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Guidelines for perioperative care in gynecologic/oncology: Enhanced Recovery After Surgery (ERAS) Society recommendations—2019 update

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► There is an online supplementary infographic to accompany this paper. To view it, please visit the journal website at https://ijgc.bmj.com/.

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HIGHLIGHTS

- Updated consensus review for the Enhanced Recovery After Surgery (ERAS) gynecologic/oncology guidelines is provided.
- Updates will inform current ERAS gynecologic/oncology protocols.

ABSTRACT

Background This is the first updated Enhanced Recovery After Surgery (ERAS) Society guideline presenting a consensus for optimal perioperative care in gynecologic/oncology surgery.

Methods A database search of publications using Embase and PubMed was performed. Studies on each item within the ERAS gynecologic/oncology protocol were selected with emphasis on meta-analyses, randomized controlled trials, and large prospective cohort studies. These studies were then reviewed and graded according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system.

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

Conclusions The updated evidence base and recommendation for items within the ERAS gynecologic/oncology perioperative care pathway are presented by the ERAS® Society in this consensus review.

INTRODUCTION

Enhanced Recovery After Surgery (ERAS) is now firmly established as a global surgical quality improvement initiative that results in both clinical improvements[1] and cost benefits to the healthcare system.[2] ERAS guidelines are based on the highest quality evidence available and as such require updating on a regular basis.[3] The ERAS Gynecologic/Oncology guidelines[4 5] were first published in February 2016. This article represents the joint efforts of the ERAS® Society (www.erassociety.org) and authors from the international ERAS Gynecology chapters to present an updated consensus review of perioperative care for gynecologic/oncology surgery based on best current evidence.

METHODS

Literature Search

Standard methodology was used as published recently for the ERAS Colorectal Guideline update.[3] Starting from the original ERAS Gynecologic/Oncology guidelines,[4 5] the first author (GN) and senior authors (PR, SD) identified topics for inclusion. International authors known for their expertise in gynecologic/oncology perioperative care were invited to participate in the guideline update. The literature search 1966–2018 used Embase and PubMed to search medical subject headings including "gynecology", "gynecologic oncology", and all previous pre-, intra-, and post-operative ERAS Gynecologic/Oncology items. Reference lists of all eligible articles were crosschecked for other relevant studies. Meta-analyses, systematic reviews, randomized controlled studies, non-randomized controlled studies, reviews, and case series were considered for each individual topic. One or two authors reviewed the evidence base for each item. The quality of evidence for each item was then reviewed and crosschecked by the senior editorial team (GN, MS, OL, PR, and SD).

Quality Assessment

The quality of evidence and recommendations were evaluated according to the GRADE (Grading of Recommendations, Assessment, Development and Evaluation) system[6] 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.

Table 1 Differences in quality of evidence and recommendation grade between the 2016 and current updated guideline

ERAS item	Guidelines 2019 versus 2016
Preadmission information, education and counseling	The same recommendation grade but stronger quality of evidence (from low level to moderate)
Prehabilitation	New for 2019 guideline
Preoperative bowel preparation	The same recommendation grade and quality of evidence with updates to references
Preoperative fasting and carbohydrate treatment	Update to summary and recommendation including addition of new references
Venous thromboembolism prophylaxis	Update to summary and recommendation including addition of new information on VTE prophylaxis during chemotherapy
Surgical Site Infection (SSI) reduction bundles	New for 2019 guideline (includes antimicrobial prophylaxis, skin prep, prevention of hypothermia, avoidance of drains/tubes, control of perioperative hyperglycemia)
Standard anesthetic protocol	Update to summary and recommendation
Minimally invasive surgery	The same recommendation grade but stronger quality of evidence (from low level to high)
Perioperative fluid management/GDFT	Update including new information on the role of Goal Directed Fluid Therapy (GDFT)
Opioid sparing postoperative analgesia	This item is redesigned for the 2019 update and now includes recommendation grade and quality of evidence for several analgesic methods
Perioperative nutrition	Update including new information on the role of immunonutrition
Prevention of postoperative ileus	Change in both recommendation grade and quality of evidence (now strong/high)
Patient Reported Outcomes (PROs)	New for 2019 guideline (including functional recovery)
Pelvic Exenteration and HIPEC	New for 2019 guideline
Discharge Pathways	New for 2019 guideline
Audit and reporting	New for 2019 guideline

ERAS, Enhanced Recovery After Surgery.

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 quality of evidence (high, moderate, low) but also on the balance between desirable and undesirable effects, and on values and preferences of practitioners. Thus, strong recommendations may be reached from low-quality data and vice versa.

Table 2 ERAS items not updated in 2019 guideline (no change in recommendation/evidence)

ERAS item	Recommendation
Pre-operative optimization[4]	Smoking and alcohol consumption (alcohol abusers) should be stopped 4 weeks before surgery
	Smoking—Evidence level: high; Recommendation: strong
	Alcohol—Evidence level: moderate; Recommendation: strong
	Anemia should be actively identified, investigated, and corrected pre-operatively
	Evidence level: high; Recommendation: strong
Pre-anesthetic medication[4]	Routine administration of sedatives to reduce anxiety pre-operatively should be avoided
	Evidence level: low; Recommendation: strong
Nausea and vomiting prophylaxis[4]	A multimodal approach to post-operative nausea and vomiting with >2 antiemetic agents should be used for patients undergoing gynecologic procedures
	Evidence level: moderate; Recommendation: strong
Urinary drainage[5]	Urinary catheters should be used for post-operative bladder drainage for a short period preferably <24 hours post-op
	Evidence level: low; Recommendation: strong
Early mobilization[5]	Patients should be encouraged to mobilize within 24 hours of surgery
	Evidence level: low; Recommendation: strong

ERAS, Enhanced Recovery After Surgery.

RESULTS

The evidence base, recommendations, evidence level, and recommendation grade are provided for each individual ERAS item below.Table 1 shows all the ERAS items with emphasis on changes for the 2019 guideline update. Table 2 shows items (pre-operative optimization, pre-anesthetic medication, nausea and vomiting prophylaxis, urinary drainage, and early mobilization)[4 5] that did not receive an update because there was no change to the recommendation and evidence base.

1. Pre-admission Information, Education, and Counseling

The goal of pre-operative counseling is to set expectations about surgical and anesthetic procedures, as well as provide information regarding a care plan in the post-operative period. Pre-operative education and psychological preparation can reduce anxiety and increase patient satisfaction, which may improve fatigue and facilitate early discharge.[7–9] Pre-operative education is also effective in reducing pain and nausea, and improving well-being when added to an existing ERAS protocol.[10 11] Written information was determined to be superior to verbal in one randomized clinical trial in gynecologic oncology surgery.[12] Ideally, patients should receive

information in both written and oral form. The patient and a relative or care provider should meet with all members of the team including the surgeon, anesthetist, dietician, and nurse. Studies have shown that patients with gynecologic cancer prefer to be well informed, and support from a nurse at the time of diagnosis can reduce stress levels for up to 6 months.[13 14]

Summary and Recommendation:
Interventions and endpoints in this field vary widely. However, most studies show that **counseling provides beneficial effects with no evidence of harm**. It is recommended that patients should routinely receive dedicated pre-operative counseling.

