Original Article

Effect of the enhanced recovery after surgery protocol on recovery after laparoscopic myomectomy: a systematic review and meta-analysis

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Background: Surgery is the recommended treatment for uterine leiomyoma but it still has issues like postoperative complications and slow recovery. The enhanced recovery after surgery (ERAS) protocol could probably reduce traumatic stress and promote the rapid postoperative recovery of patients, but there are controversies for the results of different studies. This meta-analysis was performed to resolve the controversies and provide evidence for the application of ERAS in gynecology.

Methods: The PubMed, Embase, Ovid, CNKI (China), Wanfang Data (China), and Google Scholar databases were searched to recruit all studies on the application of ERAS in laparoscopic myomectomy up to November 2021. The inclusion criteria of studies was established according to the PICOS principles. the Cochrane RoB 2.0 and Newcastle-Ottawa Scale (NOS) scale were used to assess the bias of the studies, RevMan 5.3 software was used for meta-analysis.

Results: Ten studies that met the criteria were finally included with 1,441 participants. Eight of them were randomized controlled trials (RCTs) and two were cohort studies, all of them were with low level of bias. Meta-analysis showed that ERAS protocol after laparoscopic myomectomy could significantly shorten the first time getting out of bed after surgery [mean difference (MD) =−4.85; 95% confidence interval (CI): (−7.35, −2.36); P=0.0001], the first defecation time after surgery [MD =−4.69; 95% CI: (−5.68, −3.69); P<0.00001], and the postoperative hospital stay [MD =−1.32, 95% CI: (−2.08, −0.56); P=0.0007]. It could also markedly reduce the patient readmission rate [odds ratio (OR) =0.42; 95% CI: (0.23, 0.76); P=0.004], and notably reduced the incidence of complications [OR =0.37; 95% CI: (0.22, 0.61); Z=3.82; P=0.0001]. Yet, the cost of the ERAS protocol was not significantly different from that of routine care [MD =−127.76, 95% CI: (−997.19, 741.66); P=0.77].

Discussion: The application of ERAS protocol after gynecological laparoscopic myomectomy can shorten the first defecation time, first time out of bed, hospital stay, and reduce the readmission rate as well as the incidence of postoperative complications, without additional costs. But still there was heterogeneity among the studies, the topic still deserved further exploration.

Keywords: Enhanced recovery after surgery (ERAS); laparoscopy; myomectomy

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Introduction

Uterine leiomyoma is a benign tumor formed by the proliferation of uterine smooth muscle tissue, which is often more common in women aged 30–50 years and rare in people under 20 years of age (1). Some patients have no obvious symptoms, while others may have abnormal menstruation, increased leucorrhea, lower abdominal distension, and other phenomena. If the uterine fibroids are large, they may compress the bladder and ureter, resulting in frequent urination, urgent urination or dysuria, or constipation due to compression of the rectum (2). Surgical resection is one of the preferred treatments for uterine fibroids, and laparoscopic myomectomy has the advantages of faster postoperative recovery, less intraoperative injury, and less pain than laparotomy, and its effect has been confirmed by a large number of clinical studies (3,4). However, study (5) has reported that some patients still experience slow postoperative recovery as well as certain complications after laparoscopic myomectomy, which prolongs the hospital stay and reduces the quality of life of these patients.

The concept of enhanced recovery after surgery (ERAS) has been widely used and extensively promoted in recent years, and its core idea is to optimize the nursing measures during the perioperative period, and reduce the body stress response caused by nursing and surgical treatment during the perioperative period, in order to facilitate the rapid recovery of patients (6). The concept of ERAS is more common in the field of general surgery, and it is rarely applied in intestinal surgery. Compared with traditional nursing treatment, ERAS has the advantages of alleviating patients' pain, reducing traumatic stress, promoting the rapid recovery of patients after surgery, shortening the length of hospital stay, and reducing the incidence of complications and hospitalization costs in intestinal surgery (7). However, the results of ERAS protocol in the field of gynecology are controversy. A study by Boitano *et al.* (8) showed the application of ERAS protocol could significantly decrease the length of stay in hospital, the complications rate were lower than usual care, while a study by Bisch *et al.* (9) showed no significant difference for the complications rate, and the cost for ERAS protocol was even higher. and thus, we conducted a systematic review and meta-analysis of recent studies on the application of this concept in myomectomy surgery to provide a basis for the selection of clinical surgery. We present the following article in accordance with the PRISMA reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-168/rc).

