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Enhanced recovery after surgery (ERAS®) in gynecologic oncology – Practical considerations for program development

G. Nelson [a,*], S.C. Dowdy [b], J. Lasala [c], G. Mena [c], J. Bakkum-Gamez [b], L.A. Meyer [d], M.D. Iniesta [d], P.T. Ramirez [d]

[a] Department of Gynecologic Oncology, Tom Baker Cancer Centre, Calgary, Alberta, Canada
[b] Division of Gynecologic Oncology, Mayo Clinic College of Medicine, Rochester, MN, United States
[c] Department of Anesthesiology and Perioperative Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, United States
[d] Department of Gynecologic Oncology and Reproductive Medicine, The University of Texas MD Anderson Cancer Center, Houston, TX, United States

HIGHLIGHTS

- There is widespread interest in the ERAS® guidelines for gynecologic oncology.
- Many clinical departments still struggle with how to initiate their ERAS® program.
- These recommendations will help translate the ERAS® guidelines into practice.

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There has been widespread interest in the Enhanced Recovery After Surgery (ERAS®) guidelines in gynecologic oncology [1,2] as evidenced by these articles being among the most downloaded from the *Journal* since February 2016 [3]. Despite this, many clinical departments still grapple with how to initiate their ERAS® program, particularly as it relates to translating the guidelines into an actual protocol.

To date there have been few programs that have fully implemented a structured ERAS® program in gynecologic oncology – remembering that a formal program requires three elements: i) an ERAS® protocol, ii) an audit system (database) to review protocol compliance and clinical outcomes, and iii) an ERAS® team that iterates towards improved compliance and outcomes [4,5,6].

In order to address the growing demand for assistance in initiating an ERAS® program, we describe below a series of recommendations to serve as a primer for program development. While these recommendations are primarily aimed at patients undergoing laparotomy for gynecologic cancer, the majority of the recommendations are equally applicable to those undergoing minimally invasive surgery.

1. ERAS® protocol

Some protocol recommendations are quite prescriptive and include dosages and timing of administration, while others are more general and will require discussion among the ERAS® team prior to implementation. In rare instances, no standard of care exists and more than one option is provided.

1.1. Preoperative interventions

All patients should undergo extensive counseling by the surgeon, advanced practice provider, clinical nurse, and anesthesiologist regarding anticipated expectations of the patient and the healthcare team. An informational brochure that addresses patient expectations and provides education regarding the ERAS® protocol should be provided in each patient's preoperative information package.

The use of preoperative bowel preparation continues to be an area of controversy in which no standard of care exists. A multitude of randomized trials have demonstrated that mechanical bowel preparation alone has no impact on rates of surgical site infection (SSI) or enteric leak, but may result in electrolyte imbalances and dehydration, and interfere with maintenance of euvolemia [7]. Retrospective data has shown that combining mechanical bowel preparation with oral antibiotics is associated with reduced rates of SSI and enteric leak [8]. However, some gynecologic oncology practices have published very low rates of SSI and enteric leak despite omission of mechanical bowel preparation and oral antibiotics [9]. Thus, the decision for bowel preparation must be

* Corresponding author at: Tom Baker Cancer Centre, 1331 29th St NW, Calgary, Alberta T2N 4N2, Canada.
E-mail address: gsnelson@ucalgary.ca (G. Nelson).

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made according to the stance taken at each institution and, if included, should contain an oral antibiotic component.

Eliminating prolonged fasting prior to surgery remains an obstacle at many institutions. Anesthesiologists should be aware that the recommendations below are taken directly from the American Society of Anesthesiologist's own guidelines [10].

