

SİSTEMATİK DERLEME / SYSTEMATIC REVIEW

Enhanced Recovery After Surgery (ERAS) in Gynecologic Surgery: A Systematic Review

Jinekolojik Cerrahide Ameliyat Sonrası Erken İyileşme: Sistemantik Derleme

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Abstract

Enhanced recovery after surgery (ERAS) protocol aims to accelerate early recovery and improves postoperative patient outcomes. This protocol, which includes components such as reduction and prevention of postoperative complications, early mobilization, multimodal management of nausea and vomiting, positively affects surgical processes when used in patients undergoing gynaecological surgery. The aim of the present study was to use recent and relevant literature for examining the use of ERAS protocols in patients undergoing gynaecological surgery. Therefore, a systematic review was conducted to identify articles examining ERAS protocols used in patients who underwent gynaecological surgery. Electronic searches were performed in PubMed, Science Direct, MEDLINE, and Google Scholar between January 2015 and January 2021. The primary outcome was length of hospital stay. Secondary outcomes included early recovery, postoperative complications, pain management and narcotic drugs use. Twelve studies were included in the systematic review. Most of the included studies were randomized controlled trials. While six of the studies use all components of fast-track surgery protocols, others used postoperative analgesia, postoperative nausea and vomiting, early mobilization, fluid and carbohydrate loading components. When the results of the studies were examined, it was determined that these protocols shortened the length of hospital stay, provided early recovery and early mobilization, reduced nausea and vomiting, and decreased narcotic drugs use by providing appropriate pain management following gynaecological surgery. ERAS protocols need to be used in this patient group in order to achieve better results in the treatment and in the care of patients who have undergone gynaecological surgery.

Keywords: Enhanced recovery after surgery, gynaecology, gynaecological surgery, systematic review.

Öz

Ameliyat sonrası iyileşme protokolü (ERAS), erken iyileşmeyi hızlandırmayı ve ameliyat sonrası hasta sonuçlarını iyileştirmeyi amaçlar. Postoperatif komplikasyonların azaltılması ve önlenmesi, erken mobilizasyon, bulantı ve kusmanın multimodal yönetimi gibi bileşenleri içeren bu protokol, jinekolojik cerrahi geçiren hastalarda kullanıldığında cerrahi süreçleri olumlu etkiler. Bu çalışmanın amacı, jinekolojik cerrahi geçiren hastalarda ERAS protokollerinin kullanımını inceleme açısından güncel ve ilgili literatürü kullanmaktır. Bu nedenle, jinekolojik cerrahi geçiren hastalarda kullanılan ERAS protokollerini inceleyen makaleleri belirlemek için sistemantik bir inceleme yapıldı. Ocak 2015 ile Ocak 2021 arasında PubMed, Science Direct, MEDLINE ve Google Scholar'da elektronik aramalar gerçekleştirildi. Birincil sonuç hastanede kalış süresiydi. İkincil sonuçlar erken iyileşme, postoperatif komplikasyonlar, ağrı yönetimi ve narkotik ilaçların kullanımını içermektedir. Sistemantik derlemeye 12 çalışma dahil edildi. Dahil edilen çalışmaların çoğu randomize kontrollü çalışmaydı. Çalışmaların altısı hızlandırılmış bakım protokollerinin tüm bileşenlerini kullanırken, diğerleri postoperatif analjezi, postoperatif bulantı ve kusma, erken mobilizasyon, sıvı ve karbonhidrat yüklemesi bileşenleri kullanmaktaydı. Çalışmaların sonuçları incelendiğinde bu protokollerin jinekolojik cerrahi sonrası hastanede kalış süresini kısalttığı, erken iyileşme ve erken mobilizasyon sağladığı, bulantı ve kusmayı azalttığı ve uygun ağrı yönetimini sağlayarak narkotik kullanımını azalttığı belirlendi. Jinekolojik cerrahi geçiren hastaların tedavi ve bakımlarında daha iyi sonuçlar elde edebilmek için bu hasta grubunda ERAS protokollerinin kullanılması gerekmektedir.

Anahtar Kelimeler: Ameliyat sonrası erken iyileşme, jinekoloji, jinekolojik cerrahi, sistemantik derleme.

