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A Call for New Standard of Care in Perioperative Gynecologic Oncology Practice: Impact of Enhanced Recovery After Surgery (ERAS) Programs

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Abstract

Enhanced recovery after surgery (ERAS) programs aim to hasten functional recovery and improve postoperative outcomes. However, there is a paucity of data on ERAS programs in gynecologic surgery. We reviewed the published literature on ERAS programs in colorectal surgery, general gynecologic surgery, and gynecologic oncology surgery to evaluate the impact of such programs on outcomes, and to identify key elements in establishing a successful ERAS program. ERAS programs are associated with shorter length of hospital stay, a reduction in overall health care costs, and improvements in patient satisfaction. We suggest an ERAS program for gynecologic oncology practice involving preoperative, intraoperative, and postoperative strategies including; preadmission counseling, avoidance of preoperative bowel preparation, use of opioid-sparing multimodal perioperative analgesia (including loco-regional analgesia), intraoperative goal-directed fluid therapy (GDT), and use of minimally invasive surgical techniques with avoidance of routine use of nasogastric tube, drains and/or catheters. Postoperatively, it is important to encourage early feeding, early mobilization, timely removal of tubes and drains, if present, and function oriented multimodal analgesia regimens. Successful implementation of an ERAS program requires a multidisciplinary team effort and active participation of the patient in their goal-oriented functional recovery program. However, future outcome studies should evaluate the efficacy of an intervention within the pathway, include objective measures of symptom burden and

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control, study measures of functional recovery, and quantify outcomes of the program in relation to the rates of adherence to the key elements of care in gynecologic oncology such as oncologic outcomes and return to intended oncologic therapy (RIOT).

INTRODUCTION

The concept of a multimodal approach to improve functional rehabilitation after surgery was first introduced by Kehlet in the 1990s [1]. Kehlet suggested that a focus on early postoperative rehabilitation and nutrition, use of regional analgesia, and avoiding the use of recovery-limiting procedures (such as liberal use of intravenous fluids, and placement of a urinary bladder catheter and drains) might lead to accelerated recovery and reduced postoperative morbidity and costs.

Since the publication of Kehlet's review [1], a number of centers have published their experience and outcomes with ERAS programs, mainly for patients undergoing colorectal surgery but also for patients undergoing other major surgical procedures including gynecologic or gynecologic oncology surgery. The main goals of ERAS programs described to date are to reduce the length of hospital stay after surgery and speed patients' return to normal daily activities without increasing complications, readmission rates, or cost. To achieve these goals, ERAS programs focus primarily on reducing perioperative stress, achieving satisfactory pain control, resumption of normal gastrointestinal function, and early mobilization. A recent publication by the Royal College of Obstetricians and Gynecologist [2] reviews the main elements of ERAS and suggests that ERAS programs offer safe, high-quality perioperative care, and should become standard practice for all women undergoing elective gynecologic surgery. However, there are no randomized controlled trials to date of the benefits of an ERAS program over standard care in gynecologic oncology surgery.

We reviewed the published literature on ERAS programs in colorectal surgery, general gynecology, and gynecologic oncology to evaluate the impact of such programs on outcomes, as well as to identify key elements in establishing a successful ERAS program in gynecology patients undergoing surgery, especially those affected by gynecologic cancer.

METHODS

We searched the Medline, EMBASE, PubMed, and Cochrane Library databases for articles published in English with the following keywords: *enhanced recovery*, *ERAS*, *fast-track surgery*. These were combined with the keywords anesthesia, *colorectal surgery, gynecologic surgery*, or *gynecologic oncology*. Our search was limited to the period from January 2000 through December 2015.

From the articles identified, we selected reports of randomized controlled trials, case-control studies, and case series that reported on any of the following parameters in the context of an established ERAS or fast-track surgery program: length of hospital stay, postoperative pain and analgesia, bowel function, perioperative complications, readmissions rates, and cost analysis. We excluded case reports and reports that mentioned an ERAS parameter but not in

the context of an established ERAS program. Finally, we reviewed the key elements in ERAS program, and we evaluated the impact of such program.

