Gynecologic Oncology 140 (2016) 313–322

Contents lists available at ScienceDirect

Gynecologic Oncology

journal homepage: www.elsevier.com/locate/ygyno

Guidelines for pre- and intra-operative care in gynecologic/oncology surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations — Part I

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HIGHLIGHTS

- We provide evidence supporting pre- and intra-operative management of patients undergoing gynecologic/oncology surgery.
- This guideline will help integrate knowledge into practice, align perioperative care, and encourage future investigations.

ARTICLE INFO

Article history:
Received 29 August 2015
Received in revised form 19 October 2015
Accepted 17 November 2015
Available online 18 November 2015

Keywords:
Enhanced Recovery After Surgery
Gynecologic/oncology
Evidence based perioperative care

1. Introduction

The systematic implementation of an evidence-based perioperative care protocol (or "enhanced recovery pathway," ERP), such as that developed by the Enhanced Recovery After Surgery (ERAS®) Society, has resulted in an average reduction in length of stay of 2.5 days and a decrease in complications by as much as 50% for patients undergoing colorectal surgery [1,2]. These benefits are achieved by reducing surgical stress, maintaining normal physiological function postoperatively, and enhancing mobilization after surgery [3]. Furthermore, use of ERP has resulted in a mean savings of $2245 (1651€) per patient [4]. ERAS® protocols have been published for rectal, urological, pancreatic and gastric surgeries [5–8]. Given the proven benefit to both the patient and the healthcare system, several international groups are currently working with the ERAS® Society to develop protocols specific for breast and reconstructive surgery, head and neck cancer, thoracic, hepatobiliary, and orthopedic surgery.

A recent review of ERP in gynecologic oncology [9] showed marked dissimilarities among the protocols and highlighted the need to develop a standardized, evidence-based guideline for our specialty. Standardizing perioperative care helps to ensure that all patients receive optimal treatment and is required to measure compliance. Auditing compliance has proven to be a key factor to successfully implement and sustain an ERAS® protocol. The goal of this article is to critically review existing evidence and make recommendations for elements of pre- and intra-operative care in our specialty. This effort forms the basis of the ERAS® Guideline for pre- and intra-operative care in gynecologic/oncology surgery.

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http://dx.doi.org/10.1016/j.ygyno.2015.11.015

2. Methods

2.1. Literature search

The authors convened in July 2014 to discuss topics for inclusion — the topic list was based on the ERAS® colonic surgery [1] and rectal/pelvic [5] guidelines which were used as templates. After the topics were agreed upon they were then allocated among the group according to expertise. The literature search (1966–2014) used Embase and PubMed to search medical subject headings including "gynecology", "gynecologic oncology" and all pre- and intra-operative ERAS® items (see Table 1). Reference lists of all eligible articles were crosschecked for other relevant studies.

2.2. Study selection

Titles and abstracts were screened by individual reviewers to identify potentially relevant articles. Discrepancies in judgment were resolved by the lead (GN) and senior authors (OL, SD). Meta-analyses, systematic reviews, randomized controlled studies, non-randomized controlled studies, reviews, and case series were considered for each individual topic.

2.3. Quality assessment and data analyses

The quality of evidence and recommendations were evaluated according to the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system (see Tables 2a and 2b) [10] whereby recommendations are given as follows: Strong recommendations indicate that the panel is confident that the desirable effects of adherence to a recommendation outweigh the undesirable effects. Weak recommendations indicate that 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 and very low, but also on the balance between desirable and undesirable effects. As such, consistent with other ERAS® Guideline Working groups [1,6], in some cases strong recommendations may be reached from low-quality data and vice versa. Of note, this would be considered a modified GRADE evaluation since we did not consider resource utilization when making our recommendations [11].

3. Results

The evidence base, recommendations, evidence level, and recommendation grade are provided for each individual ERAS® item below.

Table 1
Guidelines for pre- and intraoperative care in gynecologic/oncology surgery: Enhanced Recovery After Surgery (ERAS®) Society recommendations.

