergies?

The rate of patient reported penicillin allergy in the United States is 13% [22]. However, true IgE-mediated allergy with anaphylaxis or other severe reactions are rare. Over 95% of patients who report an allergy tolerate penicillins and other β -lactam antibiotics [23,24]. β -lactam antibiotics are drugs which inhibit bacterial cell wall synthesis and include penicillins, cephalosporins, carbapenems, monobactams and β -lactamase inhibitors [25]. Cefazolin, a first-generation cephalosporin, and ertapenem, a carbapenem, are commonly used for antibiotic prophylaxis prior to gynecologic or gynecologic oncology surgery [24]. Even if an allergy to penicillin is suspected based on the history, the rate of dual penicillin and cephalosporin allergy is only 0.7% [26]. The explanation for this lack of cross-reactivity is that the penicillin R1 side chain drives the allergic response, not the β -lactam ring structure shared with other β -lactam antibiotics [26–31]. Cefazolin and ertapenem do not share the R1 chain with penicillin and have a low risk of cross-reactivity [27,29–32]. This also applies to most second

generation or later cephalosporins, the other carbapenems and monobactams (except for aztreonam and ceftazidime) [27,29–32].

Anstey et al. reviewed data from 8770 patients with a reported penicillin allergy who received antibiotic prophylaxis prior to surgery [28]; 6925 patients received antibiotic prophylaxis with either penicillin ($n = 176$), cefazolin ($n = 2570$), another first or second-generation cephalosporin ($n = 3552$), a third, fourth or fifth generation cephalosporin ($n = 334$) or a carbapenem ($n = 293$). The overall rate of anaphylaxis was 0.01% with one patient reacting to cefazolin [28]. Recognizing the low risk of cross-reactivity and the higher rates of surgical site infection when alternative antibiotics are used for surgical prophylaxis due to a reported allergy to penicillin [33], the Centers for Disease Control and Prevention and the Joint Task Force on Practice Parameters from the American Academy of Allergy, Asthma and Immunology have issued statements recommending use of most cephalosporins, carbapenems, monobactams and β -lactamase inhibitors in patients with a reported history of penicillin allergy [34,35]. Penicillin allergic patients should only avoid cefazolin when there is a history of penicillin induced severe cutaneous adverse reactions (such as Stevens Johnson Syndrome) or verified cefazolin allergy [36].

Recommendation: Patients with a reported penicillin allergy should receive the standard surgical antibiotic prophylaxis including cefazolin or ertapenem when indicated.

3.4. What is the best approach to intraoperative analgesia?

Regional anesthetic techniques have evolved over the last decade after the introduction of real-time ultrasound guided imaging [37], leading to improvements in efficacy, safety, and simplicity [38]. This evidence has propelled the access and use of regional anesthesia in the anesthesiology field as rising evidence demonstrates effective suppression of the sympathetic/adrenergic and inflammatory response to surgery and its potential benefits on various patient outcomes, including morbidity, cancer recurrence and persistent postoperative pain [39].

In addition to neuraxial anesthesia, there has been a rise in the use of fascial plane blocks for the management of acute pain in abdominal and pelvic surgery, such as the transversus abdominis plane (TAP) block [40] and Erector Spinae (ESP) block [41] as an alternative for providing adequate analgesia. Choice of analgesia must include considerations of surgical approach (laparotomy vs. MIS) and potential side effects which may compromise other ERAS principles.

Evidence supporting the use of TAP blocks is conflicting [42–46]. Some investigations have shown that TAP blocks reduce postoperative opioid consumption in the first 2 h [47], others up to 24 h after surgery [48–50]. However, comparing TAP block to placebo following laparoscopic or robotic hysterectomy, one investigation failed to show improvements in postoperative analgesia, while a meta-analysis showed only modest reduction in postoperative pain with TAP blocks [51]. Furthermore, in patients undergoing open resection for gynecologic malignancy, there was no significant difference in median 24-h opioid consumption or LOS for patients randomized to TAP blocks, casting doubt on their efficacy in the setting of large laparotomy incisions [42,52].

