Gynecologic ERAS Preoperative Interventions

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Abstract: Enhanced recovery after surgery (ERAS) protocols have been widely adopted within gynecologic surgery to optimize perioperative outcomes. This chapter discusses the evidence behind preoperative gynecologic ERAS elements, including preadmission counseling, comorbidity optimization, fasting guidelines, preoperative medications, and prehabilitation. Much of the evidence is extrapolated from colorectal and other surgical populations but has been supported within gynecology. Prehabilitation is the newest element, aimed at improving preoperative functional status through exercise, nutrition, and psychological support, with gynecology-specific evidence emerging to support inclusion within ERAS protocols. Preoperative interventions are the foundation of ERAS bundles, and adherence to these elements should be encouraged.

Key Words: ERAS, preoperative, anemia, fasting, premedication, prehabilitation

(*Clin Obstet Gynecol* 2025;68:479–490)

Enhanced recovery after surgery (ERAS) programs have become the standard within many surgical specialties, providing a bundle of perioperative interventions aimed at improving patient outcomes and facilitating postoperative recovery. The preoperative period is an opportunity to positively impact patients' surgical trajectory before they even enter the operating room (OR). This chapter focuses on the following preoperative ERAS components within gynecologic surgery: preadmission counseling, management of comorbidities, preoperative fasting and carbohydrate treatment, and preoperative medications. Special attention is given to prehabilitation, which has not yet been formally incorporated into gynecologic ERAS guidelines but is gaining popularity and holds great potential as an ERAS adjunct. An emphasis on gynecology-specific evidence is maintained as able, with the broader surgical literature utilized when necessary.

PREADMISSION EDUCATION AND COUNSELING

ERAS begins with preoperative education and counseling to prepare patients for their surgery and recovery. Providing information ahead of time allows patients to enter the perioperative period with appropriate expectations about their surgery, hospital stay, and postdischarge recovery course. Adequate counseling is also believed to benefit providers, as realistic patient expectations may improve success with goals like same-day discharges, adherence to activity recommendations, and decreasing calls about postoperative concerns.[1]

In an international validation of gynecologic ERAS by Wijk et al,[2] compliance with providing preadmission education had a significant association with reduced length of stay (LOS) in medium/high-complexity patients even after adjustment for covariates (−0.27 d, $P < 0.05$). This finding was supported by a systematic review of preoperative education in abdominal surgery, with not only shorter LOS but also fewer complications and improved psychological status, albeit limited by high heterogeneity.[3] A descriptive analysis of patients' perspectives after ERAS-guided gynecologic surgery noted a positive effect of clear preadmission counseling on patient's expectations and perception of high-quality care.[4] Variability in institutional infrastructure makes it unlikely that preoperative education will be standardized to the same degree as other ERAS elements, but ensuring that all ERAS patients receive counseling is essential.

The optimal form of counseling has not been determined. A randomized study in gynecologic oncology found that patients who received written information preoperatively compared with verbal preparation had shorter LOS, better satisfaction with the provided information, and decreased pain scores and analgesic use.[5] Although this study was conducted as an either-or, the ideal scenario is likely a combination of oral plus written information to provide an ongoing point of reference, which is recommended in the ERAS guidelines for gynecologic oncology, minimally invasive gynecology, and urogynecology.[1,6,7] Verbal instruction can be more personalized, with the ability to check for patients' understanding of the provided information and to answer questions, but can be easily forgotten unless accompanied by a written reference.

One proposed option to fill the need for perioperative education using a digital application (app). An ERAS app piloted for gynecologic oncology and colorectal surgery at 2 Canadian hospitals received positive feedback by both patients and providers on its utility in assisting with perioperative preparation, setting expectations, and improving patients' engagement with their care.[8] Any written information can have limitations of language barriers or reading level, and mobile apps will have additional challenges for patients who lack technological proficiency or mobile phone capability to utilize an app. Despite these possible limitations, digital ERAS apps are an interesting idea to facilitate personalized and interactive preparation, while minimizing the time burden for in-person instruction by providers. Preoperative counseling lays the groundwork for ERAS protocols to succeed, and future improvements in tailoring the provision of this information will help optimize patient preparation, expectations, and engagement with their perioperative course.

MANAGING/OPTIMIZING PREOPERATIVE COMORBIDITIES

The intent behind preoperative optimization is to improve conditions that may negatively impact a patient's

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The authors declare that they have nothing to disclose.

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DOI: 10.1097/GRF.0000000000000970

perioperative trajectory. There are many possible comorbidities that can be included within preoperative assessments. The ERAS society guidelines for gynecologic oncology address anemia, smoking, and alcohol consumption, and will therefore be the focus of this section.[6] The ability to intervene preoperatively is predicated on both patient motivation as well as sufficient time before surgery to effect change. Gynecologic oncology surgeries are more time-sensitive than operations for benign gynecologic conditions, and the benefits of optimizing comorbidities must be balanced with the risk of delaying surgery.