Item	Recommendation	Evidence level	Recommendation grade
Preoperative information education and counseling	Patients should routinely receive dedicated preoperative counseling	Low	Strong
Preoperative optimization	Smoking and alcohol consumption (alcohol abusers) should be stopped four weeks before surgery	Smoking: High Alcohol: Moderate	Strong Strong
	Anemia should be actively identified, investigated, and corrected preoperatively	High	Strong
Preoperative bowel preparation	Mechanical bowel preparation should not be used routinely even when bowel resection is planned	Moderate	Strong
Preoperative fasting and carbohydrate treatment	Clear fluids should be allowed up to 2 h and solids up to 6 h hours prior to induction of anesthesia	Solids/fluids: High	Strong
	Carbohydrate loading reduces postoperative insulin resistance and should be used routinely	Carb loading: Mod (outcome insulin resistance) Carb loading: Mod (other outcomes)	Strong
Preanesthetic medication	Routine administration of sedatives to reduce anxiety preoperatively should be avoided	Low	Strong
Thromboembolism prophylaxis	Patients at risk of VTE should receive prophylaxis with either LMWH or heparin, commenced preoperatively, combined with mechanical methods	High (Preop admin: Mod)	Strong
	Patients should be advised to consider stopping HRT or consider alternative preparations before surgery	Low	Weak
	Patients should discontinue oral contraception prior to surgery and switch to another form	High	Strong
Antimicrobial prophylaxis and skin preparation	IV antibiotics (1st generation cephalosporin or amoxi–clav) should be administered routinely within 60 min before skin incision; additional doses should be given during prolonged operations, severe blood loss and obese patients	High	Strong
	Hair clipping is preferred if hair removal is mandatory	High	Strong
	Chlorhexidine–alcohol is preferred to aqueous povidone-iodine solution for skin cleansing	High	Strong
Standard anesthetic protocol	Short acting anesthetic agents should be used to allow rapid awakening	Low	Strong
	A ventilation strategy using tidal volumes of 5–7 ml/kg with a PEEP of 4–6 cm H_2O should be employed to reduce postoperative pulmonary complications	Moderate	Strong
Postoperative nausea and vomiting	A multimodal approach to PONV with >2 antiemetic agents should be used for patients undergoing gynecologic procedures	Moderate	Strong
Minimally invasive surgery (MIS)	MIS is recommended for appropriate patients when expertise and resources are available	Morbidity: Low Recovery: High	Strong
Nasogastric intubation	Routine nasogastric intubation should be avoided	High	Strong
	Nasogastric tubes inserted during surgery should be removed before reversal of anesthesia		
Preventing intraoperative hypothermia	Maintenance of normothermia with suitable active warming devices should be used routinely	High	Strong
Perioperative fluid management	Very restrictive or liberal fluid regimes should be avoided in favor of euvolemia	High	Strong
	In major open surgery and for high risk patients where there is large blood loss (>7 ml/kg) or a SIRS response the use of advanced hemodynamic monitoring to facilitate individualized fluid therapy and optimize oxygen delivery during the perioperative period is recommended	Moderate	Strong

Table 2a
GRADE system for rating quality of evidence.

Evidence level	Definition
High quality	Further research unlikely to change confidence in estimate of effect
Moderate quality	Further research likely to have important impact on confidence in estimate of effect and may change the estimate
Low quality	Further research very likely to have important impact on confidence in estimate of effect and likely to change the estimate
Very low quality	Any estimate of effect is very uncertain

Ref. [10].

3.1. Preadmission information, education and counseling

Preoperative counseling helps to set expectations about surgical and anesthetic procedures and may diminish fear, fatigue, pain, and enhance recovery and early discharge [12]. Verbalized education, leaflets, and multimedia information containing explanations of the procedure and cognitive interventions may improve pain control, nausea and anxiety after surgery [13]. It is uncertain if formal education is superior to informal education [14], but 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 and nurse. Studies show that patients with gynecologic cancer prefer to be well informed, and support from a nurse at the time of diagnosis reduced stress levels for up to 6 months [15].

Summary and recommendation:

Although quality evidence is lacking, most studies show that counseling provides beneficial effects with no evidence of harm. It is recommended that patients should routinely receive dedicated preoperative counseling.

Evidence level:

Low.

Recommendation grade:

Strong.

3.2. Preadmission optimization

Use of tobacco, alcohol, and the presence of anemia should be routinely assessed preoperatively. Also, previously undiagnosed diabetes/hyperglycemic states are becoming increasingly common. Evidence that interventions addressing these factors prior to elective surgery reduce perioperative morbidity and mortality is presented below. For patients with gynecologic cancer, the risk of delaying surgery in order to complete preoperative optimization must be carefully considered.

3.2.1. Smoking

Smoking is associated with a high risk of postoperative complications, but the pulmonary effects of smoking can be improved within four weeks of cessation [16]. While smoking cessation interventions such as behavioral support and nicotine replacement therapy are known to result in short term smoking cessation, there is weak evidence to show that these measures decrease postoperative morbidity. A trial of varenicline showed an increase in long term smoking cessation but no evidence of a reduction in postoperative morbidity [17].

Table 2b
GRADE system for rating strength of recommendations.

Recommendation strength	Definition
Strong	When desirable effects of intervention clearly outweigh the undesirable effects, or clearly do not
Weak	When trade-offs are less certain — either because of low quality evidence or because evidence suggests desirable and undesirable effects are closely balanced

Ref. [10].