1. Introduction

Enhanced Recovery After Surgery (ERAS) was introduced more than 25 years ago by Professor Henrik Kehlet, who was a leader in colorectal surgery in Denmark. The purpose of ERAS is to limit surgical stress in the perioperative period and increase recovery (1). ERAS, also known as "fast track" or "early discharge" surgery, refers to a structured program consisting of preoperative, intraoperative, and postoperative components. Combined with a multidisciplinary and multimodal approach, the individual elements work synergistically to optimize the outcomes by reducing the physiological stress response and maintaining or rapidly restoring the core function. Since the first ERAS guideline for colorectal surgery was published in 2005, it has been repeatedly proven that advanced recovery protocols reduce the length of stay (LOS), decrease readmission rates, improve short-term morbidity, and lower healthcare costs compared to traditional management (2). ERAS protocols include preoperative counselling, anaesthesia management regarding nausea, vomiting and pain, and a standard approach for postoperative management regarding tube/catheter restriction, early mobilization, and early oral feeding (3).

Since the publication of Kehlet's review, some hospitals have published their experiences and results regarding the ERAS programs for patients undergoing major surgical procedures, particularly colorectal surgery. ERAS pathways were implemented in gynaecological, uro-gynaecological, and gynaecological oncology surgery programs and were proven as beneficial to both the patient and health care systems (4-6). In the most major gynaecological surgeries, there may be risks of postoperative complications and a prolonged hospital stay. Surgery-related morbidity significantly affects patients' outcomes, quality of life, and survival. Studies show that postoperative complications affect both recurrence rate and overall survival (7-9). A recent publication by the Royal College of Obstetricians and Gynaecologists reviews the main elements of ERAS and suggests that ERAS programs offer safe and high-quality perioperative care, thus should become standard practice for all women undergoing elective gynaecological surgery (10). We reviewed the published literature systematically regarding ERAS programs in general gynaecology and gynaecological oncology to evaluate the impact of such programs on patient outcomes. Four key questions were aimed to be answered in the present systematic review:

- 1) What are the ERAS protocols used in gynaecological surgery?
- 2) What is the effect of ERAS protocols on early recovery after gynaecological surgery?
- 3) What is the effect of ERAS protocols on preventing postoperative complications (vomiting, nausea, flatulence, defecation, infection, fever) in gynaecological surgery?
- 4) What is the effect of ERAS protocols on preventing postoperative pain and narcotic drugs use?

2. Materials and Method

The present study was performed in accordance with the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) guideline.

2.1. Eligibility criteria

Inclusion criteria: Peer-reviewed prospective and retrospective cohort studies as well as randomized and non-randomized controlled trials evaluating ERAS protocols in gynaecological surgery were evaluated for eligibility. Studies that were published (in press or online) or have been accepted for publication were included.

Exclusion criteria: Abstracts, study protocols, letters to the editor, non-peer-reviewed publications, non-English studies, case series, case reports, and non-controlled studies were excluded.

2.2. Literature Search and Data Sources

Literature search was conducted on Medline, Science Direct, Google Scholar, and PubMed databases between January 1, 2015, and January 1, 2021, using the following keywords: ERAS, enhanced recovery after surgery, enhanced recovery pathway, fast-track surgery, and gynaecological surgery. The search was limited to gynaecology by combining these search terms with the keywords 'gynaecology, gynaecological, gynaecological surgery, and gynaecological oncology'. In total, 251 studies were eligible. After carefully reading the content of the title and the abstract, 176 studies were excluded. Finally, 12 studies were included in the analysis, after excluding 64 studies due to various reasons. The flow-chart of the study was provided in Figure 1.

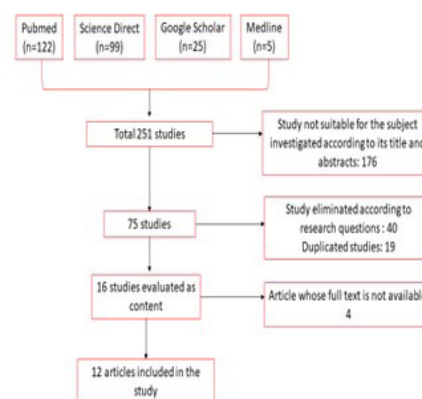


Fig. 1. Flow Chart of the Study

3. Results

The studies were ranked according to their level of scientific evidence as specified by the Healthcare Research and Quality Agency (AHRQ) (11) (Table 1). According to AHRQ classification, five of them were randomized controlled studies (Level I), two of them were prospective cohort studies (Level II), one of them was cross-sectional study (Level III), two of them were retrospective cohort studies (Level IV), one of them was retrospective observational cohort study (Level IV), and one of them was retrospective case-control study (Level IV). Studies were conducted in different countries (USA, Turkey, Egypt, China, Brazil, Sweden, and Taiwan). The number of samples included in the studies ranged between 62 and 387. The studies included a variety of gynaecological surgeries (Table 2).

