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Enhanced Recovery Pathways in Gynecology and Gynecologic Oncology

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Abstract

Importance—Enhanced recovery programs (ERPs) are considered standard of care across a variety of surgical disciplines, but ERPs have not been widely adopted in gynecology.

Objective—To describe ERP principles and the role of ERPs in gynecology and gynecologic oncology.

Evidence Acquisition—Comprehensive literature search performed using MEDLINE, the Cochrane Collaboration Database, and PubMed.

Results—Meta-analyses of a substantial number of randomized-controlled trials have shown that implementation of ERP protocols is associated with decreased length of hospital stay, a decrease in rates of postoperative complication, decreased morbidity, and cost savings while preserving patient satisfaction and quality of life.

Conclusions and Relevance—High quality evidence exists for improved outcomes among patients in ERPs. ERPs save resources and costs across the health care system. As quality metrics and bundled payments increase in healthcare, ERPs will have increasing prominence.

Target Audience

Obstetricians and gynecologists; family physicians

History and Rationale of Enhanced Recovery Programs (ERP)

“Enhanced recovery” or “fast track” surgical principles were first described in the 1990s. These ideas were pioneered by European anesthesiologists and surgeons who challenged the traditional paradigms of perioperative care, most notably the Dutch professor, Henrik Kehlet.¹ They introduced the concept that postoperative morbidity had its origins in the body's stress response to surgical injury and that the key to decreasing surgical morbidity was to (1) limit the degree of the surgical injury itself and (2) find ways to help the body

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cope by decreasing its stress response to injury.¹ The response to surgical stress is mediated by neurohormonal pathways and complement pathways leading to increased catabolism, immunosuppression, relative hypoxia, insulin resistance, and generalized organ dysfunction that can delay the body's ability to recover. Enhanced recovery programs (ERPs) are designed around interventions that help the body mitigate and cope with this surgical stress. These programs are also referred to as enhanced recovery after surgery (ERAS), multimodal postoperative management, or "fast-track" programs.

ERP protocols address preoperative patient counseling, preoperative fasting, preoperative bowel preparation, early initiation of oral intake, early postoperative mobilization, appropriate use of drains and catheters, facilitation of perioperative euvolemia and normothermia, and multimodal analgesia (Table 1). Individual interventions are combined to create a master protocol and implemented together to improve care.

ERP has been rigorously studied in many surgical specialties. Data showing benefit of ERP principles and protocols is most robust in colorectal surgery, but it has also been implemented with similar positive outcomes in a variety of other surgical specialties including vascular surgery, thoracic surgery, cardiac surgery, urology, hepatobiliary surgery, orthopedics, as well as in benign gynecology and gynecologic oncology. The National Health Service in Britain has embraced ERP as a quality improvement and service tool and considers it standard of care following surgery. They estimate that the use of ERP will allow them to increase capacity and save an additional 140,000-200,000 bed days each year while maintaining current resource levels.²

Benefits of ERP

Implementation of an ERP protocol is associated with decreased length of hospital stay, a decrease in rates of postoperative complication, decreased morbidity, and cost savings while preserving patient satisfaction and quality of life. Meta-analyses and randomized controlled trials (RCTs) of ERP pathways have shown benefit.³⁻⁷ Two of the first ERP meta-analyses in colorectal surgery found improved outcomes when ERPs were utilized compared with routine postoperative care. Two reviews found a reduction in length of hospital stay for patients in the ERP group, with no difference readmissions. They also found a significant reduction in postoperative morbidity in patients undergoing ERAS and a trend towards decreased mortality.

A recent meta-analysis included 2,376 colorectal patients from 16 randomized controlled trials. All studies compared ERP pathways to conventional postoperative care. ERP pathways were associated with a significant decrease in overall morbidity (RR = 0.60, 95% CI 0.46-0.76), medical complications (RR = 0.40 95% CI 0.27 – 0.61), and a decreased length of hospital stay of 2.28 days (95% CI 1.47- 3.09 days) with no differences in readmissions.³ Another meta-analysis included patients from RCTs in all surgical disciplines, including colorectal, orthopedics, urology and upper gastrointestinal tract surgery.⁵ This review included 38 RCTs with 5,099 patients. Patients in the ERP groups experienced decreased length of stay of an average of 1.14 days with no change in

readmission rates. ERP patients also had a decreased risk of all 30-day complications (RR = 0.71, 95% CI 0.60 – 0.86), but no reduction in mortality.