RESULTS

Colorectal Surgery

Most of the ERAS data in the literature relate to colorectal surgery. One of the first studies to evaluate ERAS was a study reported in 2000 by Basse et al. [3], who prospectively studied 60 patients undergoing elective colonic resection with an enhanced recovery program including continuous thoracic epidural analgesia, enforced early mobilization, and enteral nutrition. The median length of hospital stay was 2 days. The majority of patients (57 of 60) tolerated early enteral nutrition and experienced return of bowel function within 48 hours. Nine patients (15%) required readmission, 2 patients (3.3%) died, and 5 patients (8.3%) had complications, which included anastomotic leakage, small bowel infarction, and wound dehiscence. During the 30 days of follow-up, 73% of the patients (44 of 60) were satisfied with their postoperative care. The authors concluded that compared to traditional care, enhanced recovery program may reduce postoperative length of stay and the rate of complications in high-risk patients undergoing colonic resection. Since the report by Basse et al., a number of other investigators have reported significant reduction in postoperative length of hospital stay on implementation of ERAS programs for patients undergoing colorectal surgery [4–6].

Several versions of comprehensive evidence-based consensus review of optimal ERAS programs for patients undergoing colorectal surgery have been published over the years [7,8]. The last one by the ERAS Society in 2013 [9] discussed the evidence available for each element of the multi-modal perioperative care pathway and provided a 20-item consensus guideline. Among the key recommendations were the following:

- Patients should receive adequate preadmission information, counseling and optimization.
- Bowel preparation should not be used routinely for elective colonic resection but may be considered when low rectal resection or intraoperative colonoscopy is planned.
- Patients should engage in carbohydrate loading before midnight and 2 or 3 hours before surgery.
- Patients should refrain from consuming liquids for 2 hours prior to surgery and solids for 6 hours prior to surgery.
- Long or short-term sedative agents should not routinely be used as pre-anesthetic medication.
- Subcutaneous heparin, intermittent pneumatic compression and antibiotics should be administered as prophylactic care.
- A multimodal approach to prevent and treat postoperative nausea and vomiting should be considered.

- Surgery should consist of laparoscopy-assisted surgery or open surgery with the shortest appropriate surgical incisions, and recommends that drainage of the peritoneal cavity after colonic surgery is not routinely indicated.
- During surgery, routine placement of a nasogastric tube should be avoided, hypothermia should be prevented, and fluid management should be optimized. For patients undergoing pelvic surgery, suprapubic urinary drainage was recommended.
- After surgery, fluid overload should be avoided; in addition, administration of a laxative such as magnesium oxide may be considered.
- Encourage early mobilization as well as early enteral feeding combined with nutritional supplements. Oral nutritional supplements have been prescribed on the day before surgery and for at least the first 4 postoperative days.
- Finally, a systematic audit should be performed to establish the successful implementation of an ERAS program.

Varadhan et al. [10] recently published a meta-analysis of 6 randomized controlled trials comparing ERAS programs with conventional perioperative care in 452 patients undergoing major open colorectal surgery. The more common ERAS elements used in these trials were preoperative counseling, epidural analgesia, avoidance of routine use of nasogastric tubes or drains, and enforced postoperative mobilization and oral feeding. The authors found that ERAS was associated with a reduction in median length of hospital stay of 2.5 days and nearly a 50% reduction in complication rates. No difference was noted between the ERAS and conventional-care groups in readmission rates (relative risk [RR] for ERAS vs. conventional care, 0.80; 95% CI, 0.32–1.98; $p = 0.62$) or mortality rates (RR for ERAS vs. conventional care, 0.53; 95% CI, 0.09–3.15; $p = 0.49$).

In another recent meta-analysis, Zhuang et al. [11] analyzed 13 randomized controlled trials in which a total of 1,910 patients underwent colorectal surgery by laparoscopy or laparotomy for malignant or benign disease. To be included in the meta-analysis, trials had to implement at least 7 of the 20 items in the aforementioned ERAS Society guidelines [9]. The more common items included were preadmission counseling, avoidance of preoperative bowel preparation, preoperative carbohydrate loading, preoperative fasting, standard anesthetic protocol, avoidance of routine use of nasogastric tubes, adherence to ERAS Group guidelines for postoperative analgesia, early enteral nutrition, and early mobilization. Compared to conventional perioperative care, the ERAS program was associated with significantly reduced median number of days in hospital from surgery until discharge (weighted mean difference, −2.44 days; 95% CI, −3.06 to −1.83 days; $p < 0.00001$), total hospital stay, including additional hospital days for readmissions (weighted mean difference, −2.39 days; 95% CI, −3.70 to −1.09 days; $p = 0.0003$), total complications (RR, 0.71; 95% CI, 0.58–0.86; $p = 0.0006$), and general complications which included all complications (RR, 0.68; 95% CI, 0.56–0.82; $p < 0.0001$). No significant differences were found for readmission rates (RR for ERAS vs. conventional care, 0.93; $p = 0.88$), surgical complications, (RR for ERAS vs. conventional care, 0.90, $p = 0.29$), or mortality (RR for ERAS vs. conventional care, 1.02, $p=0.97$).

