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REVIEW PAPER / GYNECOLOGY

Meta-Analysis for the evaluation of perioperative enhanced recovery after gynaecological surgery

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ABSTRACT

Objectives: To systematically evaluate the effectiveness and safety of enhanced recovery after surgery (ERAS) in gynaecological surgery and provide a scientific basis for its clinical promotion and application in the Chinese population.

Material and methods: Systematic retrieval from CNKI, Wanfang, VIP database and other Chinese literature databases. Studies on ERAS application with a randomised controlled trial in gynaecological surgery were included in the present report. Outcome indicators: hospitalisation time, postoperative ambulation time, postoperative feeding time, postoperative exhaust time, postoperative defecation time, operation time, postoperative blood loss, postoperative morbidity, patient satisfaction, hospitalisation expenses, etc. The meta-analysis was performed using the Revman 5.3 software.

Results: A total of 24 studies were included in the analysis. The results showed that, compared with the traditional group, the ERAS group had a lower hospitalisation time (SMD = −1.67, 95% CI = −2.03 ~ −1.30, $p < 0.0001$), postoperative ambulation time (SMD = −4.16, 95% CI = −5.12 ~ −3.20, $p < 0.0001$), postoperative feeding time (SMD = −7.36, 95% CI = −9.67 ~ −5.05, $p < 0.0001$), postoperative exhaust time (SMD = −2.59, 95% CI = −3.15 ~ −2.03, $p < 0.0001$), postoperative defecation time (SMD = −2.23, 95% CI = −2.88 ~ −1.57, $p < 0.0001$), postoperative morbidity (OR = 0.22, 95% CI = 0.15 ~ 0.31, $p < 0.0001$) and hospitalisation expenses (SMD = −0.53, 95% CI = −0.78 ~ −0.28, $p < 0.0001$). The patient satisfaction was significantly improved (odds ratio = 8.11, 95% CI = 4.96 ~ 13.24, $p < 0.0001$), and there were no significant differences in intraoperative blood loss and operation time between the two groups.

Conclusions: The application of the ERAS protocol in gynaecological surgery significantly improves the effectiveness and safety of the procedure. Thus, it can be promoted and applied in clinical practice in China.
Key words: ERAS; gynaecological surgery; systematic review; meta-analysis; effect evaluation

INTRODUCTION

With the development of medical science, surgery has undergone great changes in the past three decades. Traditional open surgery has rapidly developed into minimally invasive surgery dominated by using laparoscopy, single-hole surgery and da Vinci surgical robots. In addition, the management of the perioperative period has gradually shifted to Enhanced Recovery after Surgery (ERAS), which has achieved remarkable results in improving surgical quality, patient satisfaction and health economics [1]. ERAS was first proposed by Danish surgeon Kehlet in 1997, and it is widely used in surgical clinical practice [2]. This concept is a multi-mode optimisation of perioperative treatment based on evidence-based medicine evidence and multi-disciplinary cooperation. By reducing the stress response of the surgical stress level, it avoids the occurrence of serious surgical trauma and organ failure, ensures that patients with normal physiological function, and improves the operation quality as well as patient quality of life. With its promotion in China, the ERAS protocol has achieved good clinical application results in many surgical fields, such as breast, colorectal and gastrointestinal surgery.

As a special clinical department, gynaecology has different characteristics than other departments. Minimally invasive surgery has a significant clinical application effect in the field of gynaecology, which continues to develop and innovate. However, the understanding of the concept of ERAS in the perioperative period is relatively backward and one-sided. Therefore, it is very important to deeply understand the concept of ERAS and explore its application effect in gynaecological surgery. Hence, this study uses the Meta-analysis method to expand the sample size and comprehensively analyse the effectiveness and safety of ERAS concept application in gynaecological surgery, providing a theoretical basis for the clinical practice and promotion of ERAS in the field of gynaecology.