3.2.2. Alcohol

The chronic effects of alcohol on the liver, pancreas and neurologic system are well known. In the perioperative period, effects of alcohol on cardiac function, blood clotting, immune function, and response to surgical stress contribute to excess morbidity. Intensive preoperative interventions aimed at complete alcohol cessation for at least four weeks reduces postoperative complications, but does not significantly reduce mortality or length of stay. However, only a small number of studies are available, the mechanism by which such interventions reduce complications is unknown, and the optimal timing of the interventions has yet to be determined [18].

3.2.3. Preoperative hyperglycemia

A report by the American Society of Anesthesiologists in 2012 noted that up to 40% of preoperative patients may have an abnormal blood glucose level and of the 13% with diabetes, 40% were undiagnosed [19]. For the group with previously unrecognized hyperglycemia, the risk of adverse perioperative events was higher than the risks for patients with a known diagnosis of diabetes [20]. In a small study of 120 patients undergoing colorectal surgery, elevated hemoglobin A1c (HbA1c) was associated with an increased risk of postoperative complications [21]. The benefit of tight glycemic control has not been shown conclusively but the authors of one review suggest that "it seems prudent to control blood glucose to a reasonable level preoperatively", while acknowledging that "recommendations for exact targets cannot be made" [22]. The results of a number of studies on tight glycemic control (TGC) are contradictory. Complicated and variable protocols are used to achieve glycemic control, the duration of TCG varies between studies, and there are persistent concerns with hypoglycemia. Delaying surgery to correct hyperglycemia has not been shown to improve surgical outcomes in existing larger observational datasets [23].

3.2.4. Anemia

Preoperative anemia is associated with postoperative morbidity and mortality. A comprehensive review of blood management in Europe and the NHS Blood Transfusion Committee Guidelines in the UK advocate for preoperative screening for anemia. Anemia should be identified and corrected for iron deficiency and any underlying disorder before elective surgery [24]. Treating anemia preoperatively helps to avoid adverse effects from anemia, transfusion or both. The risks are increased with the severity of the anemia [25]. The speed of response to iron therapy (oral or intravenous) is greater in more severe iron deficiency anemia and therefore prompt identification and treatment is important to reduce the need for erythropoiesis-stimulating agents or transfusion. Although not gynecological-cancer specific, both erythropoiesis-stimulating agents and perioperative transfusion have been associated with poorer outcomes for cancer patients, with a Cochrane review showing an increase in cancer recurrence following perioperative transfusion [26,27].

The recent guideline from the British Committee for Hematology showed no strong evidence of benefit from preoperative transfusion to improve surgical outcomes (in cardiac surgery patients) and, in the absence of other blood management measures, did not reduce total transfusion requirements. Where transfusion is considered to be unavoidable there is no evidence to suggest advantages of pre- over intraoperative transfusion [25]. If possible, the focus should be on preventing further blood loss intraoperatively.

Summary and recommendations:

Smoking is associated with increased postoperative morbidity and should be stopped at least four weeks before surgery.

Alcohol is associated with increased perioperative morbidity and mortality and should be avoided for at least four weeks before surgery in patients who abuse alcohol.

Anemia is associated with an increase in postoperative morbidity and mortality and should be identified, investigated, and corrected preoperatively. Iron therapy is the preferred first line treatment for the correction of iron deficiency anemia.

Evidence level:
Smoking: High.
Alcohol: Moderate (small number of studies).
Anemia: High.
Recommendation grade:
Smoking: Strong.
Alcohol: Strong.
Anemia: Strong.

3.3. Preoperative mechanical bowel preparation

Mechanical bowel preparation (MBP) often results in patient distress, may cause dehydration, and evidence of benefit to the patient is lacking. A systematic review of 18 randomized clinical trials (5805 patients) found no statistically significant evidence that patients benefit from either bowel preparation or rectal enemas [28] — the infection and anastomotic leak rates in patients with a bowel preparation was 9.6% and 4.4%, respectively, compared to 8.5% and 4.5% for those without. The authors concluded that in colonic surgery, bowel cleansing may be safely omitted. Recently, a number of large retrospective studies have suggested that oral antibiotic bowel preparation may be associated with decreased infection rates [29]. This, however, has not been verified in randomized trials investigating oral antibiotics alone (without MBP) in sufficient numbers of patients. There is some debate currently as to the benefit of bowel preparation in patients undergoing low anterior resection. In a single-blind, RCT of rectal cancer patients undergoing low anterior resection, patients were randomized to preoperative MBP versus no preparation [30]. Overall and infectious morbidity were higher in the no MBP group. However, there was no significant difference in the rate of anastomotic leakage between groups. Further studies are required in this area.

Finally, the routine use of mechanical bowel preparation before minimally invasive gynecologic surgery has not been shown to improve intraoperative visualization, bowel handling, or ease of performing the procedure [31–33].

Summary and recommendation:

Routine oral mechanical bowel preparation should not be used in gynecologic/oncology surgery, including patients with a planned enteric resection.