Vlug et al. [12] and van Bree et al. [13] evaluated both the impact of minimally invasive surgery and the impact of an ERAS program in patients undergoing a segmental colon resection. The results from these 2 trials suggested that the optimal perioperative treatment for patients requiring segmental colectomy was laparoscopy in association with an ERAS program. In both studies, patients were randomized to laparoscopic or open colectomy and to an ERAS program or standard care, resulting in 4 treatment groups: laparoscopic/ERAS, laparoscopic/standard care, open/ERAS, and open/standard care. Elements of care included in the ERAS group were: preoperative counseling; omission of bowel preparation; intake of carbohydrate-loaded drinks at the day before surgery; avoidance of preoperative fasting since midnight; omission of premedication; thoracic epidural analgesia; prevention of hypothermia; adequate perioperative fluid loading; removal of nasogastric tube before extubation; omission of abdominal drains; suprapubic catheter or no catheter; more than 500 mL of intake on postoperative day 0, including 200 mL of a carbohydrate-loaded drink; more than 15 minutes of mobilization on the day of surgery; and laxative started on the first day after surgery.

Vlug et al. [12] (n = 427) reported that the median (range) total postoperative hospital stay was significantly shorter in the laparoscopic/ERAS group (5 days [4–8 days]) than in the other 3 treatment groups (open/ERAS, 7 days [5–11 days]; laparoscopic/standard, 6 days [4.5–9.5 days]; open/standard, 7 days [6–13 days]; $p < 0.001$). Linear regression analysis identified laparoscopy as the only independent predictor of shorter postoperative hospital stay. There were no significant differences between the 4 treatment groups in morbidity, reoperation rate, readmission rate, quality of life at 2 and 4 weeks after surgery, patient satisfaction, or hospital costs. van Bree et al. [13] (n = 93) analyzed colonic transit recovery after surgery and found that median colonic transit was significantly faster in the laparoscopic/ERAS group than in the other 3 groups ($p = 0.001$). However, gastric emptying 24 hours after surgery did not differ significantly between the 4 groups ($p = 0.61$).

Some patients are not ready for early discharge despite an ERAS program. Two studies have shown that longer operation times and increased comorbidity are predictors of non-early hospital discharge after colorectal surgery. Keller et al. [14] attempted to identify predictors of non-early discharge for patients undergoing major elective laparoscopic colorectal surgery in a standardized ERAS program. This ERAS program included preoperative and postoperative patient counseling; efforts to preserve gastrointestinal function and avoid organ dysfunction; active pain control; and promotion of autonomy. A total of 548 patients were divided into those discharged within 3 days after surgery and those discharged more than 3 days after surgery. The authors reported that length of hospital stay was significantly longer in patients with high body mass index ($p = 0.0123$), comorbidities ($p = 0.0062$), higher American Society of Anesthesiologists classes ($p = 0.0014$), longer operation time ($p < 0.001$), postoperative complications ($p < 0.001$), and reoperation within 30 days ($p = 0.0004$). There were no significant differences between the length-of-stay groups in rates of intraoperative complications ($p = 0.724$), readmissions ($p = 0.187$) or mortality ($p = 1.00$). Hendry et al. [15] investigated postoperative outcomes in 1,035 patients undergoing colorectal resection in an ERAS program and demonstrated that pre-existing co-morbidity (American Society of Anesthesiologists classes III–IV) and advanced age were independent predictors of delayed mobilization ($p = 0.025$) and prolonged length of hospital stay ($p =$

0.002). Because patients with longer operation times and more co-morbidities are more likely to have non-early discharge after colorectal surgery, it is important to identify the reasons for functional limitations in these patients, and embark on specific interventions for enhancing functional recovery.

In summary, ERAS protocols have been most extensively studied and used in colorectal surgery, and the experience in colorectal surgery has demonstrated that implementation of ERAS protocols are safe and feasible, leading to a reduction of length of stay and faster recovery without increased complication and readmission rates. The most important tools implemented in ERAS programs in colorectal surgery are regional analgesia; enforced early mobilization and enteral nutrition; avoidance of mechanical bowel preparation, tubes, drains, or catheters; and use of minimally invasive surgery. Similar programs are currently being implemented and studied in other disciplines of surgery, such as orthopedic, gynecologic, vascular, and other types of abdominal surgery [16–18].