Methods

Literature inclusion criteria

The inclusion criteria were as follows: (I) we preferentially included randomized controlled trials (RCTs), cohort studies, and case-control studies, which were limited to the Chinese and English languages. Case reports, overviews, and meeting minutes were excluded, as such studies cannot provide data. We also excluded case series/uncontrolled before-after studies, since such studies have no cohort or grouping control. (II) Articles involving study subjects that were all adult female patients with benign uterine fibroids who underwent laparoscopic myomectomy, and patients with malignant uterine fibroids and cervical cancer were excluded. (III) Studies that included both ERAS and conventional perioperative care (CPC) groups. (IV) Outcomes: we used the first time out of bed, the first time to defecation, the length of hospital stay, hospitalization costs, 30-day readmission rate, and the incidence of postoperative complications as efficacy outcome indicators to evaluate the recovery of patients after care.

Search strategy

We searched the PubMed, Embase, Ovid, CNKI (China), and Wanfang Data (China) databases from the date of establishment of the database to November 2021. Additionally, we also used Google Scholar to search for relevant literature related to ERAS and myomectomy. We utilized a combination of search keywords, including (enhanced recovery after surgery/ERAS) AND (laparoscopic myomectomy/gynecologic surgery).

Literature screening and data extraction

Two researchers independently completed the screening of included studies. The initially retrieved articles were entered into NoteExpress software (V3.0.2.6390, released by Aegean Software Co., Ltd., Beijing, China); after removing the repeated literatures using this software, the unqualified studies were excluded by reading the titles and abstracts, and then the original texts and data of the remaining articles were obtained before further screening. Disagreements between the two researchers were resolved by consulting a third researcher. The final results were synthesized from the screening of the two researchers.

Next, two researchers independently completed the data extraction, and the extracted contents included: the title of the literature, the first author, the corresponding author, the publication time, the name of the publication, the contact address, the total number of samples in the study, the number of groups, the number of samples in each group, the surgical approach, the postoperative care method, as well as the ages, body mass index (BMI), ethnicities, disease types, and outcome indicators of the participants. If no data was provided in the literature but there was a data address link, the data were obtained using the link. If there was no data at all, the original author was contacted; if the data still could not be obtained, the article was excluded.

Literature bias and assessment analysis

For RCTs, the Cochrane RoB 2.0 was used to assess the bias in terms of randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The bias assessment of cohort studies were performed using the Newcastle-Ottawa Scale (NOS) with a maximum score of 9 stars. Studies with a score of 5 stars and above were considered good quality.

Statistical analysis

(I) Effect size: the odds ratio (OR) and 95% confidence interval (CI) were used to assess binary variables (readmission rate, complication rate), and the mean difference (MD) and 95% CI were used to assess continuous variables (first time out of bed after surgery, time to first defecation, length of hospital stay, hospitalization costs). (II) Synthetic analysis tools and heterogeneity detection: RevMan 5.3 software (released by The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) was used for analysis, and forest plots were used to present the analysis results. The I^2 and Q tests were applied to analyze literature heterogeneity, with $I^2>50\%$ or $P<0.1$ indicating statistically significant heterogeneity. (III) Model selection: if the heterogeneity test result indicated that the difference between studies was not statistically significant, the fixed effect model was used to obtain the combined effect value. If heterogeneity among studies was observed, the source of heterogeneity was analyzed first to determine whether a random-effects model should be used. (IV) Publication bias analysis: publication bias was visualized using a funnel plot. We also used Egger' test to statistically assessing the publication bias. (V) Heterogeneity survey and sensitivity analysis: this was analyzed using the piecemeal elimination method or general description method. Also, we performed subgroup analysis according the study type (RCT or cohort study) to investigate the heterogeneity.

Results

Literature search results and screening process

A total of 458 literatures were initially recruited in the database search. After de-duplication and screening, a total of 10 studies (10-19), with a total of 1,441 participants, met the criteria and were finally included in the meta-analysis. *Figure 1* shows the literature search results and screening process.