Evidence level: moderate
Recommendation grade: strong

2. Prehabilitation

Cancer prehabilitation has been defined as "a process on the continuum of care that occurs between the time of cancer diagnosis and the beginning of acute treatment, includes physical and psychological assessments that establish a baseline functional level, identifies impairments, and provides targeted interventions that improve a patient's health to reduce the incidence and the severity of current and future impairments".[15] Prehabilitation aims to optimize patients' physical and mental well-being in anticipation of an upcoming stressor rather than a reactive process in which care is provided to restore wellness (ie, rehabilitation).[16] There is currently no consensus-based definition, but a multimodal approach that encompasses the following principles is gaining popularity: (1) aerobic and resistance exercises to improve physical function, body composition, and cardiorespiratory fitness; (2) targeted functional exercises to minimize/prevent impairments; (3) dietary interventions to support exercise-induced anabolism as well as mitigate disease and/or treatment-related malnutrition; (4) psychological interventions to reduce stress, support behavior change, and encourage overall well-being.[17]

Recognizing the heterogeneity among prehabilitation interventions, timing, endpoints, and study populations,[16] including the absence of direct evidence that a prehabilitation intervention successfully improves the outcomes of gynecologic oncology patients under ERAS care, **a recommendation endorsing the integration of a prehabilitation program is premature**. Few gynecologic prehabilitation studies have been conducted, and available studies have focused exclusively on pre- and post-operative functional exercises with conflicting results.[18] Studies for multimodal prehabilitation before surgery in other abdominal cancers have shown a positive impact on patient outcomes. A meta-analysis in colorectal surgery found that nutrition prehabilitation with and without exercise shortened length of hospital stay by 2 days in a largely traditional (ie, non-ERAS) surgical care setting.[19] A meta-analysis of prehabilitation interventions consisting of inspiratory muscle training, aerobic exercise, and/or resistance training found that prehabilitation decreased post-operative complications after intra-abdominal operations in a traditional surgical care setting (OR 0.59, 95% CI 0.38 to 0.91; p=0.03).[20] Small prospective trials suggest that trimodal prehabilitation (exercise, nutrition, and anxiety-reduction elements) facilitates an earlier return to functional walking capacity after surgery for colorectal surgery in excess of what is achieved when ERAS is implemented alone.[21]

It is likely that patients with impaired pre-operative function will attain the greatest clinical benefit. A patient-led qualitative study suggested that patients perceived an enhanced recovery program should not be limited to the perioperative period, but should rather encompass the cancer care journey beginning at diagnosis.[22] The addition of prehabilitation to the ERAS pathway, might, therefore, confer complementary patient-oriented and functional benefits.

Summary and Recommendation:
There are no high quality studies for prehabilitation in gynecologic oncology patients. Extrapolated work in colorectal surgery shows **certain patients benefit clinically from prehabilitation but further work in gynecologic oncology is needed**.

Evidence level: low
Recommendation grade: weak

3. Pre-operative Bowel Preparation

Pre-operative bowel preparation has traditionally been used under the assumption that the reduction in the stool burden may decrease post-operative infectious morbidity including anastomotic leak following bowel surgery. Although this theoretical benefit has yet to be unequivocally substantiated, in addition to patient dissatisfaction, its use has been associated with adverse outcomes due to pre-operative dehydration and electrolyte abnormalities that can hinder post-operative recovery.

Data from randomized controlled trials on the use of bowel preparation in gynecologic surgery are limited to patients undergoing minimally invasive gynecologic surgery. These studies have conclusively shown that its use is not associated with improved intraoperative visualization, ease of bowel handling or procedure performance.[23–27]

Given the lack of data investigating the use of bowel preparation before laparotomy for gynecologic surgery, data are extrapolated from the colorectal literature. Four meta-analyses showed that the use of mechanical bowel preparation was not associated with a decrease in overall mortality, surgical site infection rate, anastomotic leak rate, or reoperation compared with no mechanical bowel preparation.[28–31] The interest in pre-operative bowel preparation was renewed in light of retrospective data suggesting that pre-operative use of oral antibiotics as bowel preparation may reduce hospital length of stay and readmissions after colorectal surgery.[32] A meta-analysis of randomized controlled trials showed that a combination of oral antibiotics with mechanical bowel preparation was associated with a lower rate of surgical site infection overall (7.2% vs 16%, p<0.001) and incisional surgical site infections (4.6% vs 12.1%, p<0.001) with comparable organ space surgical site infections (4% vs 4.8%, p=0.56).[33] Although no randomized controlled trials have compared oral antibiotics alone to no bowel preparation, retrospective studies have shown that oral antibiotics alone compared with no bowel preparation significantly reduced post-operative infectious morbidity including anastomotic leaks as well as major morbidity. The combination of oral antibiotics with mechanical bowel preparation did not offer any additional benefit in reducing post-operative infectious morbidity compared with oral antibiotics alone.[34–36] These data suggest that oral antibiotics may have value as pre-operative bowel preparation and bring into question the significance of adding mechanical bowel preparation in this setting.

Recently there has been a trend in the colorectal surgery practice towards reintroducing pre-operative bowel preparation in the form of combined oral antibiotics with mechanical bowel preparation before colonic resections. In contrast, well-established ERAS pathways in gynecologic surgery without pre-operative bowel preparations (including cases with scheduled bowel resection) have been proven safe with very low rates of anastomotic leak.[37 38] Furthermore, incorporation within established ERAS pathways of surgical site infection reduction bundles which similarly forgo bowel preparation have resulted in a significant decrease in the surgical site infection rate as low as 2.4% among ovarian cancer patients undergoing cytoreductive surgery with colonic resection, which represents the highest risk group for post-operative infectious morbidity.[39 40] Notably, this compares favorably to surgical site infection bundles which incorporate combined oral antibiotics with mechanical bowel preparation, in which infection rates decreased to 7% in a comparable high-risk ovarian cancer population.[41]

Summary and Recommendation:

Routine pre-operative bowel preparation should not be used before minimally invasive gynecologic surgery. Its use is **similarly discouraged before open laparotomy in gynecologic surgery/gynecologic oncology,** especially within an established ERAS pathway. Surgeons who feel bowel preparation is necessary should limit its use to patients in which a colon resection is planned. In these cases the use of oral antibiotics alone should be considered or combined with mechanical bowel preparation. High quality data from the colorectal literature have shown that **mechanical bowel preparation alone does not decrease post-operative morbidity and should thus be abandoned**.

Evidence level: moderate

Recommendation grade: strong

4. Pre-operative Fasting and Carbohydrate Treatment

Surgical stress following major surgery induces a marked and well-defined post-operative metabolic response. The use of pre-operative oral carbohydrates and avoiding pre-operative fasting attenuate these post-operative responses.

Several randomized controlled trials have reported that clear fluids can be safely given up to 2 hours, and a light meal up to 6 hours, before elective procedures requiring general anesthesia, in children and adults.[3 42]

Pre-operative administration of oral carbohydrates 2–3 hours before induction of anesthesia has been shown to attenuate the catabolic response induced by overnight fasting and surgery.[43] Since most investigations of oral carbohydrates used a pre-operative beverage containing 50 g carbohydrates, administration of beverages with less caloric content may not provide the anticipated clinical and metabolic benefits. Furthermore, beverages with high osmolality or fat content may slow gastric emptying.

Oral carbohydrates in randomized controlled trials have been shown to improve pre-operative well-being, reduce post-operative insulin resistance, decrease protein breakdown, better maintain lean body mass and muscle strength, and provide beneficial cardiac effects.[43] Randomized trials on oral carbohydrates have been performed in major and minor upper gastrointestinal and colorectal surgery, and orthopedic, thoracic, cardiac, neurologic, and urologic surgery. In one randomized placebo-controlled trial, less post-operative nausea and vomiting, metoclopramide consumption, and improved patient satisfaction was noted 24 hours after abdominal myomectomy.[44]

A Cochrane review of abdominal, orthopedic, and cardiac surgery studies reported that **preoperative carbohydrate treatment was associated with reduced post-operative insulin resistance, enhanced return of bowel function, and shorter hospital stay with no effect on post-operative complication rates**.[45] Large cohort studies in patients undergoing major colorectal surgery have shown that oral carbohydrates as part of an ERAS protocol significantly improved clinical outcome.[46 47]

Oral fluids including oral carbohydrates may not be administered safely in patients with documented delayed gastric emptying or gastrointestinal motility disorders as well as in patients undergoing emergency surgery. Although obese[48] and diabetic[49] patients have been included in recent studies of oral carbohydrates and no issues with regard to safety have been reported, studies are insufficient to allow a general recommendation.