High-quality evidence has persistently shown that ERP is associated with decreased length of stay and improvement or no change in rates of postoperative complication and readmission. It is intuitive that ERP is also cost saving. Decreased length of stay reduces inpatient hospital costs and decreases postoperative complications. A recent review of cardiac patients found that patients with a complication incurred \$29,876 more in costs than patients without complications. Cost analyses across a variety of surgical disciplines have confirmed the cost savings associated with ERP with savings of \$257 per vaginal hysterectomy patient, \$7,600 per ovarian cancer patient, and \$6,900 per colorectal patient.⁸⁻¹² A recent meta-analysis across a variety of surgical subspecialties confirmed that ERP are cost-effective.¹³⁻¹⁵

Data on patient satisfaction and quality of life are more limited, but the available information suggests a benefit to ERP. Due to the use of multimodal pain management strategies, ERP is consistently associated with improvements in pain scores. Patients in an ERP also have a more rapid return to baseline functional status.¹⁶⁻¹⁸ A study focusing only on quality of life in colorectal patients undergoing ERP found improved symptom scores compared with conventional care.¹⁹ ERP patients have also been found to experience decreased rates of fatigue when compared with conventional care.¹⁷ A study of gynecologic oncology patients found improvements in “autonomy”, “physical complaints” and “postoperative pain” using a validated quality of life tool.²⁰ Patient satisfaction is less well studied but the limited available data suggests no detriment to satisfaction among ERP patients.¹⁰

Important Components of ERP

Preoperative patient preparation

ERP programs require the patient to be an active participant in their recovery. Preoperative education to manage patient expectations is a key feature of ERP. Patient education is a strong component of ERP programs. Handouts and pamphlets that the patient can take with them to refer to as well as patient counseling, ideally with the surgeon, nurse, and anesthesiologist who will be present at surgery, contribute to overall improved outcomes. Materials and counseling should specifically address details about the surgical and anesthetic procedures as this has been shown to decrease patient anxiety.²¹ These should also address the patient's role in completing postoperative tasks such as pulmonary physiotherapy, early resumption of oral intake, and early mobilization. By managing patient expectations, patients become partners in achieving postoperative milestones and this results in improved outcomes such as decreased pain, shorter recovery, and decreased postoperative complications.²¹⁻²⁴

Another important part of preoperative preparation is mitigating medical comorbidities. Preoperative alcohol abuse is associated with an increased risk of postoperative morbidity. This morbidity is secondary to alcohol-induced immunosuppression as well cardiac dysfunction.^{25,26} Abstinence from alcohol for a month leading up to surgery reduces

postoperative morbidity.²⁷ Smoking is another modifiable risk factor for postoperative complication. Current smokers experience impaired wound healing and pulmonary complications. Abstinence of one-month duration from smoking prior to surgery decreases these risks.^{28,29} Optimization of cardiac function, pulmonary function, blood pressure, and diabetes should also be prioritized. Nutrition should be optimized as an albumin of greater than 3.5 g/dl is associated with improved postoperative outcomes.³⁰⁻³²

Minimizing surgical insult

Incisions lead to pain, an inflammatory response, and catabolism.¹ Thus, efforts should be made to minimize surgical trauma by using the smallest incision possible, making a transverse incision in place of a midline vertical incision, and advocating for a minimally invasive approach whenever possible.^{33,34}

Minimally invasive surgery is associated with a shorter recovery and a more rapid return to preoperative baseline functional status making it an important part of ERP. Vaginal hysterectomy is the original minimally invasive surgery and laparoscopy and robotic surgery have been widely adopted. Minimally invasive surgery offers benefits over laparotomy for benign hysterectomies and is associated with decreased complications, decreased surgical site infections, decreased risk of venous thromboembolism, shorter hospital stay, and improvement in quality of life.³⁵⁻³⁹ A recent Cochrane review concluded that a laparoscopic myomectomy is associated with less pain, less febrile morbidity, and shorter hospital stay.⁴⁰ For gynecologic cancers, robotic and laparoscopic surgery for the treatment of endometrial cancer and cervical cancer is associated with decreased blood loss, decreased postoperative complications, and decreased length of hospital stay.⁴¹⁻⁴³ A minimally invasive approach, whenever possible, is highly recommended in ERP.

Normothermia

Preventing hypothermia (< 36 degrees Celsius) is crucial to decreasing postoperative morbidity. Patients who are hypothermic during surgery have higher rates of wound infections, experience more cardiac morbidity, and have increased rates of coagulopathy and resulting bleeding.⁴⁴⁻⁴⁶ The compensatory shivering that occurs with hypothermia also increases oxygen consumption and contributes to the patient entering a catabolic state.⁴⁷ Techniques such as fluid warming before infusion, use of forced-air infusion blankets, heating mattress pads, and circulating garment systems have all been shown to be effective interventions that prevent hypothermia during surgery.⁴⁸ Prewarming the patients with a warm air blanket prior to entering the operating room has also been shown to increase core temperature prior to surgery. Monitoring body temperature throughout surgery is crucial to achieve these outcomes.