Basic characteristics of the included articles

A total of 10 studies were included in this meta-analysis, including eight RCTs and two cohort studies. The range of patients included in these studies was 80–410. The basic characteristics of the included studies are shown in *Table 1*.

Meta analysis results

First time out of bed after surgery (hours)

Five studies (11,13,15,18,19) compared the first time out of bed after surgery between the ERAS nursing model and routine nursing. The effect size was expressed by the MD, and the homogeneity test results were as follows: $I^2=95\%$, $P<0.00001$. Random effect model analysis showed that the use of the ERAS nursing model significantly shortened the first time out of bed after surgery [MD =−4.85; 95% CI: (−7.35, −2.36); Z=3.81; P=0.0001], as shown in *Figure 2*.

First defecation time after surgery (hours)

Seven articles (11-13,15,16,18,19) compared the time to first defecation between the ERAS nursing model and routine nursing. The effect size was expressed by the MD, and the homogeneity test results were as follows: $I^2=79\%$, $P<0.0001$. Random effect model analysis showed that the use of the ERAS nursing model significantly shortened the time to first defecation postoperatively [MD =−4.69; 95% CI: (−5.68, −3.69); Z=9.24; P<0.00001], as shown in *Figure 3*.

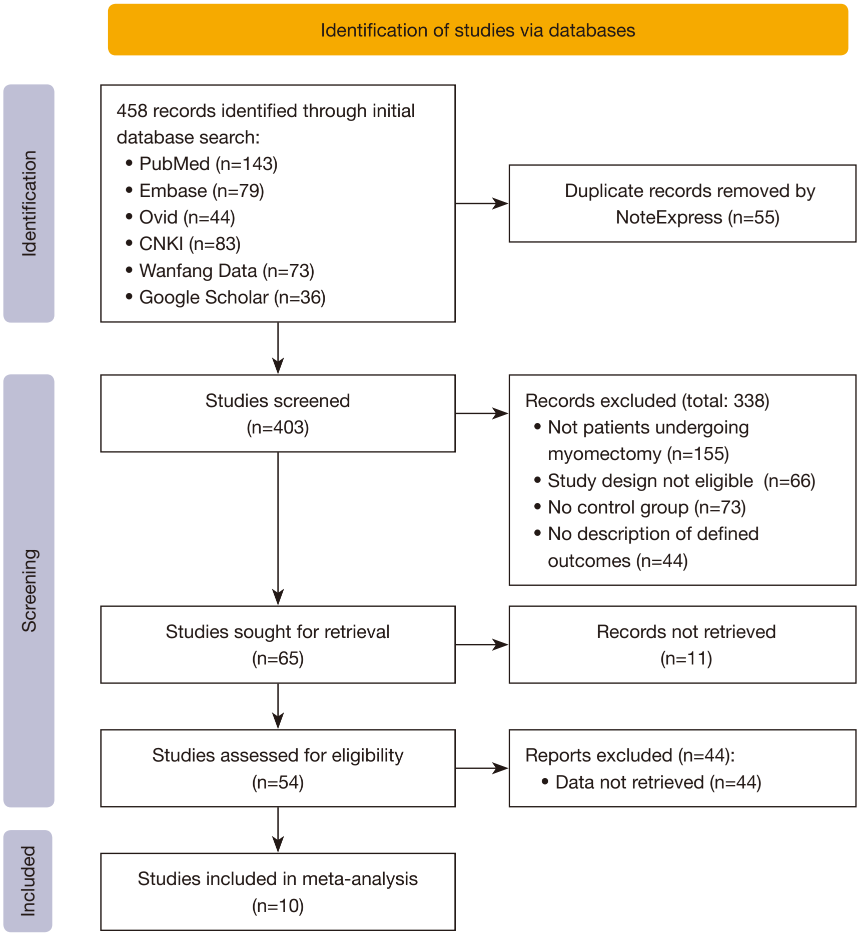

Figure 1 Literature screening flow chart.

Length of hospital stay (days)

Seven studies (11-13,15,16,18,19) compared the length of hospital stay between the ERAS nursing model and routine nursing. The effect size was expressed by the MD, and the homogeneity test results were as follows: I^2=98%, P<0.00001. Random effects model analysis showed that application of the ERAS nursing model markedly shortened the length of hospital stay after surgery [MD =−1.32; 95% CI: (−2.08, −0.56); Z=3.41; P=0.0007], as shown in *Figure 4*.