General Gynecologic Surgery

Studies of ERAS programs in general gynecologic surgery have shown that such programs significantly reduce length of hospital stay and consequently have positive economic benefits without increasing readmission and complication rates.

Length of hospital stay—Dickson et al. [19] retrospectively analyzed the impact of an ERAS program based on preoperative counseling, use of spinal anesthesia, early ambulation, and unrestricted diet in 400 patients undergoing abdominal hysterectomy for benign indications. The median length of stay decreased from 3 days (range, 1–12 days) prior to implementation of the ERAS program to 1 day (range, 1–17 days) ($p<0.001$). There were no significant differences in estimated blood loss, duration of surgery, or complication rates between the groups treated before and after program implementation.

Similar results have been documented in 2 recent case-control studies [20,21] that evaluated length of hospital stay before and after implementation of an ERAS program in patients undergoing vaginal hysterectomy. The program implemented by Relph et al. [20] focused on preoperative counseling, use of short-acting anesthetic agents and regional anesthesia, avoidance of vaginal packs and catheters, prevention of hypothermia, early mobilization, and planned discharge. The results of this trial showed a reduction in median length of stay from 42.9 hours before to 23.5 hours after program implementation ($p<0.05$). The program implemented by Yoong et al. [21] focused on the same ERAS elements as the program of Relph et al. [20], plus thromboprophylaxis and antimicrobial treatment. The results showed a reduction in median length of stay from 45.5 hours before to 22.0 hours after program implementation ($p < 0.01$).

Kondo et al. [22] performed a retrospective analysis of length of hospital stay in 161 patients undergoing laparoscopic surgery for intestinal deep infiltrating endometriosis under an ERAS program that included preadmission counseling, preoperative fasting, the use of an anesthesia protocol that included analgesic and non-steroidal anti-inflammatory drugs, maintenance of normothermia, intraoperative and postoperative fluid restriction, thromboprophylaxis, avoidance of peritoneal cavity drainage and a bladder catheter in the

postoperative period, avoidance of a nasogastric tube, prevention of postoperative nausea and vomiting, initiation of diet within 6 hours after surgery, and early mobilization. For analysis, patients were classified as having been treated conservatively (with rectal shaving, mucosal skinning or anterior disc resection; n = 102) or non-conservative group with segmental bowel resection (n = 59). The authors reported that the median length of hospital stay was shorter in the conservative group than in the non-conservative group (19 hours vs. 28 hours, $p<0.001$). Ninety-two of 102 patients (90.2%) in the conservative group versus 38 of 59 patients (64.4%) in the segmental bowel resection group were discharged on postoperative day 1. All women in the study were discharged to home by postoperative day 3. The authors concluded that implementation of an ERAS program allowed a short length of stay even in women undergoing a bowel resection.

Postoperative pain and analgesia—Post surgical pain remains one of the greatest barriers to early discharge after surgery. Reduction of post surgical pain is generally associated with earlier discharge and faster resumption of daily activities. In a prospective randomized multicenter trial, Wodlin et al. [23] evaluated postoperative symptoms in 180 patients undergoing abdominal hysterectomy for benign conditions during an ERAS program implementation. Patients were randomized to general anesthesia or spinal anesthesia with intra-thecal morphine. The study showed that the intraoperative use of a regional anesthetic was associated with significantly less postoperative discomfort, as indicated by reduced requirements for opiates, fatigue, abdominal pain, and faster recovery.

Kroon et al. [24] investigated whether intra-thecal morphine combined with low-dose total intravenous anesthesia accelerated recovery after abdominal hysterectomy in an ERAS program that emphasized patient counseling, treatment of nausea and pain, early enteral nutrition, and early mobilization. The control group consisted of patients who had a volatile-based general anesthesia in combination with an opioid intravenous patient-controlled analgesia. Patients with total intravenous anesthesia and intra-thecal morphine had a significantly shorter postoperative stay and earlier resumption of oral fluid intake. Although pain scores on a visual analogue scale were low in both groups, the median score was lower in the total intravenous anesthesia group (1 vs. 2). The authors concluded that total intravenous anesthesia in combination with intra-thecal morphine was superior to volatile anesthesia and intravenous patient-controlled analgesia in most respects.