Anemia

Anemia is a common risk factor in patients undergoing gynecologic surgery, with an overall prevalence of approximately one quarter of all patients with both benign and malignant pathologies.[9–11] Anemia is defined as a hemoglobin (Hb) < 12 g/dL in adult nonpregnant females,[12] but $\geq$ 13 g/dL regardless of sex has been suggested to be a more appropriate preoperative Hb target.[13] Although there are many causes of anemia, iron deficiency is most commonly implicated due to blood loss, inadequate intake, or functional iron deficiency from inflammation (causing anemia of inflammation, previously called anemia of chronic disease).[14]

Anemia is considered a modifiable risk factor for perioperative morbidity and mortality, with multiple large retrospective cohort studies showing anemia to be independently associated with increased 30-day morbidity and mortality in noncardiac surgery, including gynecology-specific studies of patients undergoing surgery for both malignant and benign indications.[9,11,15] Red blood cell transfusion is not recommended as a treatment strategy for anemia, as transfusions have also been independently associated with negative outcomes, including increased morbidity, mortality, wound infections, and LOS in patients undergoing major abdominal and gynecologic surgeries.[10,16,17]

Patient blood management (PBM) programs are a contemporary "three pillar" approach, with the preoperative PBM pillar focused on identification and treatment of anemia.[18] Preoperative screening is recommended in all patients other than those undergoing minor procedures, as anemia is common, treatable, and increases perioperative risk.[14,19] Incorporating laboratory evaluation into the initial preoperative visit can optimize patient convenience and allow prompt initiation of treatment.[14] Two international consensus statements on perioperative anemia recommend intravenous (IV) iron over oral formulations for treatment, which is safe and well tolerated, quickly increases iron stores and hemoglobin, and is effective in both iron deficiency and anemia of inflammation.[13,19]. Erythropoiesis-stimulating agents (ESAs) in combination with iron treatment are another treatment option in certain patients, although their use has been limited by concerns about risk of venous thromboembolism and cancer progression, so consideration of ESAs should be done in conjunction with oncologists.[14,18] For the gynecologic surgery population, preoperative anemia correction may also include medications to suppress uterine bleeding, like combined hormonal contraceptives or levonorgestrel intrauterine devices.[1] If vitamin B12 and folate deficiencies are identified in the preoperative screening, these micronutrients can also be supplemented.[14]

The benefit of preoperative optimization has been described by Guinn et al,[20] in which 127 patients treated through a preoperative anemia clinic before gynecologic and orthopedic surgery were propensity-matched 1:1 with controls. Treated patients had significantly lower rates of transfusion (12.60% vs. 26.77%, $P = 0.005$), and the gynecologic surgery subgroup also had a shorter LOS (2.2 vs. 3.1 d). This contrasts with the PREVENTT trial, an RCT of 487 patients assigned to IV iron or placebo before major abdominal surgery, in which treatment did not reduce the composite outcome of blood transfusion, death, and the number of blood transfusions within 30 days.[21] However, the median time from randomization to surgery was only 15 days, and treated patients did achieve significantly higher Hb at the time of surgery (0.47 g/dL), 8 weeks (1.07 g/dL), and 6 months (0.73 g/dL), and had significantly lower hospital readmission rates, suggesting that the measured outcomes may not have captured the benefits of IV iron supplementation.

In the Guinn and colleagues study, longer treatment times correlated with greater increases in Hb, with improved benefit up to 2 months, although delaying surgery this long may not be feasible for oncologic surgeries. Screening at least 4 weeks before surgery is recommended if possible, but evaluation and treatment are still recommended even with shorter time frames.[14,19] Given the prevalence of anemia and ability to improve this risk factor, screening at the time of surgical booking with prompt initiation of treatment should be a routine component of ERAS protocols in gynecologic surgery.

Smoking and Alcohol

Cessation of preoperative smoking and heavy alcohol consumption are strongly recommended as components of gynecologic ERAS optimization.[22] Smoking increases the risk of perioperative complications, with studies consistently indicating elevated rates of pulmonary complications, infections, and mortality.[23–25] One American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) study of 82,304 current smokers propensity-matched 1:1 to never-smokers undergoing noncardiac surgery found that smokers had 40% increased odds of 30-day major morbidity and mortality, with around double the odds of pneumonia (OR 2.09, 95% CI: 1.80-2.43) and unplanned intubation (OR 1.87, 95% CI: 1.58-2.21).[24]

Smoking cessation programs are encouraged in efforts to decrease smoking-associated risks. A Cochrane review on preoperative smoking cessation interventions found decreased postoperative complications in patients undergoing intensive intervention of weekly counseling plus optional nicotine replacement therapy (NRT) for 4 to 8 weeks before surgery (RR 0.42, 95% CI: 0.27-0.65), although this only included 210 participants in 2 trials, and trials utilizing brief interventions did not show similar benefit.[26] Another meta-analysis suggested that the risk reduction seen from smoking cessation is enhanced with longer durations of preoperative abstinence, supporting the benefit of programs ≥ 4 weeks.[27] However, even if a longer period of preoperative cessation is optimal, shorter durations are not harmful. Long-standing concern about increased perioperative risks of quitting within 8 weeks of surgery (due to increased cough and sputum production) is thought to have been borne out of misinterpretation of early studies and is not supported in the literature.[28,29]