Other analgesic options include thoracic epidural analgesia (TEA) and intrathecal analgesia which provide excellent coverage for the abdomen and pelvis with improvements in postoperative pain compared to PCA [53]. However, improvements in opioid requirements and pain scores must be weighed against potential untoward effects such as pruritus, PONV, prolonged block, urinary retention, immobility and sympathectomy, which may lead to significant hypotension and hemodynamic instability requiring the use of pressors or fluid boluses [54–56]. The need for fluid boluses is particularly common for patients undergoing evacuation of large volume ascites at the time of surgery, such as patients with ovarian cancer.

A meta-analysis on postoperative pain management in the ERAS setting revealed that epidural analgesia was associated with improved pain

scores [57]. However, complication rates were higher in the epidural group. While epidurals appeared to enhance gut function, there was no improvement in length of stay. Direct comparisons between epidural analgesia and TAP blocks favor the epidural group regarding pain scores [56]. However, the epidural group also had higher rates of hypotension, PONV, urinary retention, inability to ambulate, and increased length of stay.

A RCT comparing intrathecal morphine to thoracic epidural analgesia for midline laparotomy in gynecologic cancer showed no significant difference in pain scores with a shorter LOS for the intrathecal morphine group [58]. However, a major disadvantage to intrathecal morphine is its potential association with late onset respiratory depression, requiring careful postoperative monitoring for the first 24 h.

There is evidence that TAP blocks may be operator dependent, with one RCT showing comparable results between laparoscopic delivery of liposomal bupivacaine and ultrasound-guided TAP blocks, while others have shown poor results when performed without ultrasound guidance [59,60]. This potential operator dependence may explain why TAP blocks have shown little to no benefit compared to placebo or wound infiltration in some studies [61], while others have shown benefit even compared to epidural analgesia. For example, the EXPLANE trial of 498 patients compared TAP block with liposomal bupivacaine versus continuous epidural analgesia for major abdominal surgery. Pain scores in the first 72 h after surgery were similar in both groups, TAP block patients required more opioids, and there was more hypotension in the epidural group [62].

Direct comparisons of incisional injection of local anesthetic, TAP blocks, and TEA for locoregional pain control have failed to convincingly show a clinical benefit of TAP or epidural over incisional injection [52,62–65]. A randomized trial did not show a decrease in opioid intake or improved pain control when adding liposomal bupivacaine to standard bupivacaine as a wound injection in open gynecologic surgery. However, liposomal bupivacaine may potentially benefit patients undergoing complex cytoreduction who have been found to have more postoperative pain [66,67].

Recommendation: Techniques such as wound infiltration with local anesthetic and TAP block are preferred over TEA given the potential for complications and side effects.

3.5. How should I manage urinary drainage?

Urinary drainage via indwelling bladder catheters (IBC) is common perioperative practice in gynecologic oncology; the aim of IBCs is to facilitate urinary drainage in immobile patients, to monitor urine output, and to direct volume management. Historically, IBC were retained for several days to prevent urinary retention and promote bladder function. However, recent evidence suggests that the opposite effect is being achieved, as the number of days of IBC use directly correlates with higher risk of urinary retention, infections, and pressure injuries while dissuading mobility. In contrast, early (i.e., within 24 h, immediate) removal of intraoperatively placed IBC is associated with less IBC-related morbidity without increasing the risk of voiding dysfunction or fistulas [68–73]. An exception is critically ill patients who may still require an IBC in the acute phase to ensure accurate volume assessment.

3.5.1. Special considerations

Minimally invasive surgery: Although immediate catheter removal is common practice, there are limited studies to guide the exact timing of IBC removal in laparoscopic hysterectomy. Studies have demonstrated that prolonged catheterization increases risk of urinary tract infection (UTI), while earlier IBC removal increases risk of urinary retention compared to IBC removal on postoperative day 1 [74,75]. Liang and colleagues demonstrated a urinary retention rate of 34% when no IBC was used at all at the time of hysterectomy [75]; however, immediate IBC removal in the operating room yields clinically low rates of retention (4.6–13.5%), and these are often corrected with no intervention or

single re-catheterization [74,76]. The benefits of immediate IBC removal for ambulation, UTI prevention, patient comfort, and same day discharge may outweigh risks of transient and correctable urinary retention [74,76]. Larger studies are needed to clarify this practice, and to ascertain if IBC removal in the early postoperative period (6 h postoperatively) may optimize outcomes. There is evidence to support retrograde bladder filling following minimally invasive gynecologic surgery; this practice may reduce time to first void and time to discharge [77].