Table 1. Description of scientific levels of evidence and corresponding studies as outlined by the AHRQ

Level of Evidence	Description
Level I	Randomized controlled trials with adequate follow-up Meta-analysis of multiple randomized control trials
Level II	Non-randomized, controlled prospective trial Prospective cohort studies
Level III	Well-designed observational studies (e.g., comparative studies, correlation studies, case control studies)
Level IV	Retrospective observational studies without controls Case series
Level V	Expert opinions or committee recommendations

3.1. ERAS protocols used in gynecological surgery

The components of the ERAS multidisciplinary pathway concerning preoperative, intraoperative, and postoperative periods were shown in Table 3. Six studies used all ERAS components (13, 17-19, 21, 22). Dickson et al. (12) used postoperative analgesia, postoperative nausea and vomiting, and early mobilization components. Ismail et al. (14) and Ma et al. (15) used prevention of nausea and vomiting component. Marquini et al. (16) used fluid, and carbohydrate loading component. Chapman et al. (20) used fluid, and carbohydrate loading, prevention of nausea, and vomiting, earlier removal of catheters, and early mobilization components. Kay et al. (23) employed postoperative narcotic drugs use component.

3.2. The effect of ERAS protocols on early recovery

Seven of the studies were associated with early recovery. Carter-Brooks et al. (22) found that the ERAS group had a higher proportion of same-day discharge (25.9% vs 91.7%, $p < 0.001$) and 13.8-hour shorter LOS (25.9 ± 13.5 vs 12.1 ± 11.2 hours, $p < 0.001$). Yilmaz et al. (13) found that early mobilization on the first postoperative day was achieved in eight (26.7%) patients in the ERAS group and ERAS protocol led to a significantly shorter LOS ($p = 0.010$). In three studies, there was a significant difference in the duration of LOS (18, 19, 21). Chapman et al. (20) found that differences between ERAS and control groups regarding early mobilization ($p < 0.05$). Only one study found no significant difference between ERAS and control groups regarding early mobilization (12).

3.3. The effect of ERAS protocols on preventing postoperative complications (vomiting, nausea, flatulence, defecation, ileus, infection)

In the study of Dickson et al. (12) there were no differences in time to the first flatulence or the prevalence of emesis. In the study of Yilmaz et al. (13) time to first flatulence ($p = 0.001$), time to first defecation ($p < 0.001$), and time to eating solid food ($p < 0.001$) were all significantly

shorter in the ERAS group. In the same study, there were no significant differences between groups regarding infection. In the study of Carter-Brooks et al. (22) urinary tract infection was detected in ERAS groups. The incidence of nausea was 27.5% in the intravenous group and was 7.5% in the intraperitoneal group during the first 24 hours ($p = 0.037$). There were no significant differences in the incidence of retching or vomiting, or the need for antiemetics between the groups (14). Ma et al. (15) found that nausea and vomiting scores in the multimodal group were significantly lower at 2 ($p < 0.05$), 6 ($p < 0.01$), and 24 hours after the operation ($p < 0.01$). In the study of Wijk et al. (17) most of the patients needed a single medication for postoperative nausea at some point (53%), only 12% needed more than one dose on the day of surgery, and 6% on the first postoperative day. Kuster-Uyeda et al. (19) found that the use of nausea and vomit prophylaxis increased almost 20 times. In the study of Chapman et al. (20) there were significantly more multimodal nausea and vomiting prophylaxis compared to patients in the control group. Boitano et al. (21) found that the rate of postoperative ileus was significantly reduced in the ERAS group (2.8% vs. 15.7%; $p < 0.001$).