Perioperative diet

“NPO after midnight” has been a longstanding ingrained dogma in anesthesiology and surgery. It has been proposed that a prolonged preoperative fast would prevent gastric contents and gastric acid from remaining in the stomach and would therefore result in a decreased risk of aspiration, however current data suggests otherwise. A Cochrane review of 22 RCTs found no evidence that a shortened period of fasting was associated with an

increased risk of aspiration, regurgitation or related morbidity.⁴⁹ In fact, patients who were fasting actually retained a higher amount of gastric contents when compared with patients who were allowed to drink water prior to surgery.⁴⁹ Due to these findings, the American Society of Anesthesiology recommends a fast of 6 hours preoperatively for solid foods and that clear liquids be consumed for up to 2 hours prior to surgery.⁵⁰

A prolonged preoperative fast for up to 12 hours will cause the body to deplete its glycogen stores and the loss of readily available energy stores has been shown to adversely affect the response to surgical stress and injury. Depletion of glycogen and prolonged fasting leads to insulin resistance and hyperglycemia, which are associated with postoperative complications and morbidity.^{51,52} Minimizing the preoperative fasting period mitigates these deleterious effects. It also has the potential to increase patient quality of life and satisfaction as prolonged fasting prior to surgery is uncomfortable for patients and the changes in physiology can also increase patient anxiety.

In addition to limiting the fasting period, preoperative carbohydrate loading drinks can reverse some of the effects of the limited preoperative fasting period including preventing insulin resistance and hyperglycemia. These drinks are composed of concentrated complex carbohydrates suspended in a clear fluid and are emptied by the stomach within 30 minutes.⁵³ Four hundred milliliters of a 12.5% maltodextrin drink given 2-3 hours preoperatively has been shown to decrease insulin resistance.⁵⁴ Additional benefits include a reduction in patient anxiety as well as thirst and hunger.⁵⁵ An RCT studying colorectal patients found that length of stay was shorter for patients who received a carbohydrate loading drink (7.5 days) compared with those who fasted (10 days, $p=0.06$) or received water alone (13 days, $p<0.01$).⁵⁶

Postoperative fasting should also be avoided. Patients following an ERP are permitted and encouraged to drink clear liquids upon awakening from anesthesia and to eat a general diet upon arrival to the floor. In gynecology and gynecologic oncology populations⁵⁷⁻⁶² early enteral intake was associated with a faster return of bowel function and a decreased length of stay without increase in postoperative complications. In a study of colorectal patients undergoing surgery, those in the early feeding group experienced a decreased length of stay, decreased rates of infection, decreased time to return of bowel function, and a trend towards decreased postoperative complications.^{63,64} Additionally early feeding was not associated with an increased risk of anastomotic leak. And while patients in the early feeding groups experienced more nausea and vomiting, this was not associated with any untoward patient outcomes.⁶¹⁻⁶³ A study of ERP in gynecologic surgery also found that patients in the ERP group experienced higher rates of nausea and vomiting compared with the conventional group, however there was no difference in postoperative satisfaction.¹⁰

Postoperative nausea and vomiting may affect as many as 70% of patients who undergo major abdominal surgery.⁶⁵ Early enteral intake is very important to decrease time spent in a catabolic state and decrease insulin resistance. A multimodal prophylactic approach to postoperative nausea and vomiting includes both pharmacologic and non-pharmacologic techniques. Use of greater than 2 anti-emetics in combination has a more potent effect than less than 2 antiemetics.⁶⁶ Dexamethasone is also an important prophylactic agent in control

of postoperative nausea and vomiting. Additional non-pharmacologic approaches such as avoiding inhalational anesthetics and an increased use of propofol are important as well.

Mechanical bowel preparation

In anticipation of colorectal surgery, bowel preparation was thought to decrease risks of infection and anastomotic leaks. In gynecology, bowel preparations were thought to make bowel handling easier, improve visualization, and potentially decrease postoperative complications. However, studies have not supported these assumptions. Bowel preparation is associated dehydration, electrolyte abnormalities, and a prolonged period of fasting.⁶⁷ All of these increase catabolism and insulin resistance. Additionally, bowel preparations are cumbersome for patients and are associated with patient dissatisfaction.^{68,69}

For gynecologic surgery, a recent meta-analysis of 5 RCTs found that there was no benefit of bowel preparation in regards to visualization of the surgical field or decreases in operative time. However, patients undergoing bowel preparation did experience increased patient discomfort.^{68,70,71} The authors conclude that rectal enemas and mechanical bowel preparations can safely be abandoned in gynecologic surgery.⁷⁰ For surgery with a planned bowel resection a recent meta-analysis suggests that mechanical bowel preparation along with antibiotics may decrease rates of postoperative infectious complications. However, for mechanical bowel preparation alone, a Cochrane review of 18 RCTs found that there was no significant difference between anastomotic leak rates and infectious morbidity among patients undergoing bowel preparation or rectal enemas when compared with no preparation.⁷² A smaller prospective cohort study in colorectal patients found that mechanical bowel preparation was associated with a slower return of bowel function.⁷³ Given the alteration of physiology with no evidence of benefit and observation that there is some harm, ERPs recommend avoiding bowel preparation and rectal enemas.

Fluid balance and management

Perioperative fluid management is an important focus of ERPs. The goal in ERP is to maintain perioperative euvolemia or a zero-sum fluid balance, where the weight of the patient entering surgery should be equal to their weight exiting surgery. Both hypovolemia and hypervolemia have negative physiologic consequences. Hypovolemia is associated with decreased cardiac output, decreased oxygen delivery to tissues, and resulting organ dysfunction and damage. Hypervolemia is associated with buildup of fluid in the interstitial spaces leading to pulmonary edema and bowel wall edema leading to delayed return of bowel function.