Radical hysterectomy: Emerging evidence suggests that early catheter removal for radical hysterectomy does not increase rates of voiding dysfunction or postoperative genitourinary complications. These studies have assessed postoperative removal between 1 and 5 days [68], 48–72 h [72], 24–48 h [69,70,73], and immediate removal [71]. Early catheter removal should be considered in this population, although further comparative studies are needed. For patients experiencing urinary retention, use of transient self-catheterization can replace the reinsertion of IBC [68–70,73]. Time to voiding recovery is not influenced by the type of surgical approach (open vs. MIS) [72].

Cytoreductive procedures: Randomized trials of patients undergoing cytoreduction for gynecologic malignancy have demonstrated safety of IBC removal within 24 h [78,79]. In cases of partial bladder resection or ureteric reimplantation, IBC retention for 5–14 days may be indicated to facilitate bladder healing [80].

Recommendation: Indwelling bladder catheters should be removed as early as possible in the postoperative period (on the day of surgery for MIS, and no later than POD1 for laparotomy) unless contraindications exist.

3.6. What is appropriate venous thromboembolism (VTE) prophylaxis?

Venous thromboembolism (VTE) is a life-threatening complication of gynecologic surgery. Patients undergoing surgery for gynecologic cancer are at high risk of VTE due to predisposing factors such as upregulated procoagulant pathways inherent to malignancy or neoadjuvant chemotherapy [81], and venous stasis because of mechanical venous compression from large pelvic masses. While the rates of VTE within 30 days after surgery appear to be <1% among gynecologic cancer patients who undergo MIS [82–84], the rate of VTE in the perioperative setting of ovarian cancer is as high as 10% at initial diagnosis [85,86].

The predominant risk stratification method, the Caprini score [87], was developed in the open general surgery patient populations and does not consider the advancements in MIS and ERAS.

3.6.1. Perioperative prophylaxis

Many patients undergoing gynecologic surgery will be at least moderate to high risk as defined by the Caprini score (moderate 3–4, high ≥ 5), and pharmacologic prophylaxis and/or mechanical prophylaxis are recommended [88].

3.6.2. Extended duration prophylaxis (28 days)

All patients undergoing a laparotomy for gynecologic cancer should receive 28 days of extended VTE prophylaxis. This is supported by American College of Chest Physician guidelines for VTE prophylaxis in non-orthopedic surgical patients [88], the SGO Clinical Practice Statement [89], the ACOG Practice Bulletin [90] and ERAS guidelines [3].

Level one data supporting extended duration pharmacologic prophylaxis was generated in the ENOXACAN II double-blind, placebo controlled RCT [91]. Analyzing the impact of a prospective practice change among patients undergoing laparotomy for gynecologic cancers, Schmeler, et al. demonstrated a 78% reduction (from 2.7% to 0.6%) in clinically diagnosed VTE within 30 days of surgery when prophylactic dose LMWH was started within 24 h of surgery and continued for 28 days postop [92]. However, 90-day VTE rates were unchanged.

Two RCTs comparing prophylactic dose LMWH to prophylactic dose direct-acting oral anticoagulants (DOACs) in the setting of gynecologic

cancer surgery demonstrated equivalency of these agents for VTE prevention and no difference in major bleeding events [93,94]. In the first trial, patients were randomized to 28 days of prophylactic dose apixaban (2.5 mg po BID) vs. enoxaparin (40 mg SQ). VTE rates were 1.0% and 1.5%, respectively, and the major bleeding events rate was 0.5% in each arm. Patients randomized to apixaban reported greater convenience and less pain [93]. The second trial compared prophylactic dose DOAC (rivaroxaban 10 mg po daily) vs. LMWH (enoxaparin 40 mg SQ daily) for 30 days following major gynecologic cancer surgery. While the trial was stopped early due to lower-than-expected VTE occurrences, the VTE rate was no different between groups (3.5% v 4.4%, respectively) [94]. Taken together, extended prophylaxis with either LMWH or DOAC appears effective and safe.