Summary and Recommendation:

Patients should be encouraged to eat a light meal up until 6 hours, and consume clear fluids including oral carbohydrate drinks up until 2 hours, before initiation of anesthesia. Patients with delayed gastric emptying should fast overnight or 8 hours before surgery. Oral carbohydrates reduce insulin resistance and improve well-being and should be used routinely (extrapolated from non-gynecological surgery data). There are insufficient data to make recommendations in diabetic patients.

Quality of Evidence:

6–8 hour fasting for solids and 2 hours for clear fluids including oral carbohydrate drinks (in patients without delayed gastric emptying): high

Oral carbohydrate drinks improving insulin resistance and well-being: moderate

Oral carbohydrate drinks improving recovery time and reducing complications: low

Recommendation Grade:

Avoiding overnight fasting: strong

Administration of pre-operative oral carbohydrates: strong

Administration of pre-operative oral carbohydrates in well controlled diabetic patients: weak

5. Venous Thromboembolism Prophylaxis

Venous thromboembolism (VTE) is a major risk in gynecologic oncology patients with rates up to 3–4% in cervical cancer, 4–9% in endometrial cancer, and 17–38% in ovarian cancer.[50–55] Approximately 3% of women with a new ovarian cancer diagnosis will have a concomitant VTE diagnosed before they start cancer treatment[52]; the risk of VTE approaches 12% during neoadjuvant chemotherapy[55] and extends through at least the full course of primary therapy.[56] The extended risk of VTE was also demonstrated in an analysis from the Million Women Study that showed the risk of VTE at 12 weeks post-operatively was 1/85 for cancer surgery and 1/365 for gynecologic surgery.[57] The presence of malignancy, higher body mass index, age, pelvic surgery, extra-pelvic disease, histology, pre-operative corticosteroids, receipt of chemotherapy, immobility, and a hypercoagulable state have all been identified as

independent risk factors for VTE and are common among women undergoing gynecologic surgery, especially for cancer.[58 59] **All gynecologic oncology patients who undergo major surgery lasting longer than 30 min should receive dual VTE mechanical prophylaxis and chemoprophylaxis** with either low molecular weight heparin or unfractionated heparin and dual prophylaxis should continue throughout the hospital stay.[59–61]

Perioperative prophylaxis should include dual modality prophylaxis[61] and should begin before the induction of anesthesia. A retrospective study comparing pre-operative versus post-operative initiation of prophylactic anticoagulation in patients undergoing surgery for gynecologic cancer showed a decreased rate of deep venous thrombosis (1.9% vs 8%; p=0.04) and a decreased rate of deep venous thrombosis-associated deaths (0 vs 2; p<0.001) among those who received pre-operative prophylaxis.[62] Similarly, in a large retrospective surgical oncology study of 2058 patients who underwent surgery for cancer and received pre-operative heparin compared with 4960 historical controls, the rate of deep venous thrombosis and pulmonary embolism among those who received pre-operative prophylaxis was significantly lower.[63] Importantly, prophylactic anticoagulation has not been shown to increase the risk of intraoperative bleeding, thrombocytopenia, and epidural hematoma.[64 65] Therefore, epidural catheter placement and removal should be timed according to the last dose of heparin.[64 65] The use of mechanical prophylaxis, specifically pneumatic compression devices, has been shown to decrease the rate of VTE when compared with no prophylaxis within the first 5 post-operative days. The efficacy of mechanical prophylaxis is equivalent to heparin alone, and leads to the greatest VTE risk reduction when combined with heparin in gynecologic oncology patients.[66–68] Graduated compression stockings, when fitted properly, also appear to decrease the rate of deep venous thrombosis in hospitalized patients, especially when combined with another method of VTE prophylaxis.[69]

The risk of VTE extends beyond the post-operative hospital stay in patients undergoing cancer surgery.[56 70 71] The randomized controlled trial ENOXACAN II demonstrated a 60% reduction in the VTE rate in patients undergoing surgery for cancer who received 28 days of low molecular weight heparin compared with those who received only 10 days of low molecular weight heparin.[72] Additionally, a Cochrane review, a systematic review, and meta-analysis showed that extended prophylaxis for 28 days decreased overall VTE, deep venous thrombosis, and symptomatic VTE.[73–75] Women undergoing gynecologic cancer surgery meet high-risk American College of Chest Physicians (ACCP) criteria and the ACCP, American Society of Clinical Oncology, and National Comprehensive Cancer Network guidelines[59 61 76] recommend extended, 28-day chemoprophylaxis. While the role of extended prophylaxis in minimally invasive gynecologic surgery remains debated, VTE rates are in the range of 0.5% or less and do not appear to be modulated based on whether or not prophylaxis was given.[77–80] Additionally, although direct-acting oral anticoagulants are a recommended therapy for VTE when diagnosed in patients with active cancer,[81–83] the role for direct-acting oral anticoagulants for post-operative prophylaxis is currently limited to orthopedic surgery literature and requires further study in gynecologic surgery.[84]

Gynecologic cancer patients often start adjuvant chemotherapy within 3–5 weeks of surgery and prophylaxis during ambulatory chemotherapy remains understudied. The risk of VTE extends beyond the traditional 30 day post-operative complication window in these patients[56 71] and is inherently present among those undergoing neoadjuvant chemotherapy for ovarian cancer.[55] Extended low molecular weight heparin has been shown in two randomized, placebo controlled trials in solid tumors to reduce VTE during chemotherapy by 50%.[85 86] The recently published randomized, placebo-controlled AVERT trial of prophylactic apixaban during solid tumor chemotherapy demonstrated a 60% reduction in VTE in those randomized to apixaban.[87] However, VTE guidelines specific to gynecologic cancer are lacking.

Summary and Recommendation:
Patients at increased risk of VTE should receive dual mechanical prophylaxis and chemoprophylaxis with either low molecular weight heparin or unfractionated heparin. **Prophylaxis should be initiated pre-operatively and continued post-operatively. Extended chemoprophylaxis (28 days post-op) should be prescribed to patients who meet high-risk ACCP criteria, including patients with advanced ovarian cancer**. Further studies on extended post-operative prophylaxis with direct-acting oral anticoagulants, and guidelines on VTE prophylaxis during ambulatory chemotherapy for gynecologic cancer, are needed.

Evidence Level:
Stockings, pneumatic compression devices, low molecular weight heparin: high
Pre-operative administration: moderate
Post-operative extended prophylaxis with low molecular weight heparin: high
Post-operative extended prophylaxis with direct-acting oral anticoagulants: low

Recommendation Grade:
Perioperative deep venous thrombosis prophylaxis: strong
Extended (28-day) prophylaxis in high-risk patients: strong
Direct-acting oral anticoagulant prophylaxis: weak

6. Surgical Site Infection Reduction Bundles

Surgical site infections are defined as infections of the surgical incision or organ space that develop within 30 days of surgery.[88] Surgical site infections are associated with increased patient morbidity, mortality, and healthcare expenditures and occur in up to 20–30% of gynecologic oncology patients undergoing a laparotomy.[89–93] Surgical site infection reduction bundles have been demonstrated to decrease the risk of developing a surgical site infection in an additive fashion.[39 41 91 94–98] Surgical site infection bundle elements include antimicrobial prophylaxis, skin preparation, avoiding hypothermia, avoiding surgical drains, and reducing perioperative hyperglycemia.