The optimal design of smoking cessation programs remains undefined, although 2 recent systematic reviews of perioperative smoking cessation interventions indicated that

inclusion of counseling sessions is likely the most efficacious for successful abstinence, with additional benefit from NRT.[30,31] Importantly, those who participate in intensive interventions are also more likely to quit long-term, with 6 to 12 month postoperative abstinence rates between 25.0% and 36.4% versus 13.0% for patients in brief interventions.[30] The perioperative period is a time when patients are more motivated to make behavior changes and may be more likely to be successful with smoking cessation.[32] Individuals should be encouraged to quit smoking regardless of the duration before surgery, and any success with long-term abstinence will have positive health benefits that extend far beyond the perioperative period.

The deleterious perioperative effects of heavy alcohol consumption have also long been established, with higher morbidity including bleeding, infections, and cardiopulmonary compromise.[33] A meta-analysis of 31 studies published between 2000 and 2011 confirmed that even with modern surgical practices, preoperative alcohol consumption is still associated with increased postoperative complications.[34] Intensive preoperative alcohol cessation interventions, including pharmacologic treatment and motivational counseling for at least 4 weeks preoperatively, decreased complications and increased postoperative alcohol abstinence in 3 Danish studies, although these only included 140 total patients.[35] A systematic review of preoperative behavioral interventions also suggested promising results, but the evidence is not robust.[36] Effective alcohol cessation interventions have yet to be optimized and should be an area of continued research.

PREOPERATIVE FASTING AND CARBOHYDRATE TREATMENT

Avoidance of prolonged perioperative fasting and provision of preoperative carbohydrate loading are recommended to attenuate the surgical stress response and improve patient-centered outcomes like hunger and thirst.[37,38] The gynecologic oncology ERAS guidelines on preoperative fasting align with the recommendations of the American Society of Anesthesiology (ASA) for healthy patients undergoing elective surgery, which permit clear liquids up to 2 hours before surgery and a light meal up to 6 hours prior, with at least 8 hours of fasting for a full meal, including any fried or fatty foods.[39]

The gynecologic ERAS recommendation for carbohydrate-containing fluid consumption is drawn from the broader surgical literature. Two meta-analyses with over 1500 patients each supported a reduction in hospital LOS and improved postoperative insulin sensitivity, with no change in postoperative complications, in patients receiving preoperative carbohydrate treatment.[40,41] Although the included trials in both meta-analyses were noted to be limited by study heterogeneity and risk of bias, these pooled findings do suggest that carbohydrate treatment favorably affects glucose metabolism as well as postoperative trajectories, and importantly, without increasing complications.

Preoperative carbohydrate beverages have additional benefits in patient-reported outcomes. Studies consistently illustrate decreased hunger compared with fasting or non-carbohydrate fluid intake, and improved thirst in comparison to fasting.[42–44] The role of carbohydrates in decreasing postoperative nausea and vomiting has not been as consistently demonstrated.[40,44] Although there is a trend for superiority of clear liquids over preoperative fasting, a strong advantage of carbohydrate loading over water has not been shown.[45]

Importantly, consumption of carbohydrate beverages does not increase residual gastric volume at 2 hours in comparison to water, affirming its safety as a preoperative fluid option. An RCT of 64 patients undergoing elective ambulatory surgery assessing gastric emptying after 200 mL of a carbohydrate beverage versus water found that both groups had returned to baseline by 2 hours postingestion, despite the carbohydrate group having significantly higher gastric cross-sectional area (CSA) at 1 hour.[43] The equivalence of carbohydrate-containing fluids to water has been corroborated even in obese patients.[46] The ASA supports the safety and benefit of drinking up to 400 mL of carbohydrate-containing clear liquids up to 2 hours before elective procedures.[44] Patients with diabetes are excluded from the ASA guidelines, but provision of preoperative carbohydrate treatment to patients with type 2 diabetes has not been shown to delay gastric emptying nor increase postoperative insulin requirements or complications.[47,48] Appropriate timing for consumption of carbohydrate beverages is predicated on planned OR start time, so OR delays extend patients' fasting duration from clear liquids. Despite this potential issue, published institutional experiences with gynecologic ERAS report high levels of compliance with the recommendation for carbohydrate loading within 2 hours before surgery.[49–52]

One specific population to mention is patients using glucagon-like peptide-1 receptor antagonists (GLP-1RAs). The explosion of GLP-1RAs in diabetes and for weight loss has led to concerns about the risk of aspiration given the delayed gastric emptying time and gastrointestinal side effects of these drugs.[53] Initial guidance by the ASA favored holding GLP-1RAs before surgery.[54] More recently, a multisociety consensus for the management of patients on GLP-1RAs suggests that patients without additional risk factors for delayed gastric emptying and aspiration continue their GLP-1RA, and to consider use of a liquid diet for at least 24 hours preoperatively in lieu of holding GLP-1RAs in patients who do have elevated risk, with additional day-of-surgery recommendations based on patient symptoms and clinical concern.[55] The current guidance is based on consensus, so future studies will be needed to provide evidence-based recommendations.