Evidence level:
Moderate (extrapolated from results in colorectal patients).
Recommendation grade:
Strong.

3.4. Preoperative fasting and carbohydrate treatment

Scientific evidence has shown that intake of clear fluids until 2 h before surgery does not increase gastric content, reduce gastric fluid pH, or increase complication rates. Hence, in patients without conditions associated with delayed gastric emptying, the intake of clear fluids until 2 h before the induction of anesthesia as well as a 6 h fast for solid food is now recommended [34].

In order to reduce postoperative insulin resistance and associated increased risks for complications, carbohydrate loading before surgery has been advocated to achieve a metabolically fed state. In the last decade an increasing number of original studies, systematic reviews, and meta-analyses have shown that carbohydrate loading attenuates the increase in insulin resistance related to surgery, and hence should be used routinely in major abdominal surgery [1,35]. Carbohydrate drinks for preoperative use should be properly tested as not all carbohydrate drinks have the same effects on gastric emptying. Although no studies have been performed in patients undergoing major gynecological surgery, these findings are considered valid for gynecologic patients given similarities in patient characteristics. Randomized trials have demonstrated that preoperative carbohydrates improve wellbeing and reduce nausea and vomiting [36]. No studies have specifically addressed diabetic patients, although limited data indicate it is likely to be safe in well controlled diabetics.

Summary and recommendation:

Patients should be permitted to drink clear fluids until 2 h before anesthesia and surgery.

Patients should abstain from solids 6 h prior to induction of anesthesia.

Oral carbohydrate loading reduces postoperative insulin resistance, improves preoperative wellbeing, and should be used routinely.

Insufficient data is available for diabetic patients.

Evidence level:
Solids and fluids: High.
Carbohydrate loading, primary outcome insulin resistance: Moderate.
Carbohydrate loading other outcomes: Moderate.
Recommendation grade:
Fasting guidelines: Strong.
Carbohydrate loading: Strong.

3.5. Preanesthetic medication

Preoperative medications are widely used in major gynecological surgery to decrease anxiety. However, routine administration of long-acting sedatives within 12 h of surgery should be avoided due to its effects on immediate postoperative recovery [37]. In 2009, a Cochrane review of short-acting oral anxiolytics for outpatient surgery concluded that patients were successfully discharged. However, an impairment in psychomotor function was observed in some studies up to 4 h postoperatively, which may negatively influence the patient's ability to ambulate, eat and drink [37]. The use of short acting anxiolytics to address severe preoperative anxiety may be appropriate on a case by case basis.

Summary and recommendation:

Routine administration of sedatives to reduce anxiety preoperatively should be avoided in order to hasten postoperative recovery.

Evidence level:
Low.
Recommendation grade:
Strong.

3.6. Thromboembolism prophylaxis

Venous thromboembolism (VTE) is a major risk in gynecologic oncology patients with rates as high as 8% in endometrial cancer [38] and 38% in ovarian cancer [39]. An analysis from the Million Women study showed an increased risk of VTE 12 weeks postoperatively, with a risk of 1/85 for oncologic surgery and 1/365 for gynecologic surgery [40]. Patients undergoing oncologic surgery were at over 90 times the risk of VTE in the first 6 weeks. All gynecologic oncology patients with major surgery >30 min should receive VTE prophylaxis with either low molecular weight heparin (LMWH) or heparin [41]. Prophylaxis should be commenced preoperatively, combined with mechanical methods, and continued post-operatively [42].

3.6.1. Preoperative anticoagulation

Only one retrospective study has examined preoperative versus postoperative anticoagulation in gynecologic oncology, showing a decreased rate of DVT (8% vs. 1.9%; $p = 0.04$) and a decreased rate of DVT associated deaths (0 vs. 2; $p < 0.001$) when given preoperatively; all patients in this study received combined prophylaxis with medical and mechanical methods [43].

3.6.2. Intraoperative prophylaxis

Prophylactic anticoagulation has not been shown to increase risks of hemorrhage, thrombocytopenia or epidural hematoma. Low dose prophylactic heparin has been commonly used with less than 10 cases of reported spinal hematomas; however given the serious sequelae associated with spinal hematomas, epidural catheters and spinal anesthetics should not be placed or removed 12 h before or after the last dose of therapeutic heparin [44].

Pneumatic compression stockings reduce the rate of VTE when compared to observation within the first 5 days postoperatively [45]. Their efficacy is equivalent to heparin [46] and improved when combined with heparin [47] in gynecologic oncology patients.