3.4. The effect of ERAS protocols on preventing postoperative pain and narcotic drugs use

Dickson et al. (12) found that there was no significant difference between the narcotic drugs used during postoperative days 0 and 1; less morphine equivalents were used in the intervention group on day 2 compared to control group ($p = 0.050$). In the study of Modesitt et al. (18), a decrease was observed in the intraoperative use of morphine (0.3 vs. 12.7 mg; $p < 0.001$), and postoperative pain scores (3.7 vs. 5.0; $p < 0.001$). Boitano et al. (21) found significant differences between modes of pain control. In the control group, the majority of patients received either a Patient Controlled Analgesia (PCA) (47.2%) or an epidural analgesia (50.3%). In the ERAS group, 78.2% of patients received an intrathecal morphine injection, 7.3% received a Transvers Abdominis Plane (TAP) block, 14.5% required a PCA, and no patients received epidural analgesia. Kay et al. (23) found that pain management in the postoperative period, ERAS groups used less narcotic drugs in the 24 hours prior to discharge ($p < 0.01$).

3.5. Other Findings

Fluid and carbohydrate loading was evaluated in the study of Marquini et al. (16) and there were significant differences in the coefficient of variation for the HOMA-IR index in the control group (17.27%; $p < 0.01$) compared to the intervention group (8.46%; $p < 0.05$). Kuster-Uyeda et al. (19) found that the fasting time was reduced approximately 10 hours with the ERAS components.

Two studies were evaluated intraoperative intravenous fluids between ERAS and control groups. Modesitt et al. (18) found that the ERAS groups less used intraoperative intravenous fluids (2917.5 mL vs. 1410 mL; $p < 0.001$) and Boitano et al. (21) found that control groups received significantly more intravenous fluids intraoperatively (2272 mL vs. 1986 mL; $p = 0.010$).

Table 2. Summary of Included Studies

First Author/ Year	Country	Study Design and Evidence Levels	Participants	Type of surgery	ERAS Components	Results	Conclusion
Dickson et al ¹²	USA	Prospective randomized controlled study (I)	103	Gynaecologic Oncology	Postoperative analgesia, Postoperative nausea and vomiting, Early mobilization	There was no significant difference between the narcotic used during postoperative days 0 and 1; less morphine equivalents were used in the intervention group on day 2 compared to control group (p=0.05). There was no statistical difference in time to early mobilization between groups. There was also no difference in time to first flatus or the prevalence of emesis.	ERAS protocol was applicable after laparotomy in the gynaecologic oncology service.
Yilmaz et al ¹³	Turkey	Prospective randomized controlled study (I)	62	Abdominal Hysterectomy	All components	Pre and postoperative intravenous fluids were significantly lower in the ERAS group (p<0.001). Time to first flatus (p=0.001), time to first defecation (p<0.001), and time to eating solid food (p<0.001) were all significantly shorter in the ERAS group. Early mobilization on the first postoperative day was achieved in eight (26.7%) patients in the ERAS group. ERAS protocol led to a significantly shorter LOS (p=0.010). There was no significant difference between groups regarding infection.	Postoperative compliance and complications between ERAS and control group revealed that introducing the ERAS protocol led to a significantly shorter LOS without any signs of increasing complications.
Ismail et al ¹⁴	Egypt	Randomized controlled study (I)	80	Gynaecological Laparoscopic Surgery	Prevention of nausea and vomiting	The incidence of nausea was 27.5% in the intravenous group, was 7.5% in the intraperitoneal group in the first 24 hours (p=0.037). There were no significant differences in the incidence of retching or vomiting, or the need for antiemetic between the groups.	Intraperitoneal dexmethasone following gynaecological laparoscopy reduces the incidence of postoperative nausea.
Ma et al ¹⁵	China	Randomized controlled study (I)	153	Gynaecological Laparoscopic Surgery	Prevention of nausea, and vomiting	The nausea and vomiting scores in the multimodal group were significantly lower at 2 (p<0.05), 6, and 24 hours after the operation (both p<0.01). The incidence of nausea and vomiting was significantly lower in the multimodal group than the control group (p<0.01). Patients in the multimodal group less frequently required antiemetic than the control group (p<0.01).	The scores of nausea and vomiting in the multimodal group were lower than those in the control group.
Marquini et al ¹⁶	Brazil	Randomized controlled study (I)	80	Gynaecologic Surgery	Fluid and carbohydrate loading	There was a significant difference in the coefficient of variation for the HOMAR index in the control group (17.27%; p<0.01) compared to intervention group (8.46%; p<0.05).	Preoperative fasting with liquid containing carbohydrate and protein before gynaecologic surgeries may provide metabolic stability with lower variation in insulin resistance than inert solution.
Wijk et al ¹⁷	Sweden	Prospective cohort study (II)	121	Abdominal Hysterectomy and Salpingo-Oophorectomy	All components	Preoperative and perioperative compliance with the ERAS protocol was generally high (82–100%). Most of the patients needed a single medication for postoperative nausea at some point (53%), only 12% needed more than one dose on the day of surgery and 6% on the first postoperative day.	The ERAS protocol may be equally feasible to patients with a malignant or with a benign disease.