PREOPERATIVE MEDICATIONS

One of the key tenets in ERAS pathways is utilization of multimodal analgesia to manage postoperative pain without reliance on opioid medications. In the first gynecologic oncology ERAS guidelines in 2016, multimodal analgesia was only mentioned in regard to the postoperative setting.[56] The 2019 update added a specific preoperative recommendation for the routine administration of oral acetaminophen, celecoxib, and gabapentin.[6] In the 2023 update, clarifying preoperative medication recommendations was addressed as one of 9 implementation challenges for gynecologic ERAS.[57] Acetaminophen and nonsteroidal anti-inflammatories (NSAIDs) were given strong recommendation grades, with a high level of evidence within gynecology for NSAIDs, and a low level for acetaminophen. Gabapentin was still included as part of preoperative medication recommendations, although this update cautioned on the risks of gabapentinoids in the elderly.

Acetaminophen

Although acetaminophen is routinely included within ERAS premedication bundles, its use in the preoperative setting has not been prospectively studied specifically within patients undergoing gynecologic surgery, but instead inferred from colorectal surgery.[58] In Ban et al's[58] evidence review for the Agency for Healthcare Research (AHRQ) for colorectal surgery, they note 2 studies supporting preoperative acetaminophen within elective surgical patients. A 2008 Cochrane review found single dose oral acetaminophen to be effective analgesia for around 4 hours for about half of patients with acute postoperative pain, without any serious side effects.[59] In addition, a 2015 systematic review and meta-analysis comparing preventive versus postincision acetaminophen showed a moderate clinically significant reduction in 24-hour opioid consumption, lower pain scores up to 2 hours postoperatively, and decreased incidence of postoperative vomiting.[60] The included studies were limited by a potential risk of bias, and the results of the meta-analysis were suggested to be considered preliminary. Notably, all the studies utilized intravenous administration of acetaminophen, though this route is more costly and has not been shown to have superior analgesic efficacy to oral, including within studies of both open and minimally invasive gynecologic surgery.[61–63] Inclusion of acetaminophen as a premedication within gynecologic ERAS protocols is an inexpensive and safe intervention that facilitates nonopioid multimodal analgesia.

Nonsteroidal Anti-inflammatories

The 2023 gynecologic/oncology ERAS guidelines update does not clarify a preference for preoperative NSAID type, although many published protocols specifically suggest celecoxib, the only COX-2 inhibitor available in the United States.[49,50,64–66] COX-2 inhibitors do not directly affect platelet function, and thus do not significantly increase the risk of perioperative bleeding.[67] The 2019 review for the AHRQ by Grant et al[68] notes 3 RCTs in gynecologic surgery supporting COX-2 selective inhibitors for preoperative analgesia. Two studies utilized preoperative parecoxib injections versus placebo; one included 120 patients before exploratory laparotomy, and the other in 268 patients before laparoscopic gynecologic surgery.[69,70] Both trials found significantly lower mean 24-hour postoperative meperidine consumption in the parecoxib group (27.50 +/- 19.36 mg vs. 48.75 +/- 28.15 mg for the laparotomy trial and 26.3 +/- 28.1 mg vs. 39.1 +/- 34.6 mg for the laparoscopy trial; both $P < 0.001$). Pain scores up to 24 hours postoperatively were only significantly decreased in the trial of patients undergoing laparotomy. The third study evaluated rofecoxib versus placebo administered preoperatively and for the first 4 postoperative days in patients undergoing total abdominal hysterectomy or myomectomy.[71] The rofecoxib group had a significantly lower postoperative opioid requirement and improved pain control, as well as significant improvement in other secondary clinical outcomes like time to first flatus and bowel movement. Rofecoxib was withdrawn from the worldwide market in 2004 due to concerns for cardiovascular adverse events, but celecoxib remains available as a COX-2 selective inhibitor,[72] and extrapolating the study findings to celecoxib suggests preoperative benefit. Two clinical trials in chronic NSAID users have suggested a similar cardiovascular safety profile between celecoxib and nonselective NSAIDs, which implies a reasonable cardiovascular safety profile for a single preoperative dose.[73,74] Importantly, the combination of acetaminophen plus NSAIDs has been shown to have increased analgesic efficacy over either alone.[75]