MATERIAL AND METHODS

Retrieval strategy

In accordance with the Cochrane Handbook for Systematic Reviews [3], relevant pieces of literature dated up to September 2021 were systematically retrieved from CNKI, Wanfang and VIP databases. Key words: ERAS; enhanced Recovery after Surgery; gynaecological surgery, etc. In addition, literature that met the inclusion and exclusion criteria was obtained by reading relevant systematic evaluation articles.

Inclusion and exclusion criteria

Inclusion criteria:

1. The subjects were female patients who underwent gynaecological surgery;
2. the intervention measures were gynaecological operations on endometrial cancer, cervical cancer, endometriosis, uterine fibroids, ovarian cancer, gynaecological tumours, etc.;
3. the control group was treated with traditional or conventional strategies;
4. the outcome indicators included hospitalisation time, hospitalisation expenses, postoperative recovery time, and incidence of postoperative complications; and
5. the research types include randomised controlled trials (RCTs).

Exclusion criteria:

1. The research types were descriptive studies, systematic reviews, case reports and other non-original studies;
2. the control groups lacked traditional strategies; and
3. there were no relevant outcome indicators, or the literature was incomplete.

Literature screening and data extraction

Two researchers (Wu XF and Liu LL) independently screened the literature according to the criteria. In case of a disagreement between the two, a third researcher (Zhou F) was invited to discuss and reach a consensus. After literature screening, the data were extracted by two researchers; this included literature information, demographic characteristics of the subjects, surgical methods, related outcome indicators and research types.

Quality evaluation

RCT quality was assessed using the Cochrane bias risk assessment tool [4]. The evaluation items included random sequence generation, assignment concealment, blind method for researchers and subjects, blind method for results, completeness of outcome data, optional reporting of study results and other sources of bias. The evaluation grades of each item were divided into low risk, unknown risk and high risk. Finally, the literature quality was divided into A, B and C according to the evaluation results. Level A represented low deviation, i.e., four or more items that meet quality standards = low risk. Level B represented moderate bias, i.e., meeting two to three quality criteria = low risk. Level C represented high bias, i.e., the quality standard for one or more items = high risk.

Statistical Analysis

The statistical analysis was conducted using the Revman 5.3 software. The odds ratio (OR) and weighted mean difference were used to indicate the effect of count data and measurement data, respectively. The 95% confidence interval (CI) was used to estimate effect range. The heterogeneity test used the combination of χ^2 test and I^2 to determine the size of heterogeneity. $I^2 < 50\%$ meant that the included studies were not homogeneous; these were analysed using a random effects model. If heterogeneity was large, subgroup analysis or sensitivity analysis were used. The funnel plot was used to evaluate the publication bias of the analysis if the number of included pieces of literature was ≥ 10.

RESULTS

Characteristics of included literature

Through the search of keywords, a total of 1352 articles were retrieved, and 601 repetitive articles were preliminarily excluded. A total of 479 articles were excluded by reading literature titles, abstracts, conference abstracts, animal experiments and case reports. After further reading the full text, there were 24 articles (excluding non-randomised controlled articles, unreported related outcome indicators, unmet inclusion criteria and incomplete data) [5–28]. The document retrieval flow chart is shown in Figure 1. "Flow chart of document retrieval".

In the 24 studies included in the present report, the ERAS concept was used for perioperative treatment in the experimental group (n = 1632), and the traditional or conventional concept was used for perioperative treatment in the control group (n = 1636). The basic characteristics of the included literature are shown in Table 1.

Quality evaluation results

According to the Cochrane bias risk tool, the quality level of the 24 studies included in this analysis was evaluated: 9 studies = A, 11 studies = B and 4 studies = C. Bias was mainly caused by the absence of a blind method and group hiding. The detailed evaluation results are shown in Table 2.