3.6.3. Special circumstances

3.6.3.1. Hormone replacement therapy (HRT). A Cochrane review on long term hormone therapy for perimenopausal and postmenopausal women showed an elevated risk of thromboembolism in women treated with continuous combined HRT or estrogen used alone [48]. Extrapolating from this evidence, the use of HRT is viewed as a perioperative risk factor for thromboembolism [49]. In the United Kingdom both the National Institute for Health and Clinical Excellence (NICE) and the Royal College of Obstetricians and Gynecologists (RCOG) suggest that patients discontinue HRT 4 weeks before surgery, but stop short of a direct recommendation [50,51]. These recommendations acknowledge the paucity of direct evidence of HRT as a risk factor and emphasize the importance of discussing the risks and benefits of stopping HRT. Changing from an oral to a transdermal estrogen preparation may reduce thromboembolic risk; of note, most patients taking HRT will meet criteria to receive thromboprophylaxis.

3.6.3.2. Combined oral hormonal contraception. Combined oral hormonal contraception is a risk factor for postoperative thromboembolism. The risk of thromboembolism varies according to progesterone type, with levonorgestrel, norethisterone, and norgestimate associated with the lowest risk. Women should be encouraged to use an alternative form of contraception preoperatively. Continued use of combined oral hormonal contraception is an indication for thromboprophylaxis [50,51].

Summary and recommendation:

Patients at risk of VTE should receive prophylaxis with either LMWH or heparin, commenced preoperatively, combined with mechanical methods, and continued post-operatively.

HRT is a relative risk factor for postoperative thromboembolism and patients should be advised to consider stopping or switching to alternative preparations before surgery, taking into account the risks and benefits. If HRT is continued, thromboprophylaxis should be considered.

Combined oral hormonal contraception is a risk factor for thromboembolism. Patients should change to another form of contraception prior to surgery. If continued to the time of surgery, thromboprophylaxis should be prescribed.

Evidence level:

Stockings, pneumatic compression, LMWH: High.
Preoperative administration: Moderate.
HRT: Low.
Combined oral hormonal contraception: High.

Recommendation grade:

Pre-operative DVT prophylaxis: Strong.
HRT: Weak.
Combined oral hormonal contraception: Strong.

3.7. Antimicrobial prophylaxis and skin preparation

Most surgical interventions for gynecologic malignancies include total hysterectomy which is classified as a clean contaminated, or type II incision. Surgical site infections (SSI) in gynecology involve skin flora, vaginal flora, or enteric bacteria when the colon is entered. Prophylactic antibiotics should therefore be broad spectrum. Many studies and meta-analyses have demonstrated the benefits of antibiotic prophylaxis in reducing surgical site infection after vaginal or abdominal hysterectomy [52]. Cephalosporins are the most commonly recommended antibiotic class given their broad spectrum, low cost, and low allergenic potential [53]. Cefazolin is generally recommended for gynecologic interventions where antibiotic prophylaxis is mandatory. Amoxicillin–clavulanic acid has been shown to be equivalent to cefazolin and can also be used [54]. Antibiotics are administered intravenously within 1 h [55] before skin incision (usually at the time of anesthesia induction). The dose should be increased in obese patients (BMI > 35 or >100 kg) [56], and repeated after 1–2 times the half-life of the chosen medication in prolonged operations (eg. 3 h for cefazolin, half-life: 1.8 h) and in case of blood loss >1500 ml [57]. For patients allergic to penicillin/cephalosporin, a combination of clindamycin and gentamycin IV or a quinolone (eg. ciprofloxacin) can be used. Laparoscopic operations not contaminated by the genitourinary or digestive tracts do not require antimicrobial prophylaxis [58].

Skin preparation before surgery traditionally includes a shower, hair removal and the use of skin antiseptic solution. One Cochrane review addressed the topic of showering or bathing with different antiseptic solutions before surgery [59]. Showering using plain soap is as effective as chlorhexidine in reducing surgical site infection. Compared to shaving, hair clipping in the operating room immediately prior to surgery is associated with lower rates of SSI [60]. However, there is no clear evidence that hair removal reduces SSI, irrespective of the method chosen (shaving, hair clipping or depilatory cream). Therefore, hair removal should be avoided and if deemed necessary hair clipping is preferred.

Skin antiseptic is highly recommended. A RCT showed a 40% reduction in SSI when using chlorhexidine gluconate and isopropyl alcohol 70% compared to an aqueous solution of 10% povidone-iodine for skin cleansing in different clean-contaminated interventions [61]. Chlorhexidine–alcohol therefore is preferred over aqueous povidone-iodine solution although care must be taken to avoid ignition when electrocautery is used [62].

Summary and recommendation:

IV antibiotics should be administered routinely within 60 min before skin incision. The dose should be repeated in case of prolonged operations or severe blood loss and increased in obese patients.

Hair clipping is preferred if hair removal is mandatory.

Chlorhexidine–alcohol is preferred to aqueous povidone-iodine solution for skin cleansing.

Evidence level:

Antibiotic prophylaxis: High.
Hair clipping: High.
Chlorhexidine–alcohol: High.

Recommendation grade:

Antibiotic prophylaxis: Strong.
Hair clipping: Strong.
Chlorhexidine–alcohol: Strong.