Gabapentin

Gabapentin was originally a mainstay of ERAS preoperative medication regimens, including within gynecology. A 2014 systematic review and meta-analysis of RCTs of patients undergoing a total abdominal hysterectomy, with or without bilateral salpingo-oophorectomy, found an opioid-sparing effect of preoperative gabapentin administration, with a significant decrease in morphine consumption at 24 hours.[76] Multiple other studies within both open and minimally invasive gynecologic surgery supported these positive findings.[77–79] Meta-analyses of gabapentinoids also found that both gabapentin and pregabalin significantly reduce postoperative nausea and vomiting in patients undergoing general anesthesia, though with significantly increased risks of sedation/somnolence and visual disturbance, respectively.[80,81] However, a 2020 meta-analysis of 281 randomized control trials failed to show a clinically meaningful difference in pain with gabapentinoid use and noted an increased rate of adverse events, particularly dizziness and visual disturbance.[82] Furthermore, a large cohort study of over 237,872 adults age 65 and older found a significant increase in the risk of delirium, new antipsychotic use, and pneumonia after major surgery in patients who received perioperative gabapentin.[83] Another large cohort study of over 5 million surgical admissions also showed an increased risk of opioid-related adverse events, including overdose in patients concomitantly using gabapentinoids and opioids [adjusted hazard ratio 1.95 (95% CI: 1.49-2.55)].[84] Even though the overall rate of adverse events was low, the potentiation of central nervous system and respiratory depression is concerning, particularly if the clinical benefits of gabapentin are less notable than originally believed. Although the most recent gynecologic ERAS update still recommends gabapentin except for the elderly,[57] a subsequent update may see this recommendation removed entirely.

Sedatives

Avoiding routine administration of preoperative sedatives has been consistently recommended in all versions of the gynecologic/oncology ERAS guidelines.[6,22,57] A 2009 Cochrane review of premedication for anxiety in adults undergoing day surgery under general anesthesia demonstrated a prolonged return of psychomotor function in those receiving premedication, though this was not reflected in a delay in discharge.[85] Of note, the included studies are almost all from the late twentieth century and many reflect outdated premedication practices, giving limited applicability in today's practice. Concern about an association with postoperative delirium has led to recommendations against perioperative benzodiazepine use in older adults, which is the most commonly utilized category of preoperative sedative.[86] A 2024 RCT of 607 patients between 65 and 80 years old receiving either a single dose of preoperative oral midazolam versus placebo found no difference in any adverse events or complications between the groups, including delirium on postoperative day one [1 of 304 ($< 1\%$) vs. 3 of 303 (1%)], though these events were analyzed as secondary outcomes.[87] Neither did they find a difference in their primary outcome of global perioperative patient

satisfaction between the groups (mean 69.5 vs. 69.6; mean difference, −0.2; 95% CI: −1.9 to 1.6; $P = 0.85$). A 2025 large prospective cohort study of 5663 patients investigating the risk of postoperative delirium in adults age 65 and older undergoing noncardiac surgery did not show a significant association between receiving intravenous midazolam in the OR and the occurrence of postoperative delirium within 7 days of surgery (adjusted risk ratio, 1.09; 95% CI: 0.91-1.33; $P = 0.35$).[88] Although these studies challenge prior beliefs about the risks of perioperative midazolam, avoiding standard administration of preoperative anxiolytics is reasonable.

PREHABILITATION

Prehabilitation is gaining traction as an adjunct to successful ERAS protocols and is a natural response to the enormous body of literature demonstrating that patients who are more physically active and functional (eg, higher VO2 max) have better surgical outcomes.[89–93] Whether or not physical fitness is a modifiable determinant of outcomes, or a more general sign of overall health and well-being, is the focus of recent, ongoing, and planned trials in prehabilitation.

Although the exact elements may vary, prehabilitation programs include interventions undertaken during the preoperative period aimed at the triad of exercise, nutrition, and psychological status, with the aim of decreasing the degree of postoperative decline by optimizing preoperative status.[94] Management of additional perioperative comorbidities like tobacco and alcohol use or chronic diseases has also been included under the umbrella of prehabilitation.[95–97] A 2024 review of existing RCTs on prehabilitation suggests the following common definition: "prehabilitation is a process from diagnosis to surgery, consisting of one or more preoperative interventions of exercise, nutrition, psychological strategies, and respiratory training, that aims to enhance functional capacity and physiological reserve to allow patients to withstand surgical stressors, improve postoperative outcomes, and facilitate recovery."[98]

Prehabilitation in Non-gynecology Populations

Like the development of enhanced recovery programs, much of the established research on prehabilitation is within colorectal surgery.[99–104] Most studies have been performed within the context of a perioperative enhanced recovery program in addition to the prehabilitation and rehabilitation interventions. A 2023 Cochrane review of prehabilitation in colorectal surgery concluded with a moderate level of evidence that prehabilitation improves preoperative functional status, but only a low level of evidence that this improvement continues postoperatively.[97]

The PREHAB trial, published shortly after the Cochrane review, assessed postoperative complications and functional recovery in 251 patients with nonmetastatic colorectal cancer who underwent a 4-week supervised multimodal prehabilitation program compared with standard care incorporating perioperative ERAS.[105] Patients in the prehabilitation group had a significantly lower rate of severe complications, and a lower, though nonsignificant difference in overall complication rate. A trend towards increased 6MWD at 4 weeks postoperatively was noted in the prehabilitation group (16 m, $P = 0.07$), and significantly more patients improved compared with their baseline. The trial's prespecified sample size of 714 patients was not reached due to restrictions related to the COVID-19 pandemic, limiting interpretation of the results, but this is still the largest RCT on multimodal prehabilitation within colorectal surgery.