Historically, surgeons and anesthesiologists have recommended a liberal fluid policy during surgery to prevent hypoperfusion. Patients entered the operating in negative fluid balance given the prolonged preoperative fasting period and prescription of a bowel preparation. However, once patients are resuscitated in the operating room, the principles of diffusion mean that much of the given fluid leaks into the interstitial space leading to morbidity. Additionally, traditional teaching regarding necessary urine output goals in the operative and postoperative period did not account for the body's natural response to surgical stress as a period of transient oliguria driven by the release of antidiuretic hormone. As a result, many

patients cared for according to traditional practice are net fluid balance positive upon exiting the operating room.

In contrast, ERP calls for a zero-sum fluid balance which is obtained by minimizing crystalloid administration, and increasing the use of colloids. When necessary, infusion of balanced crystalloids such as lactated ringers in place of normal saline is recommended to lower the sodium content and decrease the risk of developing electrolytes abnormalities. Other key principles in a zero-sum balance fluid policy include increasing the use of vasopressors in place of crystalloid for treatment of hypotension in a euvoletic patient (such as an epidural), and the use of flow measurements to provide resuscitation according goal-directed therapy.

Goal-directed fluid therapy refers to using minimally invasive devices such as esophageal dopplers to measure cardiac output during surgery. Fluid management is directed towards maintaining an optimal cardiac output. The patient is progressively challenged with small boluses of colloid while measuring stroke volume. An increase of greater than 10% in stroke volume means that the patient is on the point in the Starling curve where they are still fluid responsive and thus increased fluid delivery will continue to improve their cardiac output. Progressive colloid challenges are infused until the cardiac output response is less than 10%. At this point the patient is considered to be fluid balanced. Further resuscitation is based upon measuring cardiac output. Meta-analyses of goal directed therapy among patients undergoing major abdominal surgery have shown decreased length of stay, fewer complications, fewer ICU admissions, more rapid return of bowel function, and decreased postoperative nausea and vomiting.⁷⁴⁻⁷⁶

Additional fluid paradigms have been described as either liberal or restrictive although these protocols have variable definitions. In general, a restrictive fluid policy is associated with improved outcomes compared with the traditional surgical paradigm, but it is clear that the best outcomes are achieved when patients are fluid balanced.⁷⁷ In colorectal patients, an RCT examined a zero-balance fluid pathway compared to traditional care and found that patients in the zero-balance group experienced fewer cardiopulmonary complications, fewer tissue-healing complications, and a trend towards decreased mortality.⁷⁸ A meta-analysis of 9 RCTs found that both restrictive fluid policies and goal-directed fluid policies were associated with decreased postoperative morbidity (OR 0.41 95% CI 0.22-0.77 and 0.43 95% 0.26-0.71).⁷⁹ A smaller randomized trial in colorectal patients found that weight gain of as little as 3 kilograms was associated with slower return of bowel function and prolonged hospitalization.⁸⁰ Given the morbidity associated with fluid overload, ERPs recommend that minimal fluids be given in the operating room, enteral feeding be undertaken immediately, and intravenous fluids be removed as quickly as possible, often with first oral intake or postoperative day one at the latest.

Pain management

High quality postoperative pain control is crucial to achieve the goals of early mobilization and early feeding. Pain management strategies focus on decreasing the total amount of intravenous opioids as opioids are associated with impaired gastrointestinal function and nausea and vomiting. Opioids can also cloud the patient's sensorium making mobilization

more difficult and depressing the respiratory drive. ERPs decrease the amount of opioids used by combining regional anesthetics techniques with multimodal pharmacologic pain management.

Multimodal pain management should take advantage of the anti-inflammatory pathways by using NSAIDs and acetaminophen as adjuncts. A systematic literature review of 60 RCTs found that use of anti-inflammatory adjuncts in addition to morphine PCA decreased the amount of morphine used by patients in a 24-hour period by 6.34 mg when Tylenol was used, 10.2 mg when NSAIDs were prescribed, and 10.9 mg when COX-2 inhibitors were used.⁸¹ In another meta-analysis, investigating ketorolac, 27 double blind RCTs including 2,314 patients found that patients receiving ketorolac experienced improved pain control compared to patients receiving opioids alone.⁸² Some surgeons may be reluctant to use ketorolac given the perceived risk of bleeding. However, in this meta-analysis, there was no difference in the rate of bleeding complications between patients receiving ketorolac and those in the control group.⁸²

Regional anesthesia is a mainstay of ERP. Neural blockades are a very effective way to prevent the catabolic response to pain. In major abdominal surgery utilizing a midline laparotomy, thoracic epidural anesthesia (TEA) is considered standard of care by the vast majority of ERPs.^{34,83} Pain control is superior to intravenous opioid PCA and several meta-analyses have found that postoperative nausea and vomiting is decreased, time to return of bowel function is shortened, and postoperative insulin resistance is decreased. However, if not managed properly, TEA can conflict with some of the other components of ERP. If hypotension secondary to sympathetic blockade is treated with fluid bolus, fluid overload can result and undermine the goal of zero-sum fluid balance. For this reason, current ERP guidelines recommend the use of vasopressors in place of a fluid bolus to raise blood pressure in the euvoletic hypotensive patient with an epidural.^{34,83} Additionally, patients can have difficulty with ambulation and urinary retention which can paradoxically lengthen hospital stay and impair recovery.