Bowel function—Another important factor determining the return to daily activities after surgery is the resumption of bowel function. Kroon et al. [24] evaluated the type of anesthesia and its impact on resumption of oral fluid intake in patients undergoing abdominal hysterectomy in an ERAS program. The total intravenous anesthesia group demonstrated a shorter median time to resumption of oral fluid intake than the patient-controlled analgesia group (4h vs. 5h, $p<0.01$). In a comparison of general anesthesia with spinal anesthesia in 180 patients undergoing abdominal hysterectomy for benign conditions in an ERAS program, Wodlin et al. [23] reported significantly more vomiting episodes during the day of surgery in the spinal anesthesia group. Despite this increase in vomiting in spinal anesthesia group; less requirements of opioid analgesics, less postoperative discomfort, and faster recovery were found in this group compared with general anesthesia.

Complication and readmission rates—When an ERAS program is implemented, it is important to ensure that by promoting and implementing strategies to achieve a faster recovery, one does not increase the risk of complications or readmissions. Nilson et al. [25] prospectively investigated the incidence and type of postoperative complications in 162 women undergoing abdominal hysterectomy for benign conditions in an ERAS program. The authors reported that 25% of patients developed minor postoperative complications, mostly infections and wound healing problems, and 9.7% of patients developed major complications. These rates are comparable to those in the FINHYST study, which examined complications in 5,279 hysterectomies for benign conditions performed in hospitals in Finland in 2006 [26]. In the study by Nilson et al. [25], the risk of postoperative complications was higher in women with obesity (odds ratio [OR], 8.83), prior laparotomy (OR, 2.92), increase in body weight on the first postoperative day (OR, 1.52), longer duration of hospital stay, or longer time with a urinary catheter. The readmission rate was 2.5%. These results are in agreement with results of other studies of abdominal hysterectomy for benign conditions without an ERAS program.

Two studies compared readmission rates in patients undergoing vaginal hysterectomy before and after implementation of an ERAS program. Yoong et al. [21] reported a readmission rate of 4% before and 0% after implementation of an ERAS program. Relph et al. [20] reported a readmission rate of 6.7% before and 0% after implementation of an ERAS program. Relph et al. [20] reported that ERAS patients had a higher rate of attending the emergency department for minor symptoms following discharge (15.6% vs. 0%, $p<0.05$). Yoong et al. [21] also found a higher rate of visits to the emergency department in ERAS patients, but the difference was not statistically significant (12% vs. 0%, $p>0.05$).

In the study by Kondo et al. [22] in which patients undergoing laparoscopic surgery for intestinal deep infiltrating endometriosis with application of an ERAS program were divided into 2 groups for analysis, conservative surgery and segmental bowel resection, the median readmission rate was low in both groups: 6.8% in the segmental bowel resection group and 1% in the conservative surgery group ($p=0.04$). The rate of need for reoperation was similar in the 2 groups (3.4% for segmental bowel resection and 1% for conservative surgery; $p=0.28$).

Cost analysis—When an ERAS program is implemented, it is also critically important to evaluate the cost of establishing such a program as a standard practice. Assuming there is faster resumption of daily activities, faster return of bowel function, and shorter length of hospital stay, these results will result in lower overall cost. However, one must also consider the initial cost of setting up the program that will include education/training of the staff and an ongoing audit of the program incorporating new tools to evaluate symptom burden/control and indices of functional recovery into routine clinical practice.

Rhou et al. [27] reported a retrospective study of direct intraoperative and postoperative costs in 50 women who underwent a total laparoscopic hysterectomy without an ERAS program and 50 women who underwent open hysterectomy with an ERAS program. Total laparoscopic hysterectomy without an ERAS program had a higher intraoperative cost ($p < 0.001$) but a lower postoperative cost ($p < 0.001$), but total costs did not differ between the 2

surgical groups (p = 0.068). However, there was a significant decrease in cost in the laparoscopic group after the initial 25 cases, and when patients from this learning period were excluded, laparoscopic hysterectomy without an ERAS program had a lower total cost than open hysterectomy with an ERAS program (p < 0.001).

In the aforementioned studies showing that implementation of an ERAS program for patients undergoing vaginal hysterectomy resulted in a significantly shorter length of hospital stay without an increase in the readmission rate [20, 21], the ERAS program also resulted in cost savings. Yoong et al. [21] estimated a median cost for vaginal hysterectomy of £1,148.63/US$1,722.90 before implementation of an ERAS program and £1,042.32/US $1,563.48 after implementation of an ERAS program, which translated to a median cost savings of £106.30 (9.25%) per patient with an ERAS program. In a similar analysis, Relph et al. [20] estimated that the ERAS program saved £164.86 (15.2%) per patient.