3.8. Standard anesthetic protocol

To allow rapid awakening, anesthesia should be maintained with short-acting agents such as sevoflurane or desflurane, or continuous target controlled infusions of propofol. When combined with short-acting opioid analgesics such as remifentanil, this may allow a consistently rapid recovery. Propofol-based total intravenous anesthesia has fewer postoperative side effects and the advantage of producing less postoperative nausea and vomiting [63]. Nitrous oxide is associated with postoperative nausea and vomiting (PONV) when the baseline risk of vomiting is high [64]. Both laparoscopic procedures and gynecological surgery are independent predictors of PONV [65], so it is reasonable to omit N2O during laparoscopic gynecologic surgery to prevent PONV and prophylaxis with a combination of at least 2 antiemetics should be standard. Use of bispectral index (BIS) to guide anesthetic depth may allow

reduction of anesthetic dose and hence facilitate rapid awakening [66]. Regional anesthetic techniques are opioid sparing, reducing PONV and allowing more rapid awakening [67]. Recent studies have shown a reduction in pulmonary complications in patients undergoing open abdominal surgery when a lung protective ventilation strategy is utilized (TV5-7 ml/kg with PEEP 4–6 cm H_2O) [68].

Summary and recommendation:

Short acting anesthetic agents should be used to allow rapid awakening. The addition of regional anesthesia to general anesthesia is opioid sparing, helps reduce PONV, and allows more rapid awakening.

A ventilation strategy using tidal volumes of 5–7 ml/kg with a PEEP of 4–6 cm H_2O reduces postoperative pulmonary complications.

Evidence level:

Short acting general anesthesia: Low (lack of data).

Lung protective ventilation (5–7 ml/kg): Moderate.

Recommendation:

Short acting general anesthesia: Strong.

Lung protective ventilation: Strong.

3.9. Prevention of postoperative nausea and vomiting

Postoperative nausea and vomiting (PONV) is very common and troubling for patients undergoing gynecologic surgery. Vomiting occurs in 12–30% and nausea in 22–80% [69], potentially leading to prolonged hospitalization and distress. Several risk factors have been identified for PONV including: age <50 years, gynecologic surgery, laparoscopic surgery, female gender, history of PONV or motion sickness, non-smoking, use of volatile anesthetics, long duration of anesthesia, postoperative opioid use, obesity, and use of nitrous oxide [65,69]. A patient's risk of PONV may be assessed using a validated risk score [69,70], allowing the clinician to give prophylaxis to patients deemed to be at high risk.

Strategies for reducing PONV include administration of antiemetic prophylaxis to all patients receiving abdominal surgery and emetogenic anesthetics/analgesics; this would likely include a large proportion of gynecologic or gynecologic oncology patients. The second strategy is to decrease PONV risk by avoiding general anesthesia, using propofol infusions, avoiding nitrous oxide and volatile anesthetics, reducing opioid use, and decreasing the neostigmine dose [69,71]. Although regional interventions (e.g. transversus abdominis plane block) may decrease opioid use and postoperative pain, this may not directly translate into a PONV advantage in all cases [72].

A multimodal approach to PONV prevention is quickly becoming standard of care. Antiemetics are classified into the following categories: 5HT3 antagonists, NK-1 antagonists, corticosteroids, butyrophenones, antihistamines, anticholinergics and phenothiazines [69,73]. Combinations of two or more classes of antiemetics may enhance potency (e.g. aprepitant, ondansetron, midazolam, or haloperidol combined with dexamethasone) [69,74–77]. Although dexamethasone has good efficacy for PONV and pain control, its long term effects as an immunosuppressant are unknown [69]. If nausea and vomiting occurs postoperatively, an antiemetic drug from a different class should be selected. A 5-HT3 antagonist should be administered first since it is the only category that has been well studied for existing PONV [69,77,78]. Transdermal scopolamine has also been shown to decrease the rate of PONV with application the night before or on the same day as surgery [79].

Supplemental oxygen may reduce the risk of early vomiting, but has no overall effect on PONV, and is therefore no longer recommended for the prevention of PONV [69,79]. P6 acupoint stimulation has also been shown to decrease PONV regardless of timing of administration [80]. Other therapies including music therapy, isopropyl alcohol, aromatherapy, ginger, NG decompression, proton pump inhibitor and nicotine patches have been proposed, but are not supported by current evidence [69,81–85]. Alternative non-pharmacologic therapies are not commonly used due to difficulties with access and efficacy of existing drug therapies.

Summary and recommendations:

Patients undergoing gynecologic procedures should receive prophylaxis using a multimodal approach to PONV using more than two antiemetic agents.

The risk of PONV is reduced with increased utilization of regional anesthesia, decreasing or eliminating opioids, neostigmine, volatile anesthetics, and increasing propofol use.

Evidence level:

Moderate.