6.1 Antimicrobial Prophylaxis

Appropriate antibiotic prophylaxis includes administration of a first generation cephalosporin to cover skin flora.[99 100] Cephalosporins have relatively broad coverage, are low cost, have a low allergenic potential, and are the recommended prophylaxis for simple hysterectomy.[100] Additional anaerobic coverage is recommended if the bowel is entered during pelvic surgery for cancer.[100 101] Dosage may need to be adjusted based on patient weight.[99 100] Most

antibiotics should be administered within 1 hour of incision in order to obtain the highest drug serum levels at incision.[99 100] Antibiotic redosing should be monitored for compliance based on operative time and blood loss.[99 100] Several surgical site infection reduction bundles include an emphasis on antibiotic dosing and timing of administration. Appropriate antimicrobial prophylaxis is a category 1B recommendation by the Centers for Disease Control and Prevention (CDC).[39 41 91 97 102]

Summary and Recommendation:
First generation cephalosporins should be first choice for antibiotic prophylaxis for hysterectomy and dosing should be weight-based. Antibiotic prophylaxis should be adjusted according to the planned procedure, with the addition of anaerobic coverage in the setting of pelvic cancer surgery or bowel surgery. Redosing should be performed as indicated based on duration of surgical case and blood loss.

Evidence level: high
Recommendation grade: strong

6.2 Skin Preparation

Skin preparation is intended to decrease the amount of bacterial flora present on the skin before incision. This can be accomplished through pre-operative bathing at home as well as use of a skin preparation in the operating room before incision.[99] There is level I evidence demonstrating a 40% lower surgical site infection rate associated with chlorhexidine-alcohol skin preparation compared with povidone-iodine[103] and the CDC has endorsed alcohol-based skin preparation as a category 1A recommendation.[102] Most surgical site infection reduction bundles have incorporated pre-operative bathing with a chlorhexidine-based antimicrobial soap and chlorohexidine-alcohol skin preparation before surgery.[39 41 91 97]

Summary and Recommendation:
Patients should **shower before surgery with a chlorhexidine-based antimicrobial soap and undergo a chlorohexidine-alcohol skin preparation in the operating room before surgery**.

Evidence level: high
Recommendation grade: strong

6.3 Prevention of Hypothermia

Intra-operative hypothermia has been linked to an increased risk of surgical site infections and cardiac events.[104] Various methods to avoid intraoperative hypothermia have been evaluated including forced air blanket devices, underbody warming mattresses, and warmed intravenous fluid administration.[104] In a randomized clinical trial comparing intraoperative warming only (control group) versus additional warming 2 hours before and after surgery (warming group) among patients undergoing major abdominal surgery, the rate of surgical site infections was decreased by half among those who were normothermic.[104] The CDC endorses perioperative normothermia as a category 1A recommendation.[102]

Summary and Recommendation:
Maintenance of **normothermia should be incorporated into all ERAS programs**.

Evidence level: high
Recommendation grade: strong

6.4 Avoidance of Drains/Tubes

High quality evidence is lacking to address the role of subcutaneous or peritoneal drains in decreasing surgical site infections and evidence exists that drain biofilm colonization can be detected as early as 2 hours after placement.[105] One surgical site infection reduction bundle implemented among gynecologic oncology patients included use of subcutaneous drains in obese patients. However, this surgical site infection reduction bundle also included other interventions with stronger surgical site infection reduction evidence.[94] At this point, there is insufficient evidence to recommend inclusion of a subcutaneous drain or peritoneal drain as part of a surgical site infection reduction bundle and there may be harm by introducing a foreign body conduit for bacteria to travel into a surgical wound. Nasogastric intubation increases the risk of post-operative pneumonia after elective abdominal surgery and does not reduce the risk of wound dehiscence or intestinal leaks.[106 107] As such, the use of drains should be tailored according to the surgical procedure and rationale for individualized drain placement.

Summary and Recommendation:
The use of **peritoneal drains, subcutaneous drains, and nasogastric tubes should be avoided after abdominal surgery**.

Evidence level: high
Recommendation grade: strong

6.5 Control of Perioperative Hyperglycemia

The prevalence of diabetes is 22% among the US population older than 65 years.[108–110] The high prevalence suggests the need not only to implement interventions to obtain perioperative glycemic control but also to improve pre-operative screening. Perioperative hyperglycemia has been associated with increased risk of developing surgical site infections, in both diabetic and non-diabetic patients undergoing surgery,[93 111–113] and the CDC recommends (category 1A) blood glucose levels be maintained at <200 mg/dL regardless of whether a patient is diabetic or not.[102] A recent study among gynecologic oncology patients found that implementing an intensive post-operative glycemic control initiative using a continuous insulin infusion resulted in a 35% reduction in the rate of surgical site infections among patients with diabetes.[114] Similarly, authors of another study decreased the surgical site infection rate by 55% through implementation of an initiative standardizing post-operative management of diabetic and pre-diabetic patients using a multidisciplinary team.[109] Importantly, glucose management must avoid hypoglycemia as well as hyperglycemia as both extremes have been associated with higher mortality risk.[115 116] It should be noted that other interventions that decrease insulin resistance are part of the ERAS protocol, including oral carbohydrate loading, minimally invasive surgery, early feeding, and thoracic epidural analgesia.[3]

Summary and Recommendation:
Perioperative glucose levels should be maintained under 200 mg/dL in diabetics and non-diabetics. All surgical patients should be screened for diabetes. Measures to optimize

perioperative glycemic control should be included in surgical site infection reduction bundles.

Evidence level: high

Recommendation grade: strong

7. Standard Anesthetic Protocol

The goals for the anesthesiologist are multiple: to provide hypnosis, analgesia, and optimal surgical conditions, and to optimize circulation, mean arterial pressure, and oxygen delivery, all with minimal residual anesthetic effects with rapid neurocognitive recovery and minimal nausea and vomiting. Propofol has become the standard medication for induction of general anesthesia because of its rapid onset, favorable antiemetic profile, and rapid recovery. General anesthesia can be maintained with inhalation anesthesia or total intravenous anesthesia. Short-acting inhalation agents such as sevoflurane or desflurane should be used. Continuous target controlled infusions of propofol have an additional benefit in reducing the incidence of post-operative nausea and vomiting.[117 118] Several intravenous anesthetic agents may be used in combination with propofol to provide an effective total intravenous anesthesia regimen—dexmedetomidine, ketamine, and lidocaine. In addition to its direct sedative-analgesic properties, dexmedetomidine also reduces opioid requirements and minimum alveolar concentration levels for inhalational anesthetics.[119–122]

There is potential for ketamine to have benefits in reducing chronic post-operative pain, but the optimum treatment duration and dose for different operations has yet to be identified.[123 124] Intravenous lidocaine infusion in the perioperative period decreases intraoperative anesthetic requirements, lowers pain scores, reduces post-operative analgesic requirements, and improves return of bowel function with decreased length of hospital stay.[125] There is also evidence that ketamine, lidocaine, propofol, and avoidance of inhalational anesthetic agents may lead to a reduction in cancer recurrence. However, recognizing that multiple factors influence recurrence and survival, further research is needed to define the true impact of total intravenous anesthesia in gynecological malignancies and no recommendations can be currently made.[126 127]