Hospital costs

Three articles (11,14,18) compared the cost of the ERAS nursing model with routine nursing. The cost unit used in these three studies was different [Ref. (11,18) were in RMB, while Ref. (14) was in US dollars]. The effect size was expressed by the MD, and the homogeneity test results were as follows: I^2=100%, P<0.00001. Random effect model analysis showed that the cost of the ERAS nursing model was not significantly different from that of routine nursing [MD =−127.76; 95% CI: (−997.19, 741.66); Z=0.29; P=0.77], as shown in *Figure 5*.

The subgroup analysis was perform according the study type, heterogeneity was still significant in the RCT group: I^2=62%, P=0.11.

Thirty-day readmission rate

Four articles (10,14,15,18) reported the readmission rate at 30 days postoperatively. The effect size was expressed by the OR, and the homogeneity test results were as follows: I^2=0%, P=0.40. Fixed effect model analysis showed that the use of the ERAS care model significantly reduced the patient readmission rate [OR =0.42; 95% CI: (0.23, 0.76); Z=2.85; P=0.004], as shown in *Figure 6*.

The subgroup analysis was perform according the study type, the overall effect size of the RCT subgroup [OR =1.03; 95% CI: (0.23, 4.66); Z=0.04; P=0.97] and the cohort

Table 1 Basic characteristics, object characteristics, surgical methods, and outcome indicators of the included literatures

Author	Year	Type of study	Number of patients	Number of subjects grouped (E/C)	Patient age (years)	Intervention method (E/C)	Outcome indicators	Quality score
Peters *et al.* (10)	2020	Retrospective cohort study	410	196/214	33.6±10.2	ERAS/CPC	(V)	6*
Zeng *et al.* (11)	2017	RCT	120	60/60	35.72±5.34	ERAS/CPC	(I), (II), (III), (IV), (VI)	Low risk of bias
Tang *et al.* (12)	2018	RCT	90	45/45	39.6±5.7	ERAS/CPC	(II), (III), (VI)	Low risk of bias
Liu *et al.* (13)	2020	RCT	80	40/40	46±5	ERAS/CPC	(I), (II), (III), (VI)	Low risk of bias
Chapman *et al.* (14)	2016	Retrospective cohort study	165	55/110	59.3 (20.1–83.1)	ERAS/CPC	(III), (IV), (V), (VI)	7*
Yilmaz *et al.* (15)	2020	RCT	104	51/53	39.1±10	ERAS/CPC	(I), (II), (III), (V), (VI)	Low risk of bias
Zhang *et al.* (16)	2012	RCT	116	58/58	38.26±5. 80	ERAS/CPC	(II), (III), (IV)	Low risk of bias
Chen *et al.* (17)	2020	RCT	100	50/50	45.23±1.34	ERAS/CPC	(VI)	Low risk of bias
Ren *et al.* (18)	2021	RCT	144	72/72	39.9±8.9	ERAS/CPC	(I), (II), (III), (IV), (V)	Low risk of bias
Lin *et al.* (19)	2018	RCT	112	56/56	36.89±7.52	ERAS/CPC	(I), (II), (III), (VI)	Low risk of bias

Outcomes: (I) first time out of bed after surgery; (II) first defecation time after surgery; (III) length of hospital stay; (IV) hospital costs; (V) 30-day readmission rate; (VI) complication rate. *, the NOS score was used for quality score. RCT, randomized controlled trial; E/C, experimental group/control group; ERAS, enhanced recovery after surgery; CPC, conventional perioperative care; NOS, Newcastle-Ottawa Scale.