A critique of existing prehabilitation trials spanning all surgical specialties is a lack of adherence to reporting guidelines, limiting the quality of evidence and the ability to conduct meta-analyses.[106] As such, the ERAS Society has not yet formally recommended inclusion of prehabilitation within gynecologic surgery. The 2019 update of the ERAS Society guidelines for gynecologic oncology suggested a potential clinical benefit from a prehabilitation program but refrained from an endorsement due to a paucity of gynecology-specific evidence,[6] and the 2023 update did not comment on prehabilitation.[57] Similarly, a 2022 joint consensus statement on enhanced recovery after urogynecological surgery lists prehabilitation as a weak recommendation with very low-quality evidence.[7] In contrast, the 2021 European Society of Gynaecological Oncology guidelines for the perioperative management of advanced ovarian cancer patients undergoing debulking surgery include prehabilitation with ERAS as a grade A recommendation, with a trimodal approach to prehabilitation as a grade B recommendation, although the guidelines do not reference the evidence supporting these recommendations.[107]

Prehabilitation in Gynecology

Within the existing gynecology literature, prehabilitation has been primarily focused on gynecologic oncology patients, who frequently have postoperative decline as well as associated comorbidities like anemia.[9,108] Although patients with gynecologic cancer are heterogeneous regarding their baseline status and disease state, patients with endometrial cancer have high rates of obesity,[109,110] and patients with ovarian cancer are frequently malnourished and with muscle wasting due to their often-advanced stage at the time of presentation.[111,112]

The possibility for success of a prehabilitation program requires sufficient lead time before surgery for patients to meaningfully engage with these interventions, which depends on the length of time between diagnosis and surgery. A duration of 2 to 4 weeks has been suggested for gynecologic oncology patients, specifically patients with endometrial or cervical cancer, or for patients with ovarian cancer undergoing primary debulking surgery.[96] In patients with ovarian cancer undergoing neoadjuvant chemotherapy before interval debulking surgery, this time frame may extend to several months.

Summaries of the published gynecologic surgery prehabilitation studies discussed below are in Table 1. The prehabilitation program described and utilized by Miralpeix et al[96] includes elements of medical comorbidity optimization in addition to physical, nutritional, and psychological interventions, with differing interventions according to baseline parameters. This prehabilitation program continues in the postoperative state, restarting after surgery and continuing up to 8 weeks postoperatively. In a pre-post cohort analysis of 128 patients with endometrial cancer undergoing laparoscopic surgery in an ERAS protocol, the prehabilitation group exhibited reduced median length of stay (2.0 vs. 3.0 d, $P < 0.001$) and earlier oral intake (8 vs. 16 h, $P = 0.005$) without increasing complications or readmission rate.[114] Looking specifically at the nutritional component, protein supplementation in the same group of prehabilitation patients did not lead to improvement in

TABLE 1. Characteristics of Gynecologic Prehabilitation Studies

		Number of patients				
	Study design	**Prehab**	**Control***	**Study population**	**Key components of prehabilitation intervention**	**Outcomes**
Miralpeix et al. (2022)[113]	Pre-post prospective cohort	14	15	Advanced ovarian cancer undergoing neoadjuvant chemotherapy followed by interval cytoreduction surgery	Daily exercise program (supervised or at-home based on VO2 max) Nutritional supplements + dietary recommendations or dietician referral (based on MUST) Weekly group mindfulness session + anti-anxiety exercises or psychotherapy (based on HADS)	↑ Preop protein (7.4 vs 6.8 g/dl, $p = 0.004$) ↑ Postop protein (4.9 vs 4.3 g/dl, $p = 0.005$) ↑ Postop albumin (2.8 vs 2.4 g/dl, $p = 0.021$) ↓ transfusion (14.3 vs 53.3%, $p = 0.027$) No difference in length of surgery, complications, LOS, postop pain, readmission rate, mortality
Miralpeix et al. (2023)[114]	Pre-post retrospective cohort	68	60	Endometrial cancer undergoing laparoscopic surgery	Same as above	↓ LOS (2 vs 3 days, $p = <0.001$) Earlier diet (8 vs 16 hours, $p = 0.005$) No difference in complications or readmission rate
Sole-Sedeno et al. (2023)[115]	Pre-post prospective cohort	68	60 (ERAS) 57 (pre ERAS†)	Endometrial cancer undergoing laparoscopic surgery	Same as above	No intergroup difference in pre- or postop protein, albumin, or prealbumin Note: adherence in prehabilitation group not recorded
Miralpeix et al. (2025)[116]	Prospective cohort	77	n/a	Any gynecologic cancer	Same as above, except: -Choice of CrossFit 3x/week vs daily at-home training for fit patients -Hospital-supervised training for frail patients	6MWD ↑ 20.7 m preop ($p < 0.001$) -CrossFit (33.4 m) -Hospital-supervised (27.1 m) -Home training (14.0 m) ↑ Hand grip strength ↓ Malnutrition and HADS score
Diaz-Feijoo et al. (2022)[117]	Pre-post prospective cohort	15	19	Advanced or recurrent ovarian cancer	Supervised exercise (high-intensity + resistance) Group CBT +/- psychologist referral (based on HADS) Nutritional assessment + supplementation	80% overall adherence to program ↓ LOS (5 vs 7 days, $p = 0.04$) ↓ days to chemo (25 vs 35, $p = 0.03$) No difference in complications
Sebio-Garcia et al. (2024)[118]	Ambispective cohort	35	n/a	Advanced ovarian cancer	Same as above	6MWD ↑ 33.1 m preop ($p < 0.05$) 30s Sit-to-stand test ↑ 2 reps ($p < 0.01$) HADS score ↓ 4.4 points ($p = 0.001$)
Dhanis et al. (2024)[95]	Prospective cohort	111	n/a	Ovarian, uterine, or vulvar cancer	Exercise: 3x/week supervised + aerobic non-supervised Nutritional supplements + dietary recommendations Psychologist referral	67% of eligible patients participated 85% adherence to supervised exercise 88% adherence to unsupervised exercise 93% adherence to protein supplementation, 98% to vitamins