Table 2. Summary of Included Studies(continued)

First Author/Year	Country	Study Design and Evidence Levels	Participants	Type of surgery	ERAS Components	Results	Conclusion
Modesitt et al ¹⁸	USA	Prospective cohort study (II)	136	Elective Major Gynaecologic Surgery	All components	A decrease was observed in the intraoperative use of morphine (0.3 vs. 12.7 mg; p<0.001), intraoperative intravenous fluids (2917.5 mL vs. 1410 mL; p<0.0001), postoperative pain scores (3.7 vs. 5.0; p<0.001).	ERAS protocols in gynaecologic surgery were associated with a substantial decrease in intravenous fluids and morphine administration coupled with reduction in LOS.
Kuster-Uyeda et al ¹⁹	Taiwan	Cross-sectional study (III)	387	Gynaecological Surgery	All components	After the protocol, fasting time was reduced in approximately 10 h. Patients' bowel preparation significantly less frequently, and the volume of fluids was reduced. The use of nausea and vomit prophylaxis increased almost 20 times, but only nausea episodes were reduced. The frequency of antithrombotic prophylactic therapy more than doubled. LOS decreased significantly.	The protocol implementation was associated with reductions in fasting time, bowel preparation, administration of fluids, pain, nausea and LOS.
Chapman et al ²⁰	USA	Retrospective case-control study (IV)	165	Gynaecologic Oncology	Fluid and carbohydrate loading, Prevention of nausea and vomiting, Earlier removal of catheters, Early mobilization	Patients in ERAS group used significantly more multimodal nausea and vomiting prophylaxis compared to patients in the control group. There were significant differences between ERAS and control groups regarding earlier removal of urinary catheters and early mobilization (p<0.05)	ERAS pathway is associated with significant improvements in recovery time, decreased pain despite reduced opioid use, and overall lower hospital costs.
Boltano et al ²¹	USA	Retrospective cohort study (IV)	376	Gynaecologic Oncology	All components	Control groups received significantly more intravenous fluids intraoperatively (2272 mL vs. 1986 mL; p=0.01). There was also a significant difference between modes of pain control. In the control group, the majority of patients received either a PCA (47.2%) or an epidural analgesia (50.3%). In the ERAS group, 78.2% of patients received an intrathecal morphine injection, 7.3% received a TAP block, 14.5% required a PCA, and no patients received an epidural analgesia. The rate of postoperative ileus was significantly reduced in the ERAS group (2.8% vs. 15.7%; p<0.001).	ERAS protocol decreased postoperative ileus and LOS in patients without increasing readmission rates.
Carter-Brooks et al ²²	USA	Retrospective observational cohort study (IV)	258	Uro-gynaecological Surgery	All components	ERAS group had a higher proportion of same day discharge (25.9% vs 91.7%, p<0.001) and a 13.8-hour shorter LOS (25.9±1.3.5 vs 12.1±1.2 hours; p<0.001). Women in the ERAS group were more likely to be discharged using a urethral catheter (57.9% ERAS vs 25.4% pre-ERAS, p=0.005). Urinary tract infection was detected in ERAS groups.	ERAS pathway was associated with decreased LOS, increase in the day of surgery discharge.
Kay et al ²³	USA	Retrospective cohort study (IV)	136	Open Ovarian Cancer Surgery	Postoperative narcotic drug use	For pain management in the postoperative period ERAS groups used fewer narcotic drugs in the 24 h prior to discharge (p<0.01).	ERAS protocol appears to decrease the narcotic drug needs of patients in the three months after ovarian cancer surgery.