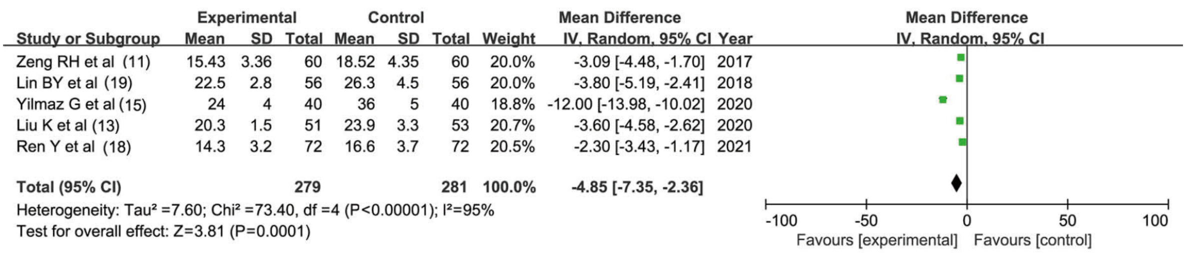

Figure 2 Effect of the ERAS care model on the first time the patient gets out of bed after surgery (11,13,15,18,19). SD, standard deviation; IV, inverse variance; CI, confidence interval; ERAS, enhanced recovery after surgery.

study subgroup [OR =0.36; 95% CI: (0.18, 0.69); Z=3.03; P=0.002].

Complication rate

Six studies (11-13,15,17,19) reported the incidence rate of postoperative complications. The effect size was expressed by the OR, and the homogeneity test results were as follows: I^2=0%, P=0.81. Fixed effect model analysis showed that the use of the ERAS nursing model significantly reduced the incidence rate of postoperative complications [OR =0.37; 95% CI: (0.22, 0.61); Z=3.82; P=0.0001], as shown in *Figure* 7.

Heterogeneity survey and sensitivity analysis

In this study, studies analyzing the first time out of bed after surgery outcome indicator (11,13,15,18,19) were deleted one-by-one, and heterogeneity still existed between the remaining literatures, which indicated that the source of heterogeneity might be related to the different characteristics of the included patients (age, disease severity) or different intervention characteristics (different implementation process of ERAS). After eliminating the included articles one-by-one, the statistical value (Z) was still significant, which indicated that the analysis of this

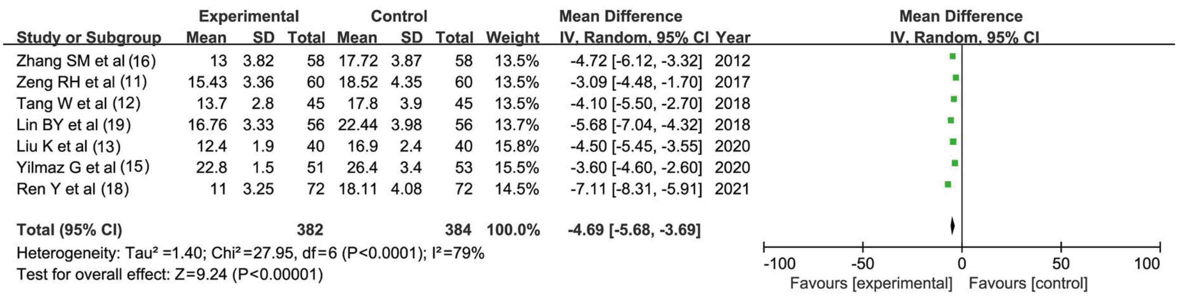

Figure 3 Effect of the ERAS care model on the first defecation time of patients after surgery (11-13,15,16,18,19). SD, standard deviation; IV, inverse variance; CI, confidence interval; ERAS, enhanced recovery after surgery.

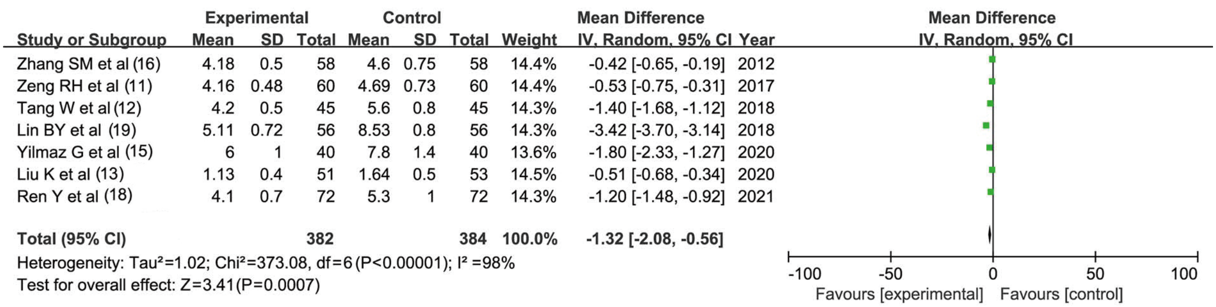

Figure 4 Effect of the ERAS care model on postoperative hospital stay of patients (11-13,15,16,18,19). SD, standard deviation; IV, inverse variance; CI, confidence interval; ERAS, enhanced recovery after surgery.