*Standard care following institutional ERAS protocol.
†Cohort before the establishment of ERAS protocol.
CBT indicates cognitive behavioral therapy; HADS, Hospital Anxiety and Depression Scale; LOS, length of stay; MUST, Malnutrition Universal Screening Tool; HADS, Hospital Anxiety and Depression Scale; LOS, length of stay; preop, preoperative; postop, postoperative; 6MWD, 6-minute walk distance; CBT, cognitive behavioral therapy.

TABLE 2. Characteristics of Gynecologic Prehabilitation Trials in Progress

	Study design	Intended sample size		Study population	Key components of prehabilitation intervention	Planned outcomes
		Prehab	Control*			
Lopes et al. (PROPER)[120]	Single-center RCT	97	97	Gynecological surgery by laparotomy	Aerobic, inspiratory, stretching exercises + muscle strengthening 3x/week Nutritional counseling + supplementation Psychological counseling + relaxation and breathing exercises	Primary endpoint: postoperative recovery time Secondary endpoints: ERAS compliance Postop complication rates ICU admission rates Physical and psychological assessments
Diaz-Feijoo et al. (SOPHIE)[121]	Multicenter RCT	73	73	Advanced ovarian cancer (primary or recurrent)	Supervised exercise (high-intensity + resistance) 2-3x/week Weekly group CBT +/- psychologist referral Nutritional assessment + supplementation	Primary endpoint: overall postop complication rate Secondary endpoints: LOS Days to chemotherapy Quality of life Physical, nutritional, and cognitive assessments Program compliance
Inci et al. (KORE-INNOVATION)[122]	Two-center prospective non-randomized controlled trial	414	198† 50‡	Ovarian, fallopian, or peritoneal cancer (primary or first recurrence)	Tailored exercise program Nutritional counseling Comprehensive medication review Individual and group psychological coaching	Primary endpoint: severe 30-day postop complications Secondary endpoints: -Postop minor complications, morbidity, or mortality -LOS -Readmission rates -ERAS compliance Health economic analysis (supply costs, surgical complications, cost-effectiveness)

*Standard care following institutional ERAS protocol.
†Historical control group.
‡Prospective control group.
RCT indicates randomized controlled trial; ERAS, enhanced recovery after surgery; postop, postoperative; ICU, intensive care unit; LOS, length of stay.

postoperative serum albumin, prealbumin, or total protein levels in comparison to ERAS-only and pre-ERAS groups.[115]

A prospective observational study including 77 gynecologic oncology patients utilizing a modified version of this prehabilitation program found a significant impact on preoperative parameters based on 6MWD, hand grip strength, nutritional index, and psychological testing.[116] The greatest improvement in 6MWD was among patients performing supervised CrossFit training (33.4 m), compared with the hospital-supervised group (27.1 m) and the home training group (14.0 m). Postoperative outcomes were not assessed, although an optimized preoperative functional status suggests a better reserve for the stress and impact of surgery.