High dose or long-acting opioids should be avoided to reduce post-operative opioid-related side effects. Short-acting opioid analgesics such as remifentanil may allow a consistently rapid recovery, but there is concern it may induce hyperalgesia. Nitrous oxide as well as being minimum alveolar concentration additive has analgesic properties but is associated with an increased rate of post-operative nausea and vomiting in a patient population with a high baseline risk.[128] Both laparoscopic procedures and gynecological surgery are independent predictors of post-operative nausea and vomiting; therefore, it is reasonable to omit nitrous oxide during laparoscopic gynecologic surgery to prevent post-operative nausea and vomiting, and prophylaxis with a combination of at least two anti-emetics should be standard.[129]

Neuromuscular blocking agents provide muscle relaxation to facilitate surgical exposure in open surgery. In laparoscopic surgery they maintain muscle paralysis through the procedure and improve operating space and allow surgery at lower intra-abdominal insufflation pressures.[130] Peripheral nerve stimulators should be used to monitor block and ensure correct reversal of neuromuscular block to reduce risks of residual muscle weakness that is a major risk for post-operative respiratory complications.[131]

Use of a bispectral index to guide anesthetic depth may allow reduction of anesthetic dose and hence facilitate rapid awakening.[132] In the elderly, there is increased focus on using this tool to reduce the dose of inhalational anesthetic to avoid the risk of post-operative cognitive dysfunction and delirium[133]; a recent randomized controlled trial, however, has called this into question.[134]

Regional anesthetic techniques are a major component of a bundle of perioperative interventions of ERAS to reduce the stress response, as well as anesthetic and opioid use. Regional analgesic techniques include neuraxial (eg, epidural, spinal), peripheral nerve blocks, and wound infiltration.[135] Multimodal non-opioid analgesia use decreases post-operative nausea and vomiting and allows more rapid recovery.[136 137]

Recent studies have shown a reduction in pulmonary complications in patients undergoing open abdominal surgery when a lung protective ventilation strategy is utilized (tidal volume 6–8 ml/kg with positive end expiratory pressure 6–8 cm H_20).[138] Randomized controlled trials have suggested that low tidal volumes, high positive end expiratory pressure, and recruitment maneuvers may be protective intraoperatively.[139]

Summary and Recommendation:

The use of **short-acting anesthetics, monitoring of neuromuscular block depth, and complete reversal is recommended**. Ventilation should use a protective strategy with tidal volumes 6–8 mL/kg and positive end expiratory pressure 6–8 cm H_2O .

Quality of evidence: Short-acting anesthetics: low

Recommendation grade: strong

Quality of evidence: Objective monitoring of the level of neuromuscular block and ensuring complete reversal: high

Recommendation grade: strong

Quality of evidence: Protective ventilation: moderate

Recommendation grade: strong

8. Minimally Invasive Surgery

A key tenet of enhanced recovery is the focus on decreasing the stress response and modifying the metabolic response to surgical insult.[1] Laparoscopic surgery has been associated with a decrease in both the inflammatory and immunomodulatory response to surgery compared with open procedures.[140 141] While some studies suggest that classic endocrine metabolic responses are less influenced by minimally invasive surgery, others have suggested that minimally invasive surgery decreases the cortisol stress response compared with moderate and highly invasive surgeries.[142]

While most reports of the gynecologic ERAS programs have focused on open surgery, there is mounting evidence that the ERAS programs are also safe and feasible for patients undergoing minimally invasive surgery, including bowel procedures.[143–145] The adoption of minimally invasive laparoscopy and robotic surgery in gynecology has led to substantial improvements in patient outcomes by decreasing intraoperative blood loss, length of stay, analgesic requirements, return of bowel function, length of hospitalization, and return to normal daily activities.[146 147]

With currently available data, it is not clear to what degree ERAS implementation has impacted outcomes for women undergoing minimally invasive surgery for gynecologic indications compared with minimally invasive surgery gynecologic procedures outside an ERAS program. Length of stay is a commonly reported metric

for assessing the impact of ERAS programs. However, same day discharge is achievable for many patients undergoing gynecologic minimally invasive surgery procedures, regardless of whether or not the procedures were performed on a formal ERAS pathway.[148] Retrospective comparative studies suggest that ERAS implementation in minimally invasive surgery demonstrated an association with improvements in length of stay and cost.[149] Another series described an association of ERAS implementation with decreased intraoperative and post-operative morphine equivalents, decreased cost, and with increased patient satisfaction.[144] Similar benefits have been identified in patients undergoing vaginal hysterectomy and urogynecologic procedures including shorter length of stay, decreased opioid intake, and higher patient satisfaction scores.[37 150 151] From a patient's perspective, undergoing minimally invasive surgery leads to faster recovery compared with open gynecologic surgery on an ERAS pathway. Patients undergoing minimally invasive surgery reported less pain, interference with walking, and fatigue compared with women undergoing open surgery on an ERAS pathway.[152]

The perioperative benefits of a minimally invasive surgery approach may be reduced by a number of elements, including uncontrolled pain, nausea and vomiting, fluid overload, limited ambulation, fatigue, and deconditioning. Age, blood loss, perioperative blood transfusion, and post-operative complications have been associated with prolonged length of stay after laparoscopic surgery.[153] Urinary retention and inadequate pain control were the two top reasons why patients undergoing gynecologic minimally invasive surgery on an ERAS pathway were not discharged on the day of surgery, with 30% of delayed discharges attributed to each.[143]

Oncologic outcomes have been found to be equivalent in women undergoing minimally invasive surgery and open procedures for endometrial cancer,[154] but not for early stage cervical cancer.[155]

Given the improvements in surgical recovery in patients undergoing minimally invasive surgery procedures compared with open surgery,[146 147 152] **minimally invasive surgery remains an important tenet of ERAS and is recommended for appropriate patients** when long-term oncologic outcomes are similar, and where expertise and resources are available.

Summary and Recommendation:
Minimally invasive surgery, **including vaginal surgery, is preferred for appropriate patients when feasible**.

Evidence level:
Morbidity: high
Recovery: high
Recommendation grade: strong

9. Perioperative Fluid Management/Goal-Directed Fluid Therapy

Intravenous fluid excess has been associated with a delayed return of bowel function, post-operative ileus, post-operative nausea and vomiting, and increased length of stay.[156–158] Conversely, hypovolemia, if undetected, may lead to post-operative complications, including acute kidney injury, surgical site infections, sepsis, and delirium, as well as prolonged hospital stay.[159–161] In order for the anesthesiologist to make decisions regarding fluid management, clinical parameters such as blood pressure are used, while the routine use of specific clinical goal-directed fluid therapy guidelines or algorithms using physiological measurements of blood flow, fluid responsiveness, and organ perfusion have not been universally adopted into clinical practice.[162–164] This has led to wide variations in fluid volume administration across surgical practices and procedures.[165]

For high-risk surgical patients, goal-directed fluid therapy—a technique used to manage hemodynamics with the use of fluids and inotropes to improve tissue perfusion and oxygenation—has been associated with improvements in short- and long-term outcomes.[166 167] One of the most important components of an ERAS program is the use of goal-directed fluid therapy; this may be facilitated by the use of minimally invasive hemodynamic monitoring to detect flow-related parameters and/or dynamic parameters of fluid responsiveness. This is done in order to titrate therapeutic interventions (intravenous fluids and/or inotropic therapy administration) to optimize end organ tissue perfusion.[168 169]

Goal-directed fluid therapy in ERAS pathways is simpler to implement as compared with patients on traditional surgical pathways. This is because patients on an ERAS pathway are not exposed to prolonged periods of fasting, or mechanical bowel preparations, and, in addition, are given carbohydrate loading solutions the night before and the morning of surgery, allowing for better hydration and a normal intravascular volume status.