It is important to note that although the data is robust for use of TEA in patients undergoing laparotomy for colorectal, hepatobiliary, thoracic, vascular and urologic indications, the data for gynecologic and gynecologic oncology procedures is less clear. One randomized study of patients undergoing radical hysterectomy found that patients undergoing epidural anesthesia had significantly shorter return to bowel function and shorter length of hospital stay.⁸⁴ However, other studies have shown that although pain scores are decreased among patients receiving epidurals, length of stay is not decreased.^{85,86} Authors at the Mayo clinic have also raised concerns about the use of epidurals in laparotomy for ovarian cancer patients. As these patients are prone to substantial fluid shifts resulting in hypotension, it is hypothesized that the detrimental effects on fluid management.^{10,87} may outweigh the relative benefit of epidurals and improvement in pain management.

The optimal ERP pain regimen for laparoscopic surgery is controversial. For many laparoscopic procedures, oral pain medications are often sufficient. However, there are times when a larger incision is required for specimen removal or for use in hand-assisted procedures. Additionally, visceral pain after laparoscopic surgery can be significant. One

RCT examined patients undergoing laparoscopic colorectal surgery and compared epidural, spinal and opioid PCA. Paradoxically, patients in the epidural group had a longer length of stay and a slower return of bowel function, but the spinal patients and PCA patients showed no difference.⁸⁸ Another study confirmed these results by comparing spinal to epidural anesthesia and found that spinal anesthesia was associated with shorter length of stay and earlier mobilization.⁸⁹ Local anesthetic techniques such as transverse abdominis plane (TAP) blocks which anesthetize the nerve supply to the anterior abdominal wall have also been proposed, but there is currently no definitive evidence to support their use.

Drains and catheters

ERPs recommend eliminating or minimizing the use of drains, tubes, and catheters. Surgeons have placed peritoneal drains to reduce postoperative fluid collections, decrease infectious morbidity, and as an adjunct to diagnose intra-abdominal bleeding and anastomotic leaks. However studies have not shown that placement of these drains is associated decreased rates of infection or postoperative fluid collections. In contrast, drains may cause infections of the abdominal cavity by tracking infection from the skin, and can cause bleeding and pain.⁸⁷ Pooled data has shown that only 1 in 20 patients with a clinical bowel leak will actually have enteric contents in their drain.⁹⁰ Peritoneal drains also impede mobilization, which is crucial for the success of ERP.⁸³

Urinary catheters should also be removed as quickly as possible, usually on the morning of postoperative day one. Prolonged catheter use is associated with an increased rate of urinary tract infection. In an RCT which examined early removal (1 day) compared to standard removal (approximately 4 days) the prevalence of urinary tract infection was increased to 12% for those in the in standard group and was only 2% in the early removal group ($p=0.004$).⁹¹ Of note, all patients in this trial had epidural catheters and there was no difference in the need for repeat catheterization, however 8% of the early removal group required a single in and out catheterization compared with only 2% in the standard group.

Traditional surgical practice involves routine placement of a nasogastric tube (NGT) with bowel rest following surgery and removal of the tube once the return of bowel function was established either by the passage of flatus or a bowel movement. However, there is high quality evidence that this practice may be detrimental. A Cochrane review examined patients undergoing abdominal surgery who received routine NGT placement versus selective use or no NGT use.⁹² Patients in the selective or no- tube group experienced an earlier return of bowel function ($p<0.0001$), a decrease in pulmonary complications ($p=0.01$), and no increased risk of anastomotic leaks or other postoperative complications. Patients in the NGT group also experienced increased discomfort. A meta-analysis of colorectal patients undergoing routine NGT decompression compared to selective NGT use confirmed these results and found no difference in return to bowel function, but a significantly increased rate of respiratory infections and complications.⁹³ Current Enhanced Recovery After Surgery society, also known as ERAS, guidelines for pelvic surgery and colorectal surgery strongly recommend against routine NGT placement. They state that “there is *no rationale* for routine nasogastric tube placement” and that all NGTs should be removed upon exiting the operating room.^{34,83} In an ERP created specifically for patients undergoing gynecologic

oncology surgery, NGT use was recommended only for patients undergoing gastric resections.¹⁰

Early Mobilization

Early mobilization is a hallmark of all ERPs. Traditional teaching and intuition suggests that early mobilization decreases pulmonary complications such as atelectasis, decreases insulin resistance, prevents loss of muscle mass, and shortens the interval to return of bowel function. Conversely, immobilization is associated with increased risk of thromboembolism and decreased oxygen delivery to tissues. However, there are no current RCTs that show that early postoperative activity results in improved postoperative outcomes. Analysis of ERPs shows that a failure to mobilize is a common reason for protocol deviation and is associated with increased length of stay suggesting that early mobilization is a key to achieve the beneficial outcomes associated with ERP.⁹⁴ Many ERPs recommend that patients get out of bed a minimum of 2 hours on the day of surgery and then 6 hours per day until discharge.^{34,95}

Which ERP interventions are most important?