3.6.3. Extended prophylaxis in patients undergoing minimally invasive gynecologic surgery?

Prospective studies support extended VTE prophylaxis in cancer surgery performed via laparotomy, but data in MIS gynecologic cancer surgery is limited to retrospective studies. Swift et al. recently published data on nearly 64,000 patients who underwent gynecologic cancer surgery and were captured within the 2013–2019 ACS-NSQIP dataset. While there was an almost 4-fold higher (2.3% v. 0.6%) 30-day VTE risk with laparotomy vs. MIS, the absolute risk of VTE within 30 days of MIS was <1% [84]. Similarly, Nick et al. demonstrated a 0.7% 6-week rate of VTE in the setting of MIS gynecologic surgery [83] and Kumar et al. demonstrated a 30-day VTE rate of 0.5% [82]. As such, there appears to be a < 1% risk of VTE among gynecologic cancer patients who undergo MIS. Extended duration pharmacologic prophylaxis would appear to have limited value in minimally invasive gynecologic surgery.

Recommendation: Patients at increased risk of VTE should receive dual prophylaxis with mechanical compression and chemoprophylaxis, initiated preoperatively. Extended chemoprophylaxis should be prescribed to patients who meet high-risk criteria or undergo laparotomy for gynecologic malignancy. Extended prophylaxis with LMWH or DOAC are equally effective and safe. Extended prophylaxis is of limited value in MIS patients.

3.7. What constitutes appropriate postoperative opioid prescribing?

Appropriate opioid prescribing after gynecologic surgery forms a cornerstone of ERAS and must be thoughtfully managed in the inpatient and outpatient settings. The value of this cannot be understated given the need to simultaneously control postoperative pain and reduce opioid administration. Minimizing opioid use prevents side effects of nausea, sedation, constipation, and fatigue while also mitigating the 6–10% risk of new, persistent opioid use in previously opioid-naïve postoperative patients [95,96]. A multimodal approach utilizing local analgesia and non-opioid alternatives as first-line therapy allows for appropriately low opioid dosing and achievement of other critical ERAS goals without affecting patient satisfaction or other patient-reported outcomes [97,98]. Synergism of non-opioid analgesics with different mechanisms of action further enhances pain control and can be at least as effective as opioids for postoperative pain [99,100]. In the inpatient postoperative setting we recommend routine, scheduled administration of oral acetaminophen and NSAIDs unless contraindicated, as well as primarily oral administration of opioids as needed. Intravenous opioids/patient-controlled analgesia (PCA) should be reserved for breakthrough pain and discontinued as soon as patients can tolerate oral medications.

To fully realize the benefits of opioid reduction using an ERAS protocol, attention must also be focused on the post-discharge period, whether same-day or after an inpatient stay [101–103]. Physicians understandably hesitate to reduce outpatient opioid prescriptions due to concerns for patient dissatisfaction or potential need for additional prescriptions. However, several investigations have shown reductions in

opioid prescriptions with no change in patients' perception of pain or opioid refills [101,103–105]. We recommend a tiered guideline approach for prescribing post-discharge opioids, guided by surgical procedure for outpatients, and opioids used in the 24 h before discharge for inpatients. With this approach, approximately half of patients will not require an opioid prescription at discharge and as few as 3 to 15 tablets may be needed (15 to 75 mg morphine equivalents) in those who would benefit from short-term opioid treatment [100,103,104,106]. Individualization with emerging pharmacogenomic data may help address inter-individual variation in response to opioids [107].

Physician variation in opioid prescriptions at discharge is well-documented and may be challenging to automate [108]. Tailored stakeholder education for physicians, trainees, advanced practice providers, nurses, pharmacists, and office staff provides an excellent launch point for any systemic change and is especially pertinent in opioid prescribing given previous misinformation [103,104,109]. For patients, preemptive psychoeducation can include preoperative expectation-setting, preparing for surgical recovery, strategizing to reduce pain and anxiety, discussing the risks of opioid treatment, and collaborative decision-making [110,111].

Recommendation: Multimodal opioid-reduction strategies for postoperative pain control are critical to employ in the inpatient and outpatient settings. Decreased post-discharge opioid prescribing is feasible with a team approach and does not affect pain control or patient satisfaction. PCA is rarely required and should be used as a last resort for patients requiring repeated treatment with IV opioids.