A population-based study[170] investigated intraoperative fluid administration practices across three surgical subspecialties and its association with post-operative recovery (64 hospitals including 8404 intestinal resections, 22 854 hysterectomies, and 1471 abdominopelvic endovascular procedures). There was a wide variation in fluid balance between hospitals ($p<0.001$, all procedures). The highest fluid balance hospitals had significantly longer adjusted post-operative length of stay than the lowest fluid balance hospitals for intestinal resections and hysterectomies. The authors concluded that high fluid balance hospitals have 12–14% longer risk-adjusted length of stay for visceral abdominal procedures, independent of complications and case complexity.

A recent multicenter randomized trial[171] compared patients on a restrictive fluid regimen with a liberal fluid strategy. The liberal fluid group had a lower rate of acute kidney injury and surgical site infection, but otherwise there were no significant differences in outcomes. However, there is insufficient evidence to determine if the liberal fluid cohort was overhydrated, and there is evidence that the restrictive cohort was underhydrated. Furthermore, differences in fluid administration between groups were small, with <1.5 L difference intraoperatively. This study, however, has provided important information emphasizing the need to achieve euvolemia, not hypo- or hypervolemia.

A study of ERAS protocol implementation in women undergoing major gynecologic surgery compared surgical outcomes before and after implementation[144]; 136 ERAS protocol patients were compared with 211 historical controls. Goal-directed fluid therapy was guided by a fluid algorithm using the Masimo pleth variability index (measure of the dynamic changes in the perfusion index that occur during one or more complete respiratory cycles). The authors concluded that implementation of ERAS protocols in gynecologic surgery was associated with a substantial decrease in intravenous fluids (917.5 mL compared with 1410 mL; $p<0.01$). National

Surgical Quality Improvement Program (NSQIP) outcomes including acute renal failure were not statistically different between groups.

Summary and Recommendation:
Perioperative **goal-directed fluid therapy reduces length of stay and complications in high-risk patients undergoing abdominal surgery**.

Evidence level:
Use of goal-directed fluid therapy in major abdominal surgery in patients with high co-morbidities or high blood loss surgery: high
Recommendation grade: strong

10. Opioid Sparing Multimodal Post-operative Analgesia

Post-operative pain after gynecologic surgery plays a major role in patient quality of life and it may also be associated with higher rates of complications, longer hospital stays, increased readmission rates, and higher cost.[172 173] When patients rely on opioid alone for post-operative analgesia, this may cause nausea, sedation, and fatigue while increasing the risk of addiction, thus leading to associated financial and social costs.[174–176] Avoiding opioid use within a multimodal post-operative analgesia pathway, with greater emphasis on non-opioid medications, preserves or improves patient experience and functional recovery after surgery.[37 177] Non-opioid alternatives include non-steroidal anti-inflammatory drugs, acetaminophen, gabapentin, and dexamethasone. Pre-operative education should stress the use of non-opioid alternatives as first-line therapy, and set expectations for post-operative pain control.

When used together, analgesics with different mechanisms of action may be synergistic, a concept which lays the foundation for post-operative pain management within ERAS protocols.[178] We recommend routine pre-operative administration of oral acetaminophen, celecoxib, and gabapentin to reduce pain and opioid requirements.[179] Intravenous acetaminophen should not be used routinely, recognizing its equivalent efficacy to the oral preparation at much higher expense. In general, oral administration of all post-operative medications in patients who can tolerate a diet is preferable to the intravenous route. While intravenous medications may be required for breakthrough pain, patient-controlled analgesia should be required in <5% of patients undergoing laparotomy. Incisional infiltration with either bupivacaine or liposomal bupivacaine has no systemic side effects when used appropriately, and should be incorporated into all ERAS protocols as a component of multimodal analgesia.[37 180]

The use of thoracic epidural analgesia and transversus abdominis plane blocks, both alternatives to local analgesia, has been frequently debated in patients undergoing major abdominal surgery. Thoracic epidural analgesia has been shown to effectively reduce post-operative pain and stress,[181 182] but with some untoward effects such as a 30% risk of failure,[183] hypotension requiring vasopressors,[184] and hindrance of early mobilization.[185] Transversus abdominis plane blocks are performed by injecting local anesthetic between the muscle layers of the trunk using ultrasound guidance, and has also been shown to reduce pain and opiate requirements after surgery.[186] However, direct comparisons of thoracic epidural analgesia, transversus abdominis plane blocks, and incisional injection have not been performed and current literature has failed to show improvements over local injection. One trial showed lower pain scores and less opioid use in patients randomized to local injection of liposomal bupivacaine compared with transversus abdominis plane blocks following total abdominal hysterectomy.[187] Other investigations in laparoscopic surgery have also failed to show improvements with transversus abdominis plane blocks.[188–191] A randomized trial of conventional epidural versus transversus abdominis plane block demonstrated a 0.5 day decreased length of stay with transversus abdominis plane blocks, likely due to a slower transition to oral analgesics with thoracic epidural analgesia.[192] The weight of current data supports the use of incisional injection over transversus abdominis plane blocks or thoracic epidural analgesia.

Patients using buprenorphine before surgery require special consideration. Buprenorphine is a mixed opioid agonist-antagonist at the mu (μ) and kappa (κ) receptors used for the treatment of opioid abuse. These pharmacodynamics prevent other opioids from binding to the κ receptor, therefore reducing the efficacy of all opioids after surgery. Management options include continuing buprenorphine through the perioperative period or discontinuation before surgery.[193] The best option for patients undergoing minor procedures with the expectation of minimal post-operative pain is to continue buprenorphine, recognizing that high doses of opioid may be required for treatment of more severe pain. While discontinuation may be the best option if significant pain is expected, it must occur at least 3–7 days pre-operatively given its long half-life, and is associated with a higher risk of relapse for patients treated for dependence. Recognizing these challenges, all patients using buprenorphine should be evaluated by a pain specialist for optimal management.

It has been recognized that there are great discrepancies in patients' responses to medications including opioids, with a contribution of inherited differences.[194] Pharmacogenomics is an emerging field in individualized medicine, generally focusing on genetic polymorphisms in drug-metabolizing enzymes, transporters, receptors, and drug targets that may explain inter-individual variation in drug efficacy and toxicity.[195] This information has emerging importance in post-surgical opioid administration, with one study showing a 50% reduction in opioid use as well as excellent analgesia using pharmacogenetic-guided input.[196]

In recent years there has been an increased focus on the reduction of outpatient opioid prescribing, especially in post-surgical patients. A number of investigations have demonstrated that surgeons overprescribe opioids at discharge, with wide variations in prescribing practices among providers.[197] It is generally accepted that 6% of opioid-naive patients will become chronic opioid users after surgery, while the rate is as high as 21% for those who require chemotherapy after surgery.[198 199] Improving opioid stewardship among surgeons and their teams is an important facet of opioid use reduction, and can be successfully implemented using standardized guidelines. A large, prospective initiative evaluated patient opioid use after surgery and found that a large proportion of patients used little or no opioids after surgery.[200]

Summary and Recommendation:
A **multimodal post-operative analgesic protocol successfully reduces opioid administration**, both in the hospital and at discharge. This can be accomplished using non-opioid oral medications and incisional injection of local anesthetic to decrease the

need for systemic medications. Emerging tools for opioid reduction, including pharmacogenomics assessment and opioid-prescribing initiatives, will improve opioid stewardship with a goal of reducing opioid dependence after surgery.