Meta-analysis results

Hospitalisation time

The results of hospitalisation time were reported in 21 articles. The random-effects model Meta-analysis showed a significantly shorter hospitalisation time in the ERAS group than in the control group (combined effect: SMD = −1.67, 95% CI= −2.03 ~ −1.30, $p < 0.0001$). There was significant heterogeneity between the literature (I^2 = 95%, $p < 0.0001$). The source of heterogeneity was not found using the sensitivity analysis and subgroup analysis, indicating that the results were relatively stable.

The publication bias analysis results showed that the left and right funnel plots were basically symmetrical (Fig. 2). There was no symmetry in certain pieces of literature, suggesting a certain publication bias; however, the risk was small.

Postoperative ambulation time

The results regarding the postoperative ambulation time (h) were reported in 14 articles. The random-effects model Meta-analysis showed a significantly earlier postoperative feeding time in the ERAS group than in the control group (combined effect: SMD = −4.16, 95% CI = −5.12 ~ −3.20, $p < 0.0001$). There was significant heterogeneity between the literature (I^2 = 98%, $p < 0.0001$). The source of heterogeneity was not found using the sensitivity analysis and subgroup analysis, indicating that the results were relatively stable.

The publication bias analysis results showed that the left and right funnel plots were basically symmetrical, indicating that the possibility of publication bias was small (Fig. 3).

Postoperative feeding time

The results regarding the postoperative feeding time (h) were reported in 9 articles. The random effects model Meta-analysis showed a significantly earlier postoperative feeding time in the ERAS group than in the control group (combined effect: SMD = −7.36, 95% CI= −9.67 ~ −5.05, $p < 0.0001$). There was significant heterogeneity between the literature ($I^2 = 99\%$, $p < 0.0001$). The source of heterogeneity was not found using the sensitivity analysis and subgroup analysis, indicating that the results were relatively stable.

Postoperative exhaust time

The results regarding the postoperative exhaust time (h) were reported in 20 articles. The random-effects model Meta-analysis showed significantly earlier postoperative venting in the ERAS group than in the control group (combined effect: SMD = −2.59, 95% CI = −3.15 ~ −2.03, $p < 0.0001$). There was significant heterogeneity between the literature ($I^2 = 97\%$, $p < 0.0001$). The source of heterogeneity was not found using the sensitivity analysis and subgroup analysis, indicating that the results were relatively stable.

In addition, the results of the analysis of subgroups who underwent minimally invasive gynaecologic surgery showed that there was no significant difference in postoperative exhaust time between the two groups (SMD = −3.04, 95% CI = −7.47 ~ 1.38). The publication bias analysis results showed that the left and right funnel plots were basically asymmetric, indicating a certain publication bias (Fig. 4).

Postoperative defecation time

The results regarding the postoperative defecation time (h) were reported in seven articles. The results of the random effects model Meta-analysis suggested a significantly earlier postoperative feeding time in the ERAS group than in the control group (combined effect: SMD = −2.23, 95% CI = −2.88 ~ −1.57, $p < 0.0001$). There was significant heterogeneity between the literature ($I^2 = 94\ \%$, $p < 0.0001$). The subgroup analysis showed that laparoscopy heterogeneity was significantly lower than combined heterogeneity ($I^2 = 0\%$) (combined effect: SMD = −1.86, 95% CI = −2.09 ~ −1.62, $p < 0.0001$).

Hospitalisation expenses

The results regarding the hospitalisation expenses (CNY 10,000) were reported in four articles. The random-effects model Meta-analysis showed significantly lower hospitalisation expenses in the ERAS group than in the control group (combined effect: SMD = −0.53, 95% CI = −0.78 ~ −0.28, $p < 0.0001$). The heterogeneity in the literature was acceptable ($I^2 = 54\%$, $p < 0.0001$).

Operation time

The results regarding the operation time (min) were reported in five articles. There was significant heterogeneity among the literatures (I^2 = 95%, $p < 0.0001$). Heterogeneity was significantly reduced after excluding one article after sensitivity analysis [27] (I^2 = 0%, p = 0.