3.8. How do I create a successful same day discharge program?

Same day discharge (SDD) is defined as discharge home on the same calendar day as the date of surgery and is a natural evolution of ERAS protocols for gynecologic oncology patients. Recent research supports SDD for minimally invasive gynecologic oncology procedures, including hysterectomy, lymph node mapping, and complete surgical staging [102,112,113]. Effective SDD programs are anchored in multidisciplinary collaboration, patient and procedure selection, and ERAS principles to facilitate rapid recovery and discharge [114]. Successful SDD programs strategically mitigate risk factors for overnight admission: patient preference, PONV, drowsiness, urinary retention, and pain [102,115]. Current evidence based SDD guidelines and best practices are as follows:

- No standardized criteria for patient selection currently exist. Patients with poorly controlled medical comorbidities (e.g., ASA IV and V; OSA non-adherent to CPAP), who require therapeutic anticoagulation, or who lack social support (patients without a caregiver for the first 24 h after discharge) are not candidates for SDD [116,117]. Frailty can be considered a contraindication to SDD since frailty is predictive of death even following low-risk surgeries [118].
- SDD is most consistently achieved when cases have a start time before 1 pm, operative duration is under 180 min, intravenous fluid administration does not exceed 1-l, minimal opioids are used, and surgery is complication-free [112,117,119].
- Patient and provider education should focus on the safety and benefits of SDD and highlight that SDD: does not increase risk of readmission, is associated with greater patient comfort and satisfaction, and decreases hospital-related complications and healthcare costs. Patient education significantly improves SDD acceptability especially when received directly from the surgeon. SDD expectation should be re-emphasized in the preoperative bay and immediately postoperatively [102,115,117,120–122].
- Preadmission discharge planning, including medication prescription and review of discharge instructions reduces patient anxiety, reduces unnecessary care, and improves timeliness of indicated care [123]. Discharge instructions should target how to distinguish normal and expected symptoms from potentially serious adverse events.

- Multimodal non-opioid analgesia (oral acetaminophen and NSAIDs) should be utilized to minimize opioid use. Gabapentinoids should be avoided for SSD patients due to adverse effects including sedation, visual disturbances, dizziness, and respiratory depression [21,124].
- Risk of PONV should be assessed using a validated tool (e.g., Apfel score). Multimodal antiemetic prophylaxis with 2–3 antiemetics from different classes, either preoperatively or intraoperatively, is standard of care. A combination of dexamethasone and ondansetron may be used for most patients; preoperative aprepitant or transdermal scopolamine are options for patients with higher Apfel scores (3 to 4). Scopolamine should be used with caution in elderly patients given the increased risk of postoperative urinary retention and delirium. For breakthrough PONV, it is recommended to use rescue antiemetics from a different class than the prophylactic drug(s) [102,125].
- Both propofol-based total intravenous anesthesia (TIVA) and inhalational anesthesia can be safely used in SSD. Compared to inhalational agents, TIVA is associated with less PONV without increasing time to tracheal extubation or time spent in PACU. When TIVA is not an option, inhalational agents combined with appropriate PONV prophylaxis can offer similar antiemetic effects. Local anesthesia has been consistently shown to decrease postoperative pain and opioid consumption [114,118].
- Traditional discharge criteria are still valid for safe and effective discharge from PACU [126].
- A telephone call to the patient by a member of the care team is most helpful between 12 and 24 h postoperatively [127]. Use of a smartphone app for remote follow-up is associated with significant reduction in preventable ED visits as well as high usability and patient satisfaction in elective colorectal surgery [119,123,126].

Studies show an achievable SSD benchmark of 70–75% or higher in gynecologic oncology. Metrics of success include LOS (defined as the time from patient entry into and discharge from the PACU), unplanned clinic and ER visits, readmission, and patient satisfaction [102,112].

Recommendation: Multidisciplinary SSD programs should be considered for minimally invasive gynecologic oncology procedures. Implementation requires multidisciplinary collaboration, education, patient and case selection, and ERAS perioperative principles.

3.9. How can I overcome barriers to ERAS implementation?

Despite the published benefits of ERAS implementation there has not been widespread uptake on a global level, especially in lower and middle-income countries [6,128]. Barriers to implementation are varied but include challenging practice settings, cultural factors, economic constraints, information/technology and data collection, and lack of support [129–131].