Evidence level:
Use of multimodal analgesia: high
Combination of acetaminophen and non-steroidal anti-inflammatory drugs: high
Incisional injection of bupivacaine: high
Thoracic epidural analgesia: moderate
Transversus abdominis plane blocks: low
Referral of patients using pre-operative buprenorphine to a pain specialist: moderate
Recommendation grade: strong

11. Perioperative Nutrition

Several randomized studies on early feeding have been performed in gynecologic oncology and ovarian cancer.[201–206] Maintenance of appropriate nutritional status post-operatively has led to improvements in return of bowel activity, reduced length of hospital stay, and equivalent complication rates as measured by wound healing, anastomotic leaks, or pulmonary complications.[203 204 207] In colorectal patients, delivery of post-operative nutrition on day 1 is an independent prognostic factor of 5-year survival and mortality.[207–209]

Perioperative nutritional supplementation, or immune nutrition, is another field of research, examining the roles of polyunsaturated fatty acids, arginine, glutamine, antioxidants, and nucleotides on the effects of inflammation and post-operative healing.[207 210 211] Arginine supplemented diets, which may improve vasodilation and tissue oxygenation, have been examined in a large systematic review, and showed a reduction in overall infection (RR 0.59) and length of hospital stay with no difference in mortality compared with a heterogeneous control group of nutrition regimens.[212] Although most of the included trials were from gastric/colon surgery, one study in gynecologic oncology supported these results.[213] Several large randomized trials in colorectal patients compared an immune nutrition/high protein diet to a high calorie supplement and found a lower rate of infection and length of stay in the immune nutrition group.[214] Higher post-operative protein intake is also associated with earlier discharge.[215] Currently there are no definitive guidelines for surgical patients as it pertains to protein needs; however, in the acute care setting guidelines have recommended up to 2.0 g of protein/kg/day and 25–30 kcal/kg/day.[207 216] It appears that a high protein diet post-operatively may reduce complications and the role of immune nutrition and arginine supplementation continues to evolve.

Summary and Recommendation:
A regular diet within the first 24 hours after gynecologic/oncology surgery is recommended. High protein diets may be considered in post-operative management of surgical patients.

Evidence level:
Feeding within first 24 hours: high
High protein diet: moderate
Recommendation grade: strong

12. Prevention of Post-operative Ileus

Return of bowel function is often the last milestone met before post-operative hospital discharge after laparotomy. Rates of post-operative ileus as high as 30% have been reported among women undergoing open gynecologic cancer surgery,[217 218] and nearly 40% among women undergoing ovarian cancer debulking requiring a bowel resection.[218] Factors that influence the return of bowel function include, but are not limited to, exposure to opioids, fluid balance, extent of peritoneal disease and complexity of surgery, receipt of transfusion, and post-operative abdomino-pelvic complications.[218]

Several interventions have been shown to decrease the risk of post-operative ileus either through direct or indirect effects. The implementation of minimally invasive surgery reduces the rate of post-operative ileus[147]; however, not all patients are candidates for minimally invasive surgery. Among patients requiring laparotomy, interventions that stimulate the enteric nervous system and reduce opioid use have been shown to enhance bowel recovery time and reduce the rate of post-operative ileus. Simple interventions of early feeding, coffee consumption, and gum chewing have been shown to be effective in decreasing the time to bowel function return.[180 217 219–223] ERAS programs that include early feeding, as well as euvolemia, early ambulation, and multi-modal analgesia, have been shown to decrease the rate of post-operative ileus by two- to five-fold with current rates ranging from 3–10% in studies of women undergoing high complexity open gynecologic cancer surgery.[180 221] Post-operative coffee consumption has been shown to reduce the rate of post-operative ileus in women undergoing gynecologic cancer surgery from 30% to 10%.[217] While the use of chewing gum is safe and inexpensive, a large well-conducted randomized trial recently showed no benefit.[224]

Blocking or reducing the effect of opioids on the gastrointestinal tract has also been shown to reduce the time to bowel recovery and reduce the rate of post-operative ileus. Alvimopan is an oral selective μ-antagonist with very low bioavailability that works directly within the gastrointestinal tract to block the negative effects of opioids on gut motility. Randomized controlled trials in colorectal surgery, bladder resection and reconstruction, and ovarian cancer surgery have all demonstrated a reduction in time to bowel recovery and post-operative ileus in the setting of alvimopan use.[225–227] Alvimopan has been approved by the US Food and Drug Administration (FDA) for perioperative, in-hospital use for patients undergoing planned bowel resection and the first dose is given pre-operatively, before opioid exposure. Reduction in opioid consumption through implementation of ERAS pathways that leverage multimodal analgesia and/or liposomal bupivacaine have also led to reduced post-operative ileus rates.[180 221] In fact, the utilization of liposomal bupivacaine instead of bupivacaine-HCl as a single intervention change in an established ERAS protocol[37] reduced total opioid consumption and also reduced post-operative ileus by 50%.[180]

Summary and Recommendation:
Drinking coffee, as well as various other elements of ERAS pathways including euvolemia, opioid-sparing analgesia, and early feeding are safe, inexpensive, and appear effective in decreasing the time to return of bowel function. Alvimopan is FDA-approved to reduce the time to bowel function return and post-operative ileus-associated morbidity in patients undergoing

planned bowel resection. Liposomal bupivacaine may reduce opioid consumption and the rate of post-operative ileus.

Evidence level: high

Recommendation grade: strong

13. Patient Reported Outcomes, Including Functional Recovery

ERAS programs aim to accelerate and support patients' return to full functional recovery. Post-operative recovery follows a specific pattern that starts with a rapid deterioration from baseline function in the immediate post-operative period and then gradually rehabilitates back to or surpasses the pre-operative baseline.[228] The recovery process is complex and encompasses the multiple dimensions of physical, emotional, economic, and social health.[229]

Surgical recovery can be conceptualized to occur in three phases: early, intermediate, and late.[230] Patients spend the majority of the recovery period outside acute hospital settings, and thus it can be challenging to monitor and evaluate surgical recovery with standard metrics. Patient reported outcomes are uniquely positioned to track and study surgical recovery in a patient-centered fashion across multiple domains and longitudinally over time across all phases of recovery. Patient reported outcome instruments measure any aspect of a patient's health status with information derived directly from the patient.[231]

To date, there is a paucity of patient reported outcome studies focusing on gynecologic patients within ERAS programs. In one study comparing women undergoing open gynecologic surgery on and off an ERAS pathway, the ERAS cohort reported significantly lower symptom burden from fatigue, as well as lower total interference composite scores (symptom interference with work, activity, walking, enjoyment of life, mood, and relations with others).[177]

Time to recovery will vary depending on the dimension or symptom being measured. For example, economic recovery and return to work may lag behind emotional or physical dimensions of recovery. In one study, patients on an ERAS pathway reported return to mild or no fatigue in 10 days compared with 30 days for the pre-ERAS cohort, while returning to mild or no interference with walking after laparotomy was reported at a median of 5 days for ERAS patients compared with 13 days in the pre-ERAS group.[177] Patients undergoing minimally invasive surgery on an ERAS pathway reported a return to mild or no interference with walking at a median of 2 days.[152]

Consistent collection and documentation of patient reported outcomes within ERAS programs can help institutions monitor, understand, and compare patterns of recovery. Patient reported outcomes, including symptom burden assessment, can also be tracked to guide individual post-operative care. The RECOvER checklist, which outlines best practices for reporting on ERAS studies, recommends including references to validation of study instruments when reporting patient reported outcomes.[232] Careful consideration of instrument selection should go beyond whether the instrument was validated in a gynecologic surgical population, but should include thoughtful evaluation of the specific content and purpose of the instrument, responsivity in the gynecologic surgical population, designed recall period, minimally important difference, and mode of administration. Timing of measures should include a pre-operative baseline assessment, with the remainder of measurements designed thoughtfully based on an *a priori* hypothesis to balance patient burden with expected fluctuations in the patient reported outcome responses. Wearable technologies that track functions such as steps, distance walked, sleep, and other physiologic processes can also contribute to the documentation and understanding of functional recovery and post-operative mobilization.