These studies provide evidence that implementation of an ERAS program in minimally invasive surgery, such as laparoscopic or vaginal surgery, can provide even greater cost benefits when compared with fast-track programs in open surgery.

Patient satisfaction—When ERAS programs are implemented, it is important to consider patient satisfaction and overall quality of life. Yoong et al. [21] compared patient satisfaction scores at 4 weeks after surgery in patients who underwent a vaginal hysterectomy before (n = 50) or after (n = 50) implementation of an ERAS program. The median satisfaction score was 8/10 in both groups, and 65% of patients in the ERAS group gave scores of greater than 9/10.

Wodlin et al. [28] used a questionnaire to evaluate health-related quality of life in their study of 180 patients who underwent abdominal hysterectomy for benign disease in an ERAS program and were randomized to general anesthesia or spinal anesthesia with intra-thecal morphine. Health-related quality of life improved significantly faster and sick leave was significantly shorter in women who had spinal anesthesia than in those who had general anesthesia

Gynecologic Oncology Surgery

There are few published data on the incorporation of ERAS programs in gynecologic oncology. Chase et al. [29] evaluated postoperative outcomes in 880 gynecologic oncology patients who underwent laparotomy with an ERAS program for suspected gynecologic malignancy. Thirty-one percent of the patients (273/880) had a preoperative diagnosis of cancer, the most common type being endometrial cancer (180/273; 66%), and 48% of the patients (366/880) had a diagnosis of cancer after surgery. Forty percent of the procedures performed were radical hysterectomy with or without bilateral salpingo-oophorectomy and omentectomy or staging bilateral salpingoo-ophorectomy with or without total hysterectomy.

The ERAS program consisted of discontinuation of patient-controlled analgesia device and urinary catheter on the morning of the first day after surgery, early feeding, early ambulation, and prompt conversion to oral analgesics with non-opioid medication. The

median length of hospital stay was 2 days (range, 0–52 days). Regression analysis showed a significant relationship between younger age and reduced length of hospital stay (R^2=0.28). The readmission rate was only 5% (44/880). The median time to readmission was 4 days. The authors concluded that these clinical pathways reduced the length of hospital stay without increasing morbidity or mortality after laparotomy for suspected gynecologic malignancy.

A Cochrane review [30] of perioperative ERAS programs for gynecologic oncology patients evaluated the main results of 3 nonrandomized clinical trials. All of them involved patients with ovarian cancer. The ERAS programs differed between studies because standard pathways were not uniform. These 3 trials showed that implementation of an ERAS program was associated with a shorter length of hospital stay and no difference in postoperative complications, mortality, or readmission rates compared with the conventional perioperative program.

Carter [31] reported a large review of every element of a 22-point ERAS program in patients undergoing laparotomy for suspected or confirmed gynecologic cancer. A total of 389 patients were evaluated, 227 of who (58%) had cancer (51% ovarian, 39% endometrial, and 9% cervical). The median length of hospital stay was 3 days with a readmission rate of 4%, and a reoperation rate of 0.5%. Twenty-eight percent of the patients were discharged on postoperative day 2. Another subgroup analysis based on pathologic analysis (endometrial cancer, ovarian cancer, cervical cancer, or benign pathology) showed that length of stay and readmission rates were similar between subgroups. In addition, the study evaluated the impact of program experience and the appointment of a clinical nurse consultant. The authors found that increasing program experience was associated with an improvement in the percentage of patients discharged on day 2 from 10% in the first year to 36% in the fifth year of the program.

One of the most recently published studies on ERAS in gynecologic oncology was a retrospective comparison between an ERAS program and conventional care in women undergoing major abdominal surgery for gynecologic malignancies or vaginal reconstructive procedures for pelvic organ prolapse, by Kalogera et al. [32]. A total of 241 women in the ERAS group (81 cytoreductive, 84 staging, and 76 vaginal surgeries) were compared with 235 women in the conventional care group. In the conventional care group, bowel preparation, caloric restriction, intraoperative hypervolemia, patient-controlled analgesia, and surgical drains and catheters were routinely employed. Postoperative nausea (55.6% vs. 38.5%, p=0.031) and vomiting (17.3% vs. 2.6%, p=0.002) were more frequent in the ERAS group than in the control group, even though the ERAS group was treated with a more aggressive regimen to prevent postoperative nausea and vomiting. Despite this increase in nausea and vomiting, 87% rated their satisfaction with nausea and vomiting control as excellent or very good, suggesting that early feeding overall is well tolerated. Women in the ERAS group had a median time to return of bowel function 1 day less than the time in the control group (p<0.001) without differences in postoperative ileus. Median length of hospital stay was 4 days less in the ERAS group than in the control group (8.7±7.6 vs. 11.9±11.9 days, p< 0.001). Almost half (46.1%) of the patients in the ERAS group were discharged the day after the surgery, compared with only 6.5% of women in the control group. The rates of