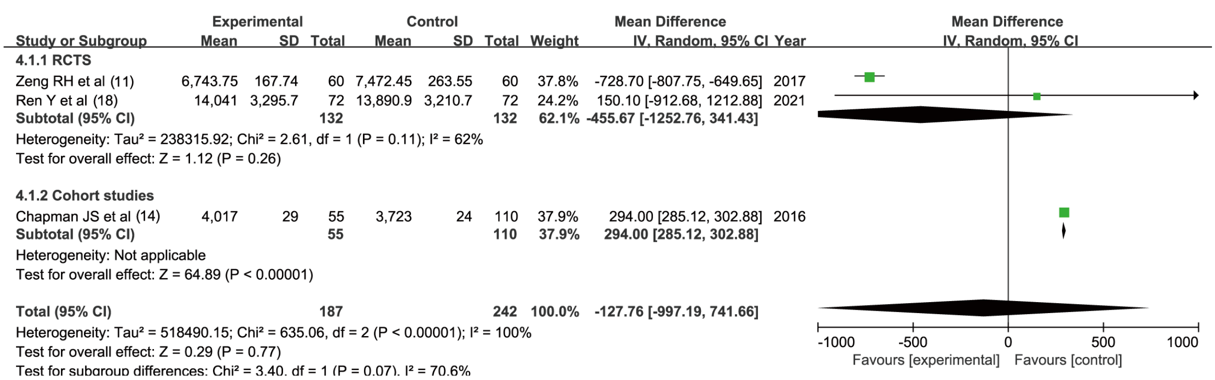

Figure 5 Cost of the ERAS care model compared to routine care (11,14,18). SD, standard deviation; IV, inverse variance; CI, confidence interval; RCTs, randomized controlled trials; ERAS, enhanced recovery after surgery.

outcome indicator was relatively stable. The quality of included studies were all good, so we didn't perform a meta regression to identify the influence of the risk of bias on the results.

Publication bias analysis

Using the outcome indicator of the first defecation time after surgery, the funnel plot showed that the literature was

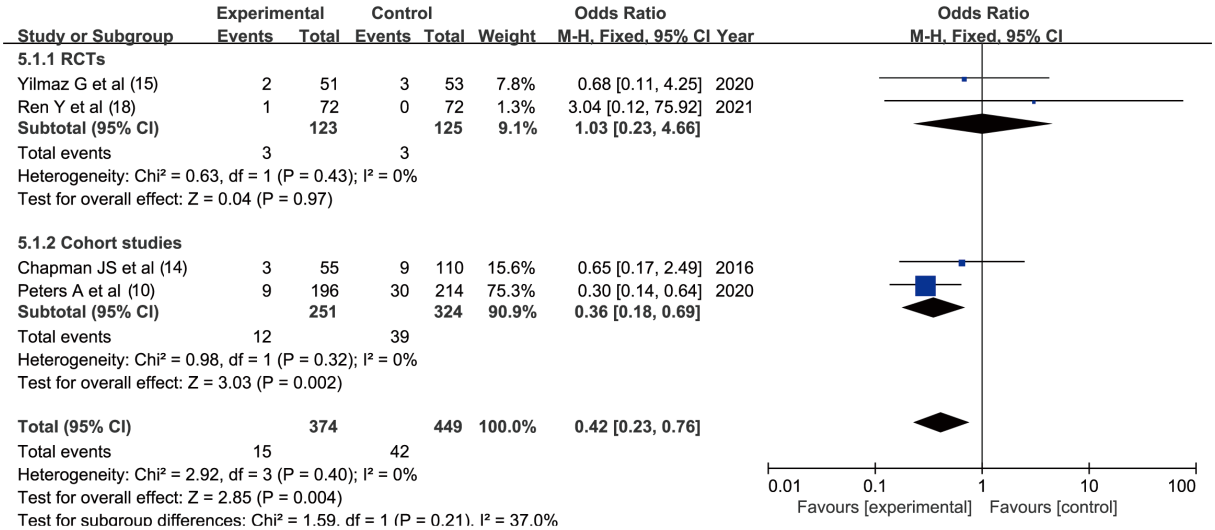

Figure 6 Effect of the ERAS care model on the postoperative readmission rate (10,14,15,18). M-H, Mantel-Haenszel; CI, confidence interval; RCTs, randomized controlled trials; ERAS, enhanced recovery after surgery.