Summary and recommendation:

Consistent collection and documentation of patient reported outcomes within ERAS programs allow institutions to monitor, understand, and compare functional recovery in a patient-centered fashion. Patient reported outcomes, including symptom burden assessment, can also be utilized to guide individual post-operative care. Validated instruments should be utilized.

Evidence level: low

Recommendation grade: strong

14. Role of ERAS in Pelvic Exenteration and Hyperthermic Intra-Peritoneal Chemotherapy

In this section of the guidelines, we focus on two procedures where the risk of perioperative complications and poor outcomes is high and thus aim to provide support for the consideration of implementation of the principles of the ERAS guidelines, highlighting a number of items considered most critical in the perioperative recovery of the patient.

Total pelvic exenteration remains one of the most extensive procedures performed in gynecologic oncology where post-operative morbidity is a major concern, with complication rates as high as 60–95%.[233 234] The post-operative 30-day mortality is 0.7% and the 90-day mortality is 2.2%.[235] The most common complications include urinary tract complications, wound dehiscence, infections, and organ system failure. Surgical complexity, hemoglobin levels, and the presence of three or more comorbidities are independently associated with severe complications.[235] A second procedure associated with high levels of perioperative morbidity is hyperthermic intra-peritoneal chemotherapy (HIPEC). Although it is considered an experimental procedure in the setting of gynecologic cancer in most centers, HIPEC is gaining increasing popularity in certain scenarios. Recent data from a prospective randomized trial evaluating the role of HIPEC in the setting of neoadjuvant chemotherapy showed that patients who underwent interval surgery plus HIPEC had an overall survival advantage over those who underwent surgery alone (45.7 months vs 33.9 months).[236] Complication rates are consistently high, with grade 3–4 morbidity in up to a third of patients.[237]

In the setting of such high complexity procedures, it is essential to implement strategies that will minimize complication rates and ideally return the patient as quickly as possible to normal daily activities. In these patients, elements such as pre-operative optimization, nutritional counseling and early post-operative feeding, perioperative fluid management, thromboembolism prophylaxis, balanced post-operative fluid therapy, perioperative glucose control, and early mobilization should ultimately translate into improved outcomes. Pre-operative counseling is a key element in compliance and thus all patients should be provided detailed information regarding the aims of the program. In patients undergoing pelvic exenteration or HIPEC therapy, insulin resistance may accentuate the already high risk of perioperative complications. Therefore, carbohydrate loading should be considered, as it may attenuate the increased insulin resistance related to such

prolonged and extensive surgery. Perioperative fluid management is also of paramount importance in major surgery and in high-risk patients. Anesthesiologists should therefore focus on the use of advanced hemodynamic monitoring to individualize fluid therapy and optimize oxygen delivery. Reduction in surgical site infection is key in patients undergoing pelvic exenteration or HIPEC therapy. Recent studies have shown that implementation of a comprehensive glycemic control initiative can lead to a decrease in surgical site infection from 14.6% to 5.7%.[109] In addition, early mobilization intuitively will promote a faster and safer recovery by reducing the risk of thromboembolic events, as well as the risk of pulmonary complications. In addition, emphasis on early ambulation will reduce muscle atrophy and will also prepare patients for a faster return to functional activity.

Summary and Recommendation:
There is currently a paucity of data on the impact of an ERAS program specifically targeting patients undergoing high complexity procedures, such as pelvic exenteration and HIPEC surgery. Further research is needed from high-volume referral centers in order to document outcomes of ERAS programs in this patient population.

Evidence level: low
Recommendation grade: weak

15. Discharge Pathways

Patients managed under an ERAS pathway are discharged in an intermediate phase of recovery, with the recovery process expected to extend into the home setting. Hospital discharge is a key transition phase for patients and caregivers. Assessing patients' readiness for discharge is an essential component of the discharge planning process.[238] Detailed education should be provided to the patient and caregiver. Important aspects of discharge education include the information content, the frequency of education, timing, and delivery method.

A decreased length of stay reduces the time available to provide discharge teaching, so it is recommended to initiate discharge education and expectations during the pre-operative visit. It is also crucial to provide tailored information to meet the needs of the individual patient. In a post-discharge follow-up study, the need to implement reliable protocols that identify patients who are at risk for poor understanding and execution of hospital discharge instructions was emphasized.[239]

A study published recently on an ERAS program for colorectal surgery showed that 93% of the patients were satisfied with the discharge information, and 90% felt they were ready for discharge.[240] Ensuring that patients' informational needs have been met before hospital discharge sets the stage for successful self-management of recovery at home.[241] With improved post-operative education and closer follow-up, it is estimated that 50% of hospital readmissions may be preventable.[242]

Summary and Recommendation:
Improved post-operative education for patients before discharge is required to facilitate patient-centered discharge planning. Such interventions may help decrease unplanned hospital visits during the immediate post-discharge period. It is recommended that patients and caregivers should routinely receive detailed education.

Evidence level: low
Recommendation grade: strong

16. ERAS Audit and Reporting

Implementation of ERAS requires coordination by a multidisciplinary team spanning the entire continuum of care from pre-operative counseling to return to normal function. Assessing adherence to specific ERAS elements is an essential component of an ERAS program. Observational studies from colorectal surgery including more than 10 000 patients have described a strong correlation between increasing compliance with ERAS guidelines and decreased rates of complications and shorter lengths of stay.[47 243] While there are no randomized studies in gynecologic oncology comparing auditing of compliance with ERAS elements to no auditing, a non-randomized Canadian prospective study of more than 500 gynecologic oncology patients using an ERAS compliance audit tool found that an increase in ERAS compliance from 56% to 77% was associated with a 31.4% reduction in adjusted length of stay and net cost savings of $952 per patient.[220] Active auditing appears to be more effective at achieving compliance than passive implementation alone.[244 245]

ERAS reporting should include enough information on compliance to define the impact of individual ERAS elements on outcomes. Insufficient reporting of compliance may lead to incorrect conclusions.[246] To improve the quality of ERAS reporting, ERAS USA and the ERAS Society have published the Reporting on ERAS Compliance, Outcomes, and Elements Research (RECOvER) Checklist. This tool delineates best practices for reporting clinical pathways and describing compliance.[232] Clinicians are encouraged to use ERAS auditing tools. Two examples include the ERAS Interactive Audit System (EIAS) (http://erassociety.org/interactive-audit/) and the Agency for Healthcare Research and Quality (AHRQ) safety program for improving surgical care and recovery (https://www.ahrq.gov/professionals/quality-patient-safety/hais/tools/enhanced-recovery/index.html).

Summary and Recommendation:
Auditing is an essential component of an ERAS program. Reports on ERAS pathways should include detailed information on the relationship between outcomes and compliance with individual ERAS elements.

Evidence level:
Use of auditing to improve compliance: high
Correlation of compliance with improved outcomes: moderate
Recommendation grade: strong

DISCUSSION

This guideline outlines the most current recommendations of the ERAS Society Group for the perioperative management of patients undergoing gynecologic/oncology surgery, and is based on the best available evidence. 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 surgical disciplines in which major abdominal surgery is routinely performed, and expert opinion from the panel. Our aim is for these guidelines

to define current standard of care and encourage investigators to address knowledge gaps. Defining best practice is challenging, yet simpler than the process of transforming best practice into routine surgical care through collaborative efforts between anesthesiologists, nurses, and surgeons. Every care team should continuously measure and analyze outcomes in order to adjust their care pathways to optimize outcomes and hasten recovery for patients undergoing gynecologic/oncology surgery.

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