An important methodologic point about most of the aforementioned studies and the ERP literature is that the studies examine entire ERP protocols in a given population and thus we do not have specific data on which of the individual ERP interventions are responsible for the improved outcomes. However, some authors have used protocol deviation to examine which specific factors within an ERP are associated with improved outcomes. In a Swedish study, failure to follow restriction of intravenous fluid and the use of a preoperative carbohydrate drink were the only independent factors that predicted poor postoperative outcome.³³ Another study of colorectal patients examined which specific factors were associated with worse outcomes in an ERP population and found that a non-functioning epidural and receiving more than the restriction limit of intravenous fluids were both independent predictors of postoperative complication in multivariate analysis.⁹⁶ Yet another study found that enforced advancement of oral intake, early mobilization, laparoscopic surgery and female sex were the only independent predictors of a shorter hospital stay.⁹⁴ From these limited data, we cannot conclude which elements of ERP are the most critical for success, but intravenous fluid management appears in two of these studies indicating that fluid management is one of the most important elements of ERPs.

ERP in Gynecology and Gynecologic Oncology

Data regarding ERP in gynecology and gynecologic oncology is relatively sparse when compared with other surgical fields and there are no published randomized trials.⁹⁷ Currently available prospective and retrospective cohort data is summarized in Table 2 and an example of an ERP protocol is for gynecology and gynecologic oncology patients is shown in Figure 1.¹⁰

Cohort studies comparing patients undergoing abdominal hysterectomy before and after implementation of an ERP have consistently found a decrease in length of stay with no difference in readmission or postoperative complication rates.⁹⁸⁻¹⁰⁰ Among patients

undergoing vaginal hysterectomy with or without pelvic organ prolapse surgery, ERP is associated with decreased length of stay and cost savings.^{10,11,101} An interesting study in this population also found that ERPs are associated with decreased nursing time required for patient care.¹⁰¹ Among patients with ovarian cancer undergoing cytoreductive surgery, participation in an ERP is associated with decreased length of stay, decreased time to return of bowel function, improved quality of life, and cost savings.^{9,10,20,102}

Implementation and the Role of Auditing of ERP

Implementation of an ERP requires coordination of a large multidisciplinary team. It requires compromise, standardization, and cooperation among large groups of people across a variety of disciplines. Pre-operative education teams, anesthesiologists, surgeons, trainees, hospital administrators, dietitians, physiotherapists, and nurses must work in concert to implement the various interventions of ERP that work synergistically to obtain the aforementioned outcomes.

Implementation of an ERP is difficult, not only due to the high degree of coordination that is required, but because many of these interventions run counter to the current practice patterns. Practice patterns can be ingrained and difficult to change. As such, auditing and monitoring ERP implementation is crucial to achieving success. Incidences of protocol deviation must be examined. Parameters audited should include protocol compliance and deviation, measuring clinical outcomes of ERP, and measuring the patient's quality of life and satisfaction. Compliance with an ERP protocol is associated with improved postoperative outcomes suggesting a dose-response relationship. A study from Sweden examined ERP compliance and found that adherence to the standardized ERP protocol resulted in lower rates of 30-day morbidity, length of stay, and readmissions.³³ Similarly, a British study of greater than 16,000 patients undergoing colorectal, orthopedic, gynecologic and urologic surgery in the United Kingdom. They found that compliance with the ERP protocol was associated with a shorter length of stay.¹⁰³ Monitoring compliance with ERP protocol is crucial to their success and all enhanced recovery societies including the Enhanced Recovery after Surgery Society and the Enhanced Recovery Partnership Program have toolkits to help institutions collect data, monitor compliance, and audit outcomes.

Future of ERP

In a health care world that is increasingly focused on evidence-based medicine, resource use, and measuring the quality of delivered care, ERP seems a natural fit across the surgical specialties. In Britain, the National Health Service has implemented the National Health Service Enhanced Recovery Partnership Program as a national quality improvement project and one can see a future in which reimbursement could be tied to ERP protocol use and compliance. High-quality level-one evidence has consistently shown that ERP is associated with decreased length of stay with no change or improvement in postoperative morbidity. ERP is evidence-based, cost saving, requires no new resources or technology, and improves patient quality of life. The cost to implementation an ERP are few whereas the benefits are tangible. As we, in the United States, move towards quality metrics, bundled payments, benchmarks, and pay for performance models, ERP is the future.

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Learning Objectives

After completing this activity, the learner will be better able to:

1. Specify the key components of enhanced recovery protocols.
2. Explain the rationale and benefit of enhanced recovery protocols across all surgical disciplines.
3. Discuss the current body of evidence regarding enhanced recovery protocols in gynecology and gynecologic oncology patients.