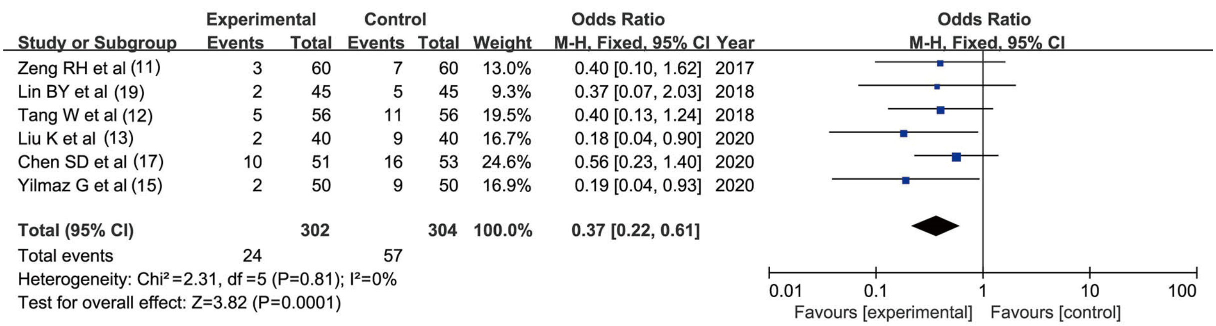

Figure 7 Impact of the ERAS care model on the incidence rate of postoperative complications (11-13,15,17,19). M-H, Mantel-Haenszel; CI, confidence interval; ERAS, enhanced recovery after surgery.

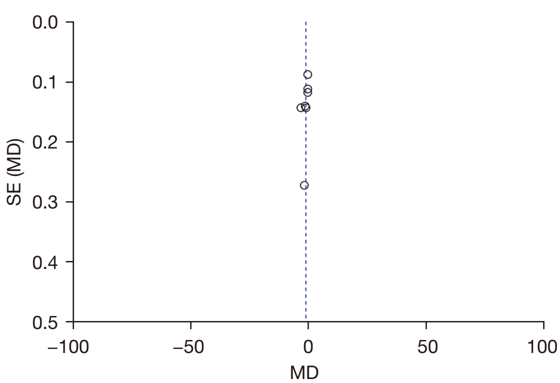

Figure 8 Funnel plot analysis. SE, standard error; MD, mean difference.

evenly distributed around the longitudinal axis, suggesting no significant publication bias, as shown in *Figure 8*.

The Egger' test showed a result of P=0.156 (>0.05), which suggesting no significant publication bias, as shown in *Figure 9*.

Discussion

Uterine leiomyoma is a benign tumor of the female cervix, the cause of which remains unclear. Although most patients have no obvious symptoms, there are still some patients at risk of micturition disorders, abortion, and infertility (20). In recent years, the laparoscopic technique has been

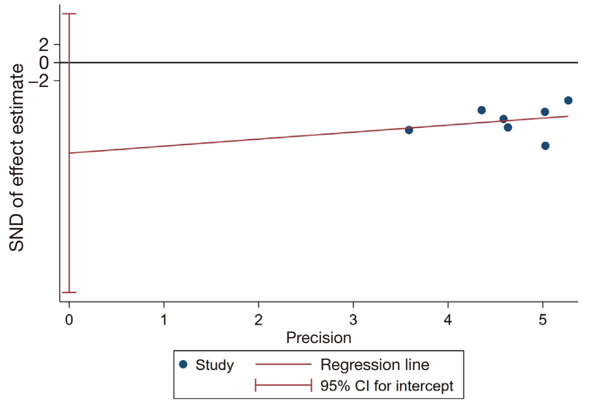

Figure 9 The Egger' test. SND, standard normal deviation; CI, confidential interval.