The original prehabilitation program described by Miralpeix et al[96] was applied in a pilot study of 29 patients with advanced ovarian cancer who underwent neoadjuvant chemotherapy followed by interval cytoreductive surgery (14 prehabilitation, 15 controls).[113] The prehabilitation group had a significant improvement in nutritional parameters of total protein levels preoperatively (7.4 vs. 6.8 g/dL, $P = 0.004$) and postoperatively (4.9 vs. 4.3 g/dL, $P = 0.005$), as well as postoperative albumin levels. These patients also had a significantly lower rate of intraoperative blood transfusion (14.3% vs. 53.3%, $P = 0.027$), with no significant differences in intraoperative complications or postoperative outcomes. Functional status was not evaluated, though this would be useful to assess in future studies; physical optimization in these patients could carry great potential benefit given the higher rates of sarcopenia in ovarian cancer patients undergoing neoadjuvant chemotherapy compared with primary cytoreductive surgery.[111] In a randomized controlled trial of patients with esophagogastric surgery, Minnella et al[119] found that an exercise and nutrition prehabilitation program led to significant improvement in both preoperative and postoperative functional status as measured by 6-minute walk test. With a majority of the patients in that trial undergoing neoadjuvant chemotherapy, the idea is plausible that ovarian cancer patients undergoing neoadjuvant therapy might see similar benefit.

Another pilot study by Díaz-Feijoo et al[117] of 15 patients with advanced ovarian cancer undergoing cytoreductive surgery who participated in a prehabilitation program had a shorter hospital length of stay compared with a historical cohort of 19 patients following only perioperative ERAS guidelines (median 5 vs. 7 d, $P = 0.04$), as well as shorter time from surgery to starting chemotherapy (median 25 vs. 35 d, $P = 0.03$). Importantly, although the outcomes from these pilot studies are limited by their small size and retrospective design, they suggest that prehabilitation programs are feasible and safe even in patients with advanced ovarian cancer.[113,117] A gynecologic oncology subgroup of a prospective cohort study participating in a multimodal prehabilitation program versus standard of care affirms the feasibility of implementing such programs in terms of recruitment, adherence, and safety.[95]

Two ongoing randomized controlled trials will be valuable to provide stronger evidence for the impact of prehabilitation in gynecologic oncology. Their primary endpoints are focused on postoperative metrics, specifically postoperative recovery time and postoperative complication rate, and will include multiple secondary endpoints for both pre- and postoperative parameters (Table 2).[120,121] The SOPHIE trial group recently published a cohort study[118] that combined a group of patients randomized to the prehabilitation arm of their trial with patients from the aforementioned pilot study by Díaz-Feijoo and colleagues.[117] Although the cohort study was assessing preoperative status, the significant improvements seen in functional capacity are encouraging that the RCT may have positive postoperative findings.

The nonrandomized KORE-INNOVATION trial (Table 2) will also include a health economic analysis of supply costs, surgical complications, and cost-effectiveness ratio, which will give valuable insight into the financial impact of prehabilitation programs.[122] A prospective study in major abdominal surgery found a cost savings of over twenty thousand dollars per patient undergoing prehabilitation,[123] and a cost-effectiveness model for patients with ovarian cancer estimated that prehabilitation was cost-effective up to $9418 per patient,[124] but there has not yet been a prospective assessment within gynecologic surgery.

The idea that preoperative optimization leads to improved postoperative status is intuitive, though the evidence supporting prehabilitation to improve clinical outcomes is not yet robust, likely due to underpowered studies. The existing studies of prehabilitation within gynecologic surgery suggest potential benefit, and importantly no harm, of inclusion of prehabilitation programs, though results have been limited and at times inconsistent. Importantly, there is an enormous body of data suggesting that preoperative physical fitness is associated with improved outcomes,[89–93] and most prehabilitation studies do demonstrate meaningful physiological changes. Given the low risk associated with exercise and strength training, it is quite reasonable to add prehabilitation to ERAS protocols. The larger trials in process will be valuable to more clearly elucidate the benefits of these multimodal preoperative programs within gynecologic surgery, particularly any incremental benefit over ERAS protocols.

CONCLUSION

The use of ERAS protocols has become widespread within gynecologic surgery, and the preoperative portion is a vital part of these perioperative bundles. Some preoperative interventions ideally begin well before surgery. Preadmission education empowers patients to feel prepared for their surgeries and helps set expectations for the perioperative period, with varying counseling options such as verbal, written, app-based, or a combination. Optimizing comorbidities is aimed at improving patients' modifiable risk profiles before they enter the OR, like screening for and treating anemia. Smoking and heavy alcohol consumption are also a focus, although the optimal cessation program has yet to be defined. Prehabilitation is an emerging optimization adjunct utilizing a bundle of structured exercise, nutritional, and psychological support to improve functional status, although it has not yet been formally incorporated into the gynecologic ERAS guidelines. In the immediate preoperative period, avoiding prolonged fasting and providing preoperative carbohydrate beverages positively impacts glucose metabolism, hunger, and thirst. In addition, acetaminophen and NSAIDs are recommended as premedication, while gabapentin has fallen out of favor due to questionable benefit and established risk. The evidence for preoperative ERAS interventions is not wholly within gynecologic surgery but is considered translatable from

colorectal surgery and general surgical populations. Preoperative interventions are essential components of gynecologic ERAS protocols and should be equally valued as intra- and postoperative elements.

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