Enhanced Recovery Pathway	
I. Preoperative diet	<ul style="list-style-type: none"> • Evening before surgery: carbohydrate loading drink; may eat until midnight • May ingest fluids up to 4 h before procedure • Eliminate use of mechanical bowel preparation; rectal enemas still performed
II. Intraoperative	
Analgesia before operative room entry	<ul style="list-style-type: none"> • Celecoxib 400 mg orally once • Acetaminophen 1,000 mg orally once • Gabapentin 600 mg orally once
Postoperative nausea and vomiting prophylaxis	<ul style="list-style-type: none"> • Before incision (± 30 min): dexamethasone 4 mg IV once plus droperidol 0.625 mg IV once • Before incision closure (± 30 min): granisetron 0.1 mg IV once
Fluid balance	<ul style="list-style-type: none"> • Goal: maintain intraoperative euvoolemia <ul style="list-style-type: none"> ◦ Decrease crystalloid administration ◦ Increase colloid administration if needed
Analgesia	<ul style="list-style-type: none"> • Opioids IV at discretion of anesthesiologist supplemented with ketamine, ketorolac, or both • After incision closure: injection of bupivacaine at incision site
Anesthesia in pelvic organ prolapse surgery	<ul style="list-style-type: none"> • Subarachnoid block containing bupivacaine and hydromorphone (40–100 micrograms) • Sedation vs “light” general anesthetic at the discretion of the anesthesiologist • Ketorolac 15 mg IV at the end of the procedure for patients able to tolerate it • No wound infiltration with bupivacaine in this cohort
III. Postoperative	
Activity	<ul style="list-style-type: none"> • Evening of surgery: out of bed greater than 2 h, including one or more walks and sitting in chair • Day after surgery and until discharge: out of bed greater than 8 h including four or more walks and sitting in chair • Patient up in chair for all meals
Diet	<ul style="list-style-type: none"> • No nasogastric tube; if nasogastric tube used intraoperatively, remove at extubation • Patient encouraged to start low residual diet 4 h after procedure • Day of surgery: one box of liquid nutritional supplement; encourage oral intake of at least 800 mL of fluid, but no more than 2,000 mL by midnight • Day after surgery until discharge: two boxes of liquid nutritional supplement; encourage daily oral intake of 1,500–2,500 mL of fluids • Osmotic laxatives: senna and docusate sodium; magnesium oxide; magnesium hydroxide as needed
Analgesia	<ul style="list-style-type: none"> • Goal: no IV patient-controlled analgesia • Oral opioids <ul style="list-style-type: none"> ◦ Oxycodone 5–10 mg orally every 4 h as needed for pain rated 4 or greater or greater than patient stated comfort goal (5 mg for pain rated 4–6 or 10 mg for pain rated 7–10); for patients who received intrathecal analgesia, start 24 h after intrathecal dose given • Scheduled acetaminophen* <ul style="list-style-type: none"> ◦ Acetaminophen 1,000 mg orally every 6 h for patients with no or mild hepatic disease; acetaminophen 1,000 mg orally twice daily for patients with moderate hepatic disease; maximum acetaminophen should not exceed 4,000 mg/24 h from all sources • Scheduled NSAIDs <ul style="list-style-type: none"> ◦ Ketorolac 15 mg IV every 6 h for four doses (start no sooner than 6 h after last intraoperative dose); then, ibuprofen 800 mg orally every 6 h (start 6 h after last ketorolac dose administered) • If patient unable to take NSAIDs <ul style="list-style-type: none"> ◦ Tramadol 100 mg orally 4 times a day (start at 6:00 AM day after surgery) for patients younger than 65 years of age and no history of renal impairment or hepatic disease; tramadol 100 mg orally twice daily (start at 6:00 AM day after surgery) for patients 65 years of age or older or creatinine clearance less than 30 mL/min or history of hepatic disease • Breakthrough pain (pain greater than 7 more than 1 h after receiving oxycodone) <ul style="list-style-type: none"> ◦ Hydromorphone 0.4 mg IV once if patient did not receive intrathecal medications; may repeat once after 20 min if first dose ineffective • IV patient-controlled analgesia <ul style="list-style-type: none"> ◦ Hydromorphone patient-controlled analgesia started only if continued pain despite 2 doses of IV hydromorphone
Fluid balance	<ul style="list-style-type: none"> • Operating room fluids discontinued on arrival to floor • Fluids at 40 mL/h until 8:00 AM on day after surgery and then discontinued • Peripheral lock IV when patient had 600 mL orally intake or at 8:00 AM on day after surgery, whichever came first
IV, intravenous; NSAIDs, nonsteroidal anti-inflammatory drugs.	
*Doses for patients greater than 80 kg and younger than 65 years of age; doses adjusted as appropriate for patients less than 80 kg or 65 years of age or older.	