widely used in obstetrics and gynecology. Compared with traditional surgery, the laparoscopic technique has the characteristics of shorter operation time, less bleeding, and faster postoperative recovery, yet there are still some complications, such as postoperative bleeding, pain, infection, and nerve injury (21). The adverse stress response of patients during surgery can promote the body to release a large number of catecholamines, glucocorticoids, glucagon, and other chemical transmitters, increase the body's metabolic rate, aggravate the possibility of complications, and is not conducive to recovery (22). Study (23) has identified patients' fear of their own disease, overnight fasting, preoperative bowel cleansing, intraoperative hypothermia, anesthesia, postoperative fasting or late eating, and other factors as stressors. Therefore, strategies aimed at improving nursing measures, reducing the body stress response (induced by surgical treatment), and achieving the rapid recovery of patients have become a particular research focus. The concept of ERAS was first discovered in bowel surgery (general surgery) and has been gradually promoted in the fields of ophthalmology, gynecology, and cardiac surgery, and its nursing effect has been confirmed (24).

In this study, we included 10 articles (including eight RCTs and two cohort studies) on the application of ERAS in uterine fibroid surgery. The results showed that compared with routine care, the ERAS nursing model could reduce the first defecation time, first time out of bed, hospital stay after surgery, readmission rate, and incidence rate of postoperative complications, highlighting that this nursing model accelerated the recovery of patients. Also, it wouldn't add costs comparing with routine care.

In the 10 included studies, the ERAS nursing methods may have been applied differently, but all followed the guidelines and consensus of ERAS in gynecological surgery proposed by the ERAS® Society (25), which involves the following: health education before and after surgery, shortening the time of fasting, using minimally invasive surgical methods, selecting reasonable anesthesia methods and postoperative analgesia, maintaining room temperature and patient insulation during surgery, strictly controlling the amount of liquid infusion, avoiding the placement of a diversion tube or removing the diversion tube as early as possible, appropriately applying anti-emetics to stop vomiting, administration of short-term antibiotic treatment to prevent infection, drinking and eating early after surgery, early postoperative activity, and early ambulation.

Preoperative timely education and psychological counselling can reduce the fear and tension of patients with uterine fibroids, gain their trust, resulting in active cooperation with the procedure. Effective maintenance of the patient's body temperature during surgery can effectively reduce the incidence of postoperative complications; thus, room temperature should be strictly maintained at about 25 ℃, and blankets should be utilized to reduce the decrease in the patient's body temperature. In the process of postoperative infusion, a series of measures (such as infusion warming) are administered to reduce the patient's stress response (26). Traditional preoperative bowel preparation and preoperative overnight fasting will aggravate the metabolic rate of the body, and hunger will increase the stress response. ERAS theory suggests that routine bowel preparation is not required for patients. Taking carbohydrates on the night before surgery and 2–3 h before surgery can reduce preoperative hunger and craving as well as other discomfort, and prevent intraoperative hypoglycemic symptoms and insulin resistance (27). In addition, pre-emptive analgesia, reasonable toilet anesthesia, and postoperative analgesia in ERAS theory encourages early postoperative eating and restoration of intestinal motility, and early ambulation can reduce the stress response and pain and accelerate patient recovery (28).

The heterogeneity survey in this study showed that heterogeneity between the included articles was minimal. Also, the sensitivity survey showed that the meta-analysis results were stable, and the publication bias evaluation results showed that there was no publication bias in the included studies. Moreover, the included cohort studies had NOS scores >5 stars, and the RCTs all had "low risk of bias" for Cochrane ROB 2.0 assessment, the quality was good, therefore, the results were reliable. However, the total number of cases included was still small, and thus, larger sample size, multi-centre, controlled clinical studies on this topic are still needed to provide stronger evidence.

Conclusions

In conclusion, the application of ERAS in gynecological laparoscopic myomectomy can shorten the time of first defecation, the time of first ambulation, and the length of hospital stay, and reduce the readmission rate and incidence rate of postoperative complications, without additional costs.

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Footnote

Reporting Checklist: The authors have completed the PRISMA reporting checklist (available at https://gs.amegroups.com/article/view/10.21037/gs-22-168/rc).

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://gs.amegroups.com/article/view/10.21037/gs-22-168/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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