Adherence to change management principles, ERAS education, identifying and recruiting local ERAS champions and leaders are keys to successful implementation of ERAS programs [132,133]. Careful planning with pre-implementation identification of local facilitators and barriers can increase successful implementation [134]. Engagement of multidisciplinary teams and strong communication with regular meetings is associated with better ERAS adherence [135]. Iterative evaluation and implementation cycles can help overcome barriers.

Communication of the economic benefits of ERAS to healthcare administrators may be a strong incentive to garner support for implementation. A return-on-investment modelling study evaluating the adoption of ERAS demonstrated cost savings with a return on investment (ROI) range of 1.05–7.31 (every dollar invested in ERAS would bring \$1.05 to \$7.31 in cost avoidance) [136]. Interestingly, the ROI was estimated to be even greater with longer time horizons of 180 or 360 days. Looking more specifically in the gynecologic oncology patient population, a meta-analysis of 7 studies demonstrated a mean cost benefit of \$2129 USD per patient [4]. In one study, the median hospital

charge for a patient decreased 15.6% in the ERAS group compared with the pre-ERAS group [137]. In this study, categorical costs were evaluated and patients in the ERAS group had lower charges for laboratory services, pharmacy services, room and board, and material goods. The decrease in length of stay associated with ERAS is a primary driver in cost reduction [138].

While resource poor settings have unique barriers to ERAS implementation including the specialized needs of socioeconomically disadvantaged individuals with many comorbidities, transient staff, and limited resources [139], there is evidence of successful implementation in settings such as safety net hospitals [140–142] and rural hospitals [143]. Health care savings noted in resource limited hospitals have shown an observed to expected cost ratio of 0.37 [142]. Guidelines specifically tailored to low and middle-income countries are available [144].

Recommendation: Barriers to successful implementation can be overcome with adherence to change management principles and education at multiple levels. Communication of the economic benefits of ERAS to healthcare administrators may be a strong incentive to garner support for implementation.

4. Discussion

This 2023 update of the ERAS® Society Guidelines for gynecologic oncology is based on the best available evidence. Consistent with the original guidelines published in 2016 and the first guideline update in 2019, in some instances, high quality data were unavailable, and recommendations were based on a combination of objective assessment of best quality evidence in gynecologic oncology surgery, consideration of data from other applicable surgical disciplines and expert opinion from the international panel. In this update, we specifically focused on addressing implementation challenges and the most controversial aspects of ERAS as defined by our clinician stakeholder groups. This guideline will have relevance for both the clinician just starting to develop their ERAS program and also the experienced ERAS champion. Iterating towards peak ERAS compliance will translate to further improvements in surgical quality outcomes for gynecologic oncology patients globally.

Declaration of Competing Interest

Dr. Nelson reports personal fees from AstraZeneca, outside the submitted work. He is the Treasurer of the ERAS® Society and Co-Chair of Enhanced Recovery Canada™.

Dr. Fotopoulou reports personal fees from Roche, AstraZeneca, MSD, Clovis, Tesaro, GSK, Ethicon; all outside the submitted work.

Dr. Taylor reports no conflicts to declare.

Dr. Glaser reports no conflicts to declare.

Dr. Bakkum-Gamez reports no conflicts to declare.

Dr. Meyer reports research funding from AstraZeneca, personal fees from GSK, stocks in Crispr, Invitae, Denali, and Bristol Myers Squibb; all outside the submitted work.

Dr. Stone reports research consulting for AstraZeneca, research funding from Pacira, personal fees from AstraZeneca, GSK; all outside the submitted work.

Dr. Mena reports research funding from Pacira, outside the submitted work.

Dr. Elias reports no conflicts to declare.

Dr. Altman reports research funding from Merck, AstraZeneca, Clovis, Pfizer, and personal fees from GSK, AstraZeneca, Merck; all outside the submitted work.

Dr. Bisch reports research funding from Pharmacosmos, Pfizer and personal fees from Merck, Johnson & Johnson, Ethicon; all outside the submitted work.

Dr. Ramirez reports no conflicts to declare.

Dr. Dowdy reports no conflicts to declare.

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