Figure 1. Example of ERP Protocol
Protocol from a recent ERP study, Kalogera et al, that was implemented in gynecology and gynecologic oncology patients

Table 1
Enhanced Recovery Protocol Components

Key components of ERP in the preoperative, intraoperative and postoperative periods

Preoperative Patient education and preadmission counseling Carbohydrate loading No prolonged fasting Avoid bowel preparation Nausea and vomiting prophylaxis
Intraoperative Zero-balance fluid policy Minimally invasive surgery No drains Normothermia Multimodal pain management Regional anesthesia Short-acting anesthetics
Postoperative Early mobilization Early enteral feeding No nasogastric tubes Early urinary catheter removal Multimodal pain management Zero-balance fluid policy Regional anesthesia Nausea and vomiting prophylaxis

Table 2
Enhanced Recovery Studies in Gynecology and Gynecologic Oncology

Summary of currently available data regarding ERP in gynecology and gynecologic oncology

Study	Patient population	Methodology	Outcomes	Results for the intervention cohorts
Dickson et al, 2012	Abdominal hysterectomy for benign conditions	Retrospective cohort study of n=176 before a "rapid recovery protocol" and n=190 after implementation	LOS Complications	LOS decreased from 3 days to 1 day, p<0.0001 No difference in postoperative complications
Miller et al, 2011	Abdominal hysterectomy for benign conditions	Retrospective cohort study of n=100 before a "hysterectomy enhanced recovery pathway" and n=123 after implementation	LOS POD1 discharges Readmission	LOS decreased from 3 days to 2 days, p<0.0001 POD1 discharges increased from 7% to 34%, p<0.0001 No difference in readmissions
Yoong et al, 2014	Vaginal hysterectomy for benign conditions	Cohort study of n=50 before a "enhanced recovery after surgery program" and n=50 after implementation	LOS Readmissions ER visits Cost	LOS decreased from 45.5 to 22.0 hours, p<0.01 No difference in readmissions or ER visits Gross cost savings of 9.25% per patient (\$159.45 per patient, no significance testing performed)
Sjetne et al, 2009	Pelvic-floor surgery and hysterectomy	Prospective cohort study of n=35 before a "enhanced recovery after surgery program" and n=90 after implementation	LOS Nursing time	LOS decreased by 28%, p<0.001 Nursing activities per stay decreased by 39%, p<0.001
Kalogera et al, 2013	Pelvic organ prolapse surgery	Prospective cohort study of n=77 before a "enhanced recovery pathway" and n=76 after implementation	LOS Complications Readmission Mortality Cost	LOS decreased from 46.1% POD1 discharges to 6.5% p<0.001 No difference in postoperative complications, readmissions or mortality No difference in cost
Wijk et al, 2014	Abdominal hysterectomy for benign and malignant conditions	Prospective cohort study of n=120 before a "enhanced recovery after surgery protocol" and n=85 after implementation	LOS Complications Readmissions Reoperation	LOS decreased by 0.3 days, p=0.011 More patients were discharged home on postoperative day 2 (73% to 56%, p=0.012) No difference in postoperative complications, readmissions or reoperation
Marx et al, 2006	Cytoreductive surgery for ovarian cancer	Prospective cohort study of n=72 before a "multimodal rehabilitation protocol" and n=69 after implementation	LOS Complications Readmissions	LOS decreased from 7.3 days to 5.4 days, p<0.05 Reduced severe medical complications from 14% to 2%, p<0.01 Reduced readmissions 10% to 3%, p<0.05
Eberhart et al, 2008	Cytoreductive surgery for ovarian cancer	Prospective cohort study of n=46 before a "fast-track rehabilitation program" and n=40 after implementation	Quality of life Complications	Improvements in scores on validated quality of life tool (PPP33 questionnaire) in regard to "autonomy", "physical complaints" and "postoperative pain" (p<0.05) No difference in postoperative complications
Gerardi et al, 2008	Cytoreductive surgery with rectosigmoid colectomy for ovarian cancer	Prospective cohort study of n=45 before a "clinical pathway" and n=19 after implementation	LOS Time to flatus Readmission Cost	LOS decreased from 10 days to 7 days, p=0.014 No difference in time to flatus No difference in readmission Cost savings of \$5,410 per patient, p=0.028
Kalogera et al, 2013	Complex cytoreductive surgery for ovarian cancer	Prospective cohort study of n=78 before a "enhanced recovery pathway" and n=81 after implementation	LOS Time to flatus Complications Readmission Mortality Cost	LOS decreased from 10.7 days to 6.5 days, p<0.001 Time to flatus decreased from 4 days to 3 days, p<0.001

Study	Patient population	Methodology	Outcomes	Results for the intervention cohorts
				No difference in postoperative complications, readmissions or mortality Cost savings of \$7,600 per patient, p=0.006
De Groot et al, 2014	Abdominal surgery for gynecologic malignancies	Cohort study of n=38 before a “enhanced recovery after surgery protocol” and n=77 after implementation	LOS Functional recovery	LOS decreased from 7 days to 5 days, p<0.001 Time to functional recovery decreased from 6 days to 3 days, p<0.001