readmission and postoperative complications were no different between the groups. The ERAS program was associated with a 30-day cost savings of more than $7,600 per patient (18.8%reduction). In addition, 95% of patients in the ERAS group rated their care as excellent or very good (patient satisfaction surveys were not available in the control group). The authors concluded that implementation of an ERAS program was associated with acceptable pain management, reduced length of stay with stable readmission and mortality rates, adequate patient satisfaction, and substantial cost reductions.

To date, there are no studies to our knowledge that evaluate physician acceptance or criticism of an enhanced recovery program in a gynecologic oncology program. However, Hughes and colleagues [33], published a survey that assessed the perceptions of care providers and patients on the relevance and importance of an ERAS program. In that study, pre- and post-operative surveys were completed by patients who underwent major hepatic, colorectal, or esophagogastric surgery. A total of 109 patients and 57 care providers completed the preoperative survey. Freedom from nausea and pain at rest were the care components rated highest by both patients and care providers.

More recently, Nelson et al. [34], published a comprehensive review of the literature regarding ERAS programs in gynecologic oncology. In their review, the authors compiled data from seven reports and found that significant improvements in patient satisfaction, length of stay (up to 4 days), and cost (up to $7,600 in savings per patient) were observed in ERAS programs compared to historical controls. They also found that morbidity, mortality, and readmission rates were no different between groups.

Recommendations for Establishing an ERAS Program

Studies to date indicate that ERAS programs are associated with more rapid recovery and shorter length of hospital stay without increased postoperative complications. Institutions considering establishing an ERAS program should consider the following factors.

Preoperative phase—To prevent perioperative complications, appropriate preoperative risk stratification, timely risk modification, and medical optimization have to be performed. Preoperative counseling of patients and care-givers (including written instructions) regarding the surgical procedure with associated complications, measures to reduce non-surgical morbidity by active patient engagement, education on balancing analgesic regimens with minimizing side effects and maintaining functionality, goal directed advancement in postoperative care to functional recovery, and clearly articulated discharge criteria are very important. Equally important is to identify barriers to discharge upon meeting discharge criteria, and availability of appropriate post-discharge help so that appropriate measures can be taken and arrangements made for appropriate care. Patients should avoid dehydration before surgery and should drink clear fluids until two hours prior to surgery if no contraindications exist. Carbohydrate loading is generally recommended, unless contraindications exist. We recommend 100 gm carbohydrate loaded drink the night before surgery and a 50 gm carbohydrate loaded drink 2 hours prior to arrival for surgery. Mechanical bowel preparation should not be used routinely. When no contraindications

exist, patients should be given multimodal pain medication adjuncts (acetaminophen, gabapentinoids, and COX-2 inhibitors) in the preoperative period.

Intraoperative phase—Key component to an ERAS program in the intraoperative period is the use of goal directed fluid therapy (implementing use of minimally invasive hemodynamic monitors to detect flow-related parameters and/or dynamic parameters of fluid responsiveness in order to titrate therapeutic interventions (intravenous fluids and/or inotropic therapy administration) to optimize end organ tissue perfusion.), multimodal opioid-sparing regimens (incorporating loco-regional techniques as appropriate), and incorporating best practices of anesthetic care and techniques. Use of thromboprophylaxis and prophylactic antibiotics per guidelines is recommended. Avoidance of routine use of drains and catheters is also suggested. However, use of drains in the setting of low anterior resection may be left to the discretion of the surgeon based on best assessment of need. It is important to also consider infusion of local anesthetic (bupivacaine) in the wound (deep and superficial injections) prior to closure. In our program, we have elected not to use routine epidurals, as these can be associated with longer anesthesia preparation time, longer time to first ambulation, and hypotension. Given that most of the data on the benefits of epidural analgesia is not in the setting of gynecologic oncology patients and the fact that these elements may all work towards detracting from the principle of faster recovery, we do not routinely recommend use of epidural analgesia.

Postoperative phase—Attention must be paid to early feeding, early mobilization, limiting formula-based intravenous fluid regimes, and providing dynamic pain control with multimodal opioid sparing analgesia regimens. Finally, before discharge, patients must be given clear postoperative instructions and emergency contacts.