Table 3. ERAS Components Followed During the Study

	Counselling before hospital admission
	Fluid, and carbohydrate loading
	Avoiding of longer fasting periods
	Avoiding bowel preparation or its application only in selective cases
	Application of antibiotic prophylaxis
Preoperative	Application of thromboprophylaxis
	Avoiding premedication
	Use of short-acting anaesthetic agents
	Application of mid-thoracic, epidural anaesthesia/analgesia
Intraoperative	Refraining from using drains
	Refraining from salt and water overload
	Maintenance of normothermia (heating the body, and use of warmed up intravenous fluids)
	Application of mid-thoracic, epidural anaesthesia/analgesia
	Refraining from use of nasogastric tube
	Prevention of nausea and vomiting
	Refraining from salt and water overload
	Earlier removal of catheters
Postoperative	Initiation of oral intake at an early period
	Use of non-opioid oral analgesics/NSAIDs
	Early mobilization
	Adherence to the protocol, and auditing results

4. Discussion

In the present study, the effects of ERAS in gynaecological surgery were examined. It was determined that half of the examined studies used all components of ERAS (25). The most frequently used ERAS components were analgesia, postoperative nausea and vomiting, early mobilization, and fluids and carbohydrate loading in the remaining studies (26). ERAS has been widely adopted internationally and was implemented in many centres and service lines around the world. Previous studies showed that ERAS shortens hospital stay, provides early mobilization, reduces nausea and vomiting, and reduce the need for analgesia (2, 27).

Many studies indicated that implementation of ERAS protocols ensured early postoperative recovery, and shortened LOS (28, 29). In the present review, it was determined that ERAS protocols provided early recovery and shortened LOS (12, 13, 18-22). In the study of Relph et al. (29) postoperative LOS after vaginal hysterectomy was an average of 42.9 hours in patients who received conventional postoperative care, and 23.5 hours in patients who were treated with ERAS protocol. Carter et al. (30) found that application of ERAS protocol enabled discharge within a short time in 72 patients who had undergone laparotomy.

Postoperative complications such as nausea and vomiting, flatus, defecation, ileus, and infection are common following gynaecological surgery. These complications negatively affect the early recovery of the patients in the postoperative period and reduce their quality of life (31). According to the Apfel's Postoperative Nausea and Vomiting (PONV) risk rating scale, gynaecological laparoscopic surgery is a highly dangerous category of PONV (32). On the other hand,

Barclay et al. (33), did not reported PONV in patients who underwent colorectal surgery. One of the most common postoperative complications are flatus and ileus (34). In the studies of Varadhan et al. (35) and Scott et al. (36), it was found that the incidence of flatus and ileus were decreased in patients who were used ERAS components. In the present study, it was determined that ERAS components decreased the incidence of postoperative complications (12-15, 17, 19-22).

In the management of pain, which is the most frequently described symptom of the patients in the postoperative period, pharmacological methods are preferred first. Opioids are used when the pain is severe. Undesirable conditions such as postoperative drug addiction and inappropriate pain management can be seen in patients at whom opioids are used frequently. ERAS components such as the use of non-opioid analgesics reduce the use of narcotic drugs in postoperative pain management (28). In the present study, it was shown that the use of non-opioids reduced the use of narcotic analgesics (12, 18, 21, 23). Meyer et al. (37) found that patients who use of ERAS components had a 72% reduction in opioid consumption.

The other findings in the present review showed that the use of fluid and carbohydrate loading were important and useful components of ERAS (16, 18, 19, 21). Fluid and carbohydrate loading was determined useful for reducing postoperative insulin resistance, regulating blood sugar, reducing patients' anxiety levels, preventing fluid-electrolyte imbalances in elderly patients, and leading to early bowel movements (38, 39).

5. Conclusion

ERAS protocols are highly recommended in gynaecological surgery, as they reduce the incidence of postoperative complications, shorten the LOS, and increase patient satisfaction. Yet, more studies are needed on ERAS and rapid fast-track protocols, which focus on evaluating long-term outcomes such as patients' experience in the surgical process, quality of life, and its positive impact on early recovery. In addition, ERAS protocols should be used in this patient group to achieve better results in treatment and care of patients who have undergone gynaecological surgery.

6. Implications for Health Professionals

The present systematic review regarding ERAS protocols applied in gynaecological surgery is a valuable study in terms of synthesizing the information whether the protocols are effective or not. Using the results of the present study, health professionals can evaluate whether ERAS protocols are effective or not, reduce postoperative complications, and accelerate the postoperative recovery process of patients following gynaecological surgery.

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Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

Authorship Contribution

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