Recommendation grade:

Strong.

3.10. Minimally invasive surgery

The introduction of laparoscopy and, more recently, robotic surgery, 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 [86,87]. However, the perioperative benefits of this approach may be reduced by a number of elements, including uncontrolled pain, nausea and vomiting, fluid overload, limited ambulation, fatigue, and deconditioning, irrespective of the existence of postoperative complications. Age, blood loss, perioperative blood transfusion, and postoperative complications have been associated with prolonged length of stay after laparoscopic surgery [88].

While most investigations of ERAS programs have been performed in open surgery, there is mounting evidence that ERAS programs are also beneficial for patients undergoing laparoscopic surgery. The LAFA (LAparoscopy and/or FAst track multimodal management vs. standard of care) trial evaluated patients requiring segmental colectomy for colon cancer. The study included four arms (laparoscopy/ERAS vs. laparoscopy/traditional vs. open/ERAS vs. open/traditional). The investigators in this study concluded that the optimal perioperative treatment for patients requiring segmental colectomy for colon cancer was laparoscopic resection in combination with an ERAS program [89]. Furthermore, several reports have shown that implementation of an ERAS program may also be of benefit in the setting of vaginal hysterectomy, including a shorter length of hospital stay and higher patient satisfaction scores [90,91].

Elements of particular value for an ERAS program in minimally invasive surgery include avoidance of prolonged nasogastric intubation (see Nasogastric intubation, below), maintenance of normothermia, normovolemia with maintenance of adequate cardiac output (impacted in minimally invasive surgery by head-down position and pneumoperitoneum), prevention of postoperative ileus, and early mobilization [1].

Summary and recommendation:

Minimally invasive surgery (MIS), including vaginal surgery is preferred for appropriate patients when feasible.

Evidence level:

Morbidity: Low.

Recovery: High.

Recommendation grade:

Strong.

3.11. Nasogastric intubation

Meta-analyses have concluded that nasogastric intubation increases the risk of postoperative pneumonia (6% vs. 3%) after elective abdominal surgery. Moreover, nasogastric decompression does not reduce the risk of wound dehiscence or intestinal leaks [92]. In a prospective randomized trial comparing early feeding to nasogastric decompression after major open gynecologic oncology surgery, the authors found no significant difference in postoperative nausea and vomiting between

the two groups. Only 10% of the early feeding arm required nasogastric tube insertion because of sub-occlusive symptoms. Conversely, 88% of patients who had a nasogastric tube experienced moderate to severe discomfort. Time to passage of flatus or stools and length of hospital stay was significantly shorter in the early diet group [93].

One exception where gastric decompression by oro- or nasogastric intubation may be of benefit is during laparoscopic or robotic surgery, whereby decompression may be used to reduce risk of gastric perforation by trochar or Veress needle insertion. The tube, however, should be removed at extubation.

Summary and recommendation:

Routine nasogastric intubation should be avoided. Nasogastric tubes inserted during surgery should be removed before reversal of anesthesia.

Evidence level:

High.

Recommendation grade:

Strong.

3.12. Preventing intraoperative hypothermia

During anesthesia and major surgery there is a high risk of hypothermia due to exposure and impairment of the normal thermoregulatory response, resulting in accelerated heat loss [94]. Hypothermia has been shown to impair drug metabolism, adversely affect coagulation, and increase bleeding, cardiac morbidity, and wound infection [94–96]. Postoperative shivering also increases oxygen consumption at a critical time and can worsen pain [95]. It is important to maintain normothermia by active methods throughout the perioperative period, including prewarming patients to avoid an initial drop in body temperature [97]. Wound infections are significantly less common with the use of active warming compared to conventional methods, with an absolute risk reduction of 13% [95]. During surgery, warming using forced air blanket devices are effective and widely used [98]. Underbody warming mattresses are also effective and avoid the use of a blanket that may interfere with surgical access, particularly in robotic surgery [99]. Intravenous fluids should be warmed using a suitable device to avoid lowering body temperature [100]. Temperature monitoring should be used to guide therapy and to avoid *hyper*thermia, which also has deleterious effects on homeostasis. Patients who have prolonged surgery with a likelihood of a Systemic Inflammatory Response (SIRS), such as open debulking procedures, are at a higher risk of developing hyperpyrexia as surgery progresses if warming is not monitored. The most convenient site to measure core temperature during gynecological surgery is the nasopharynx. Warming should be continued into the postoperative period to ensure the patient leaves the post anesthetic care unit with a temperature >36.0 °C.

Summary and recommendation:

Patient temperature monitoring is mandatory to titrate warming devices and avoid hypo- and hyperpyrexia. Maintenance of normothermia with suitable active warming devices should be used routinely.

Evidence level:

Continuous measurement of core temperature for efficacy and compliance: High.

Use of active warming devices: High.

Recommendation grade:

Strong.