Successful implementation of an ERAS program requires active involvement by a multidisciplinary team including, but not limited to, surgeons, anesthesiologists, dietitians, nurses, pharmacists, occupational therapists, a pain management team, physical therapists, and operating room staff. In addition, involving the patient at every step of the process is a fundamental part of a successful ERAS program. The “Delivering Enhanced Recovery” document published by the NHS Enhanced Recovery Partnership Programme is one such tool [35]. This guide contains the starting points to support implementation of an ERAS program as the best clinical practice for patients undergoing major surgical procedures. One should also take into consideration the impact of Patient Reported Outcomes (PROs) since these have long represented the gold standard for quality of life and patient satisfaction. PROs have become an area of increasing focus in comparative effectiveness research, health care quality assessments, and as endpoints in clinical trials. The Center for Medical Technology Policy (CMTP) recommends that prospective clinical comparative effectiveness research (CER) capture the subjective patient experience. [36] In addition, patient reported outcome measures will influence the way we deliver medical care in the future of health care reform.

Based on all of these key elements, we have implemented the ERAS program shown in Tables 1–3 in the Department of Gynecologic Oncology & Reproductive Medicine at MD

Anderson Cancer Center. An upcoming article by Nelson et al. [37], provides the ERAS Society Guidelines for patients undergoing gynecologic or gynecologic oncology surgery.

Conclusion

On the basis of current data, it appears that implementation of an ERAS program may result in an overall improvement in postoperative outcomes. However, more studies are needed that include a consistent strategy with an evaluation of the key elements of care implemented in the perioperative period, and evaluating the outcomes based on the adherence to the key elements. As ERAS is a dynamic and an evolutionary clinical care pathway, every program has to be evaluated for effectiveness and measures for continuous improvement instituted within the individual system using validated instruments that define symptom burden, quality of life, functional recovery. The implementation of a successful ERAS program may lead to a reduction in overall health care costs, faster and safer patient recovery, and ultimately improved quality of life and patient satisfaction. For patients with gynecologic cancers earlier return to baseline, or near baseline physiologic status, could improve oncological outcomes if the patient is able to resume planned adjuvant therapies without delay.

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Highlights

ERAS programs are associated with shorter hospital stay

ERAS programs may lead to a faster and safer patient recovery and improved quality of life

Patient reported outcomes may be improved after implementation of ERAS programs

Table 1

Preoperative Gynecologic Oncology Enhanced Recovery Program (ERP): MD Anderson Cancer Center

Preop	Previous Practice	ERP-GYN
Diet	NPO @ MN until surgery	No solids after midnight
		Clears 2 hrs prior to surgery
Bowel Prep	Physician discretion	None
Pre-meds	Anesthesia discretion	Tramadol ER
		Pregabalin
		Celecoxib
		Acetaminophen IV
		Heparin SQ
IVF therapy	Fluids after IV placed	Saline lock until OR

NPO=nothing by mouth; OR=operation room

Table 2

Intraoperative Gynecologic Oncology Enhanced Recovery Program (ERP): MD Anderson Cancer Center

Intraop	Previous Practice	ERP-GYN
Antibiotics	ACOG Guidelines	Same
Anesthesia	Anesthesia discretion	TIVA
		No epidurals
		Local wound infiltration
IVF therapy	Anesthesia discretion	GDT
		Noninvasive monitoring
NGT/Drains	Surgeon discretion	None

ACOG-American College of Obstetrics & Gynecology; TIVA=total intravenous anesthesia; GDT=goal-directed fluid therapy; NGT=nasogastric tube; POD=postoperative day

Table 3

Postoperative Gynecologic Oncology Enhanced Recovery Program (ERP): MD Anderson Cancer Center

Postop	Previous Practice	ERP-GYN
IVF therapy	IVFs 100 ml/hr	IVF 40 ml/hr
	KVO when tolerating diet	Saline lock (Tolerating 500 ml oral)
Analgesia	PCA vs. Epidural	Acetaminophen
		Ibuprofen
		Pregabalin
		Oxycodone
		Hydromorphone IV
Diet	Gradual advancement	Regular diet POD0
		Oral hydration
Foley Catheter	Surgeon discretion	Remove POD1
Ambulation	Patient/Physician discretion	Ambulate 8×/day
		All meals in chair
		Out of bed 8hr/day
Transfusion	Physician discretion	Restrictive
		Only for Hb<7

IVF=intravenous fluids; KVO=keep vein open; PCA=patient controlled analgesia; POD=postoperative day; Hb=hemoglobin