1.1.1. Preoperative optimization

- ☐ Bowel preparation
  - No mechanical bowel preparation [7]
  - If oral bowel preparation included, Neomycin 1 g PO + metronidazole 500 mg PO at 1:00 PM, 2:00 PM, and 10:00 PM day prior to surgery [11]
  - Rectal enema prn prior to procedure start if anticipating low anterior resection
- ☐ Evening before surgery
  - If morning case: may eat solids until midnight
  - If afternoon case: light snack (dry toast and fruit) allowed up to 6–8 h prior to procedure [10]
- ☐ Morning of surgery
  - May ingest clear fluids (excluding alcohol) up to 2–4 h before procedure
  - Carbohydrate loading drink (preferably composed of complex carbohydrates that empty readily from the stomach) 2 h prior to surgery [12–14]

1.1.2. Preoperative medications

1.1.2.1. Analgesic. (To be administered in the preoperative holding area; dose adjustment may be required based on age and/or co-morbid condition; see Fig. 1)

- ☐ Acetaminophen 1000 mg PO/IV once
- ☐ Celecoxib 400 mg PO once
- ☐ Tramadol-ER 300 mg PO once
- ☐ Gabapentin 300–600 mg PO once *or* Pregabalin 75 mg PO once

- Pregabalin 75 mg/Gabapentin 300 mg
  1. Contraindicated (CI) if hypersensitivity to Pregabalin or Gabapentin
  2. Avoid in over 65 years of age (as the risk/benefit profile for side effects is high in this patient population, although age in itself is not a CI)
- Celecoxib 400 mg (Age in itself is not a CI)
  1. CI if hypersensitivity to celecoxib (not sulfa allergy)
  2. CI if active GI bleeding
  3. CI with CrCl <30 mL/min
  4. Decrease dose to 200 mg for Child-Pugh Class B
  5. CI if Child-Pugh Class C
  6. CI in patients with NYHA Functional classification (II and above)
- Tramadol ER 300 mg
  1. CI if hypersensitivity to Tramadol
  2. Hold if history of seizure/epilepsy or risk of seizure (although this is a soft CI particularly if the history of seizure is remote, of unknown cause and the patient is currently not on treatment and asymptomatic)
  3. CI if CrCl <30 mL/min
  4. CI if Child-Pugh Class C
  5. CI with concurrent MAOI therapy (not an issue in the patient with SSRIs if dosing guidelines for Tramadol are followed)

Fig. 1. Considerations of clinical scenarios for omission or dose reduction of ERAS® protocol premedications.

For patients undergoing minimally invasive surgery, especially within the context of anticipated discharge on the day of surgery, omission of Tramadol ER and Gabapentin/Pregabalin as premedication is a reasonable consideration.

1.1.2.2. Venothromboembolic (VTE) prophylaxis.

- ☐ Heparin 5000 U SC given preoperatively or after induction of anesthesia [15]
- ☐ Sequential compression devices placed prior to induction of anesthesia

1.2. Intraoperative optimization

The specific anesthetic protocol utilized will vary between institutions, but we encourage standardization within each practice. To that aim, we have provided general guidelines focused towards recovery, rather than simply intraoperative status. Maintaining euvolemia during the entire perioperative period is particularly critical and requires excellent communication with the anesthesiology team. The use of local wound infiltration is accompanied by minimal side effects and may contribute to significant reductions in opioid requirements in the postoperative period.

1.2.1. Intraoperative prophylaxis

1.2.1.1. Antimicrobial.

- ☐ Bathe or shower with soap or antiseptic agent the night before surgery [16]
- ☐ Chlorhexidine–alcohol for skin cleansing [17]
- ☐ If no bowel resection anticipated: Cefazolin 2 g IV before incision (3 g if weight > 120 kg)
- ☐ If bowel resection anticipated: Cefazolin 2 g IV before incision (3 g if weight > 120 kg) + Metronidazole 500 mg IV *or* Ertapenem 1 g IV [18]

1.2.1.2. Antiemetic. Administer postoperative nausea and vomiting (PONV) prophylaxis using ≥2 antiemetics (multimodal approach) given that patients undergoing gynecologic oncology surgery typically are at high risk for PONV [19]. Antiemetics to choose from include:

- ☐ Aprepitant 40 mg PO at induction
- ☐ Dexamethasone 4–5 mg IV at induction
- ☐ Droperidol 0.625–1.25 mg IV end of surgery
- ☐ Ondansetron 4 mg IV end of surgery
- ☐ Promethazine 6.25–12.5 mg IV at induction or end of surgery
- ☐ Scopolamine transdermal patch prior evening or 2 h before surgery

1.2.2. Anesthesia

- ☐ Epidural or spinal where indications exist [20,21]
- ☐ Opioid sparing techniques and multimodal analgesia.
- ☐ Consideration of Total Intravenous Anesthesia (TIVA), suggestions include:
  - Propofol (main anesthetic agent) titrated to clinical effect and bispectral index (BIS) 40–60
  - Dexamethasone 10 mg IV
  - Acetaminophen 1000 mg IV q6 h
  - Dexmedetomidine 0.3 mcg/kg/h IV
  - Ketamine 10 mg/h IV
  - Lidocaine 2 mg/min IV
- ☐ Short acting anesthetic agents (e.g. sevoflurane, desflurane, nitrous oxide) should be used if TIVA not performed.

- ☐ Local wound infiltration (options):
  - Bupivicaine 0.25% with epinephrine at incision site
  - Liposomal bupivacaine 266 mg (20 mL) diluted to at least 180 mL of sterile saline injected at incision site [22]
  - Subcostal Transversus Abdominus Plane (sTAP) infiltration of Bupivicaine 0.25% with epinephrine and Transversus Abdominis Plane (TAP) infiltration to cover all 4 quadrants.

1.2.3. Best surgical practices

- ☐ Avoidance of surgical drains [23] and nasogastric tubes [24]

1.2.4. Maintenance of normothermia

- ☐ Use of active warming device (started in preoperative holding area if possible) [16]

1.2.5. Fluid therapy

- ☐ Use of lactated ringers to reduce salt load
- ☐ Very restrictive or liberal fluid regimes should be avoided
- ☐ Use of goal-directed fluid therapy (non-invasive cardiac output monitoring) where available.

1.3. Postoperative optimization

To a large extent, rapid recovery is a function of adherence to pre- and intra-operative optimization elements. Only the minimum amount of opioid should be used to achieve pain control in the postoperative period that allows for ambulation, while reducing nausea, constipation, and the potential for opioid dependence.

1.3.1. Diet

- ☐ Solid diet (regular or low fat/fiber) started postoperative day (POD) 0 [25]
- ☐ Chewing gum orally for 30 min after meals three times per day (TID) as tolerated starting on POD 0 [26]
- ☐ Oral Nutritional Supplement (e.g. Ensure Plus, Twocal HN) on POD 0 and continue until discharge
- ☐ Glycemic control to maintain blood glucose levels <200 mg/dL [16]

1.3.2. Analgesia

- ☐ Acetaminophen 1000 mg PO q6h (should not exceed 4000 mg/24 h from all sources) (start POD 0)
- ☐ Ibuprofen 400–800 mg PO q6h (start POD 1)
- ☐ Pregabalin 75 mg PO BID × 48 h (start pm POD 1)

If scheduled acetaminophen and ibuprofen ineffective (or if contraindications exist):

- ☐ Oxycodone 5–10 mg PO q4 h prn
- ☐ Tramadol 100 mg PO q4-6 h prn
- ☐ Opioid IV (e.g. hydromorphone 0.5 mg IV q30 min prn) only if PO opioid medications ineffective within 30 min
- ☐ PCA started only if patient requires two doses or more of IV opioids in a 24 h period

1.3.3. Antiemetic

- ☐ Ondansetron 4 mg PO q6 h prn nausea
- ☐ Prochlorperazine 10 mg IV q6h breakthrough nausea after 30 min Ondansetron

1.3.4. Fluid therapy

- ☐ Fluids at 40 mL/h postoperatively (typical duration 8–12 h)
- ☐ Fluid bolus of 250–500 mL for urine output <20 mL/h
- ☐ Peripheral lock IV when patient has 600 mL oral intake

1.3.5. Best surgical practices

- ☐ Remove Foley catheter POD1 in am in the absence of contraindications (i.e. bladder reconstruction) [27]

1.3.6. Activity

- ☐ Ambulate 8×/day
- ☐ All meals in chair
- ☐ Out of bed 8 h/day

1.3.7. Bowel Routine, choose one or more of the following (hold if diarrhea develops)

- ☐ Senna 1–2 tabs PO qhs
- ☐ Magnesium hydroxide 25 mL PO qhs
- ☐ Lactulose 15–30 mL PO TID
- ☐ Polyethylene glycol (PEG) 3350 17 g PO daily
- ☐ Psyllium mucilloid powder 1–2 packets PO daily

1.3.8. Venothromboembolic (VTE) prophylaxis

- ☐ Low molecular weight heparin (e.g. Dalteparin 5000 U SC daily or equivalent) starting POD 1 (regimen continued for 28 days for all patients undergoing laparotomy for cancer) [15]
- ☐ Sequential compression devices while in bed in hospital

2. ERAS® program audit

Audit is a necessary component within an ERAS® program. Either use of the ERAS® Interactive Audit System (EIAS) or a tailored database allows measurement of compliance to the individual recommendations within the ERAS® Gynecologic/Oncology guidelines [1,2]. At a minimum, the database should record each of the compliance elements and also importantly length of hospital stay (LOS), readmissions, and complications until 30 days post-discharge. It is well established that improved overall compliance is associated with reductions in both complications and hospital stay [28]. Audit allows the establishment of baseline compliance, LOS and complications pre-ERAS® implementation such that following formal implementation of the ERAS® program, efforts can be focused on areas where compliance is less than ideal and therefore iterate towards improved outcomes.

3. ERAS® team development

A critical component for any successful ERAS® program is the development of a multi-disciplinary team that facilitates input from varying expertise and perspectives with the ultimate goal of reviewing ERAS® element compliance (obtained from audit) and iterating towards improved perioperative outcomes. In order to establish such a team, the following members should be considered:

- Gynecologic oncology surgeons
- Anesthesiologists and nurse anesthetists
- Residents, fellows, advanced practice providers (NP/PAs)
- Preoperative nursing team
- Operating room nursing team
- Recovery room nursing team
- Outpatient and inpatient nursing team

- Outpatient and inpatient pharmacist
- Preoperative and postoperative dietitian
- Research data coordinators
- Data manager and statistician

It is highly recommended that the team meet consistently (at minimum every two weeks) to ensure that there is continuity of flow in addressing critical issues regarding implementation, compliance, and growth of the ERAS® program. Team members should also be leaders in their respective disciplines in order to communicate practice changes back to each stakeholder group to facilitate implementation and troubleshooting.

4. Conclusion

The initiation of an ERAS® program requires steadfast effort from the entire team along the surgical care continuum. The benefits of such efforts are well established with the majority of clinical units now consistently reporting reductions in LOS and complications [29], both of which are beneficial to the patient and healthcare system [30]. Recent economic analyses have shown that ERAS® resulted in cost-savings of US$4219-7642 per patient and highlight that ERAS® is an excellent example of value based surgery [31,32]. Some studies have even suggested there is a survival benefit when patients are cared for with an ERAS® pathway [33], although this observation requires further validation.

Finally, with more and more centers now expressing interest in developing their own ERAS® program, our hope is that this set of recommendations helps to bridge the gap that often exists when one attempts to translate guidelines into clinical practice. It is important to recognize, however, that a protocol does not equate to a program and centers aiming for success are encouraged to seek help from ERAS® Centers of Excellence and also through formal implementation programs established by organizations such as ERAS®USA and the ERAS® Society.

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