3.13. Principles of perioperative fluid balance

The aim of intravenous fluid therapy is to maintain normovolemia and reduce flux across the extracellular space. Enhanced recovery protocols and modern surgical techniques reduce the need for both total volume and duration of intravenous fluid therapy [101]. While salt and fluid overload in the postoperative period is a major cause of morbidity [102], very restrictive fluid regimes also lead to increased morbidity and mortality. There have been very few randomized trials investigating fluid therapy and hemodynamic monitoring in major gynecologic surgery. Hence recommendations are based on extrapolations from evidence in major intra-abdominal surgery. Patients undergoing colorectal resections randomized to a zero balance fluid regimen had fewer cardiopulmonary complications (7% vs. 24%; $p < 0.001$) compared to standard perioperative fluid management [103]. A meta-analysis of 9 randomized trials from nearly 1000 patients demonstrated that restrictive fluid therapy reduced morbidity (OR 0.41; $p = 0.005$) [104]. Importantly, these improvements in morbidity were not observed if fluid restriction was initiated only in the post-operative period.

Summary and recommendation:

Very restrictive or liberal fluid regimes should be avoided in favor of euvolemia.

Evidence level:

High.

Recommendation grade:

Strong.

3.14. Intraoperative fluid therapy and advanced hemodynamic monitoring

Anesthetic drugs, intermittent positive pressure ventilation, and the use of regional anesthetic techniques all have different effects on vasomotor tone causing arteriolar and venous dilatation leading to hypotension. Therefore, once intravascular volume is normalized during surgery, vasopressors should be used to maintain mean arterial pressure when needed to avoid fluid excess. Central venous catheters may be needed to administer vasopressors and can be used in the immediate post-operative period to guide fluid administration by deriving oxygen extraction from the SCVO2. The head down position and pneumoperitoneum used during MIS can cause difficulty in interpreting monitoring. The fluid requirements during MIS in gynecology surgery are reduced as compared with open surgery.

Arterial lines can be used to measure arterial blood gases giving important information about oxygenation, effective ventilation, blood pH, and lactate as a marker for cellular perfusion. Dynamic changes in arterial waveform derived values such as systolic pressure, pulse pressure and stroke volume can be useful as predictors of fluid responsiveness [105], but when noradrenaline infusions are used the fluid response does not concur with the Esophageal Doppler Monitor (EDM) [106]. There have been two studies in gynecology patients within an ERP using EDM. The first showed minimal improvement, with a reduction in length of stay from 7 to 6 days [107], but the second study showed a benefit in patients with advanced cancer including an earlier return to gut function as well as reduced length of stay [108]. The benefit from the use of EDM in fit elective patients undergoing uncomplicated surgery within an ERAS Protocol is presently unclear [109] and regular fluid challenges in anaerobically fit patients without an endpoint may lead to harm [110]. High risk patients benefit most from optimization of oxygen delivery using inotropes in addition to fluid [111].

Summary and recommendation:

In major open surgery and for high-risk patients where there is large blood loss (>7 ml/kg) or a SIRS response, the use of advanced hemodynamic monitoring to facilitate individualized fluid therapy and optimize oxygen delivery through the perioperative period is recommended.

Evidence level:

Moderate.

Recommendation grade:

Strong.

4. Discussion

This guideline outlines the recommendations of the ERAS Group for the pre- and intraoperative management of patients undergoing gynecologic and gynecologic oncology surgery, and is based on the best available evidence. However, in some instances good quality data was

not available for gynecologic/oncology patients. In these instances recommendations were made based on findings from other surgical disciplines, including colorectal surgery, in which major abdominal surgery is routinely utilized. We are hopeful that individuals and groups of surgeons will use these guidelines to help integrate existing knowledge into practice, align perioperative care, and encourage future investigations of optimal perioperative care for patients undergoing gynecologic/oncology surgery.

Conflict of interest statement

Dr. Acheson reports personal fees from Baxter UK Ltd., outside the submitted work. In addition, Dr. Acheson has a commercial (future royalties on a medical device in development) relationship with Mediplus Ltd. He has also held the following appointments: Joint National Clinical Advisor (Gynaecology) to the Enhanced Recovery Partnership Programme, Department of Health (2010–2011), and continued under NHS Improvement (2011–2013); Member of Steering Board, Enhanced Recovery ERAS (UK) (2011–2013).

Dr. Scott received honoraria for lecturing and travel expenses from Baxter Healthcare, Merck, and Deltex. He is an Executive Committee member of the ERAS Society.

Dr. Ljungqvist has an appointment with Nutricia Advisory Board, has received speakers honoraria from Nutricia, MSD, BBraun and Fresenius-Kabi. He is the current Chairman of the ERAS Society (www.erassociety.org). He founded, serves on the Board and owns stock in Encare AB that runs the ERAS Society Interactive Audit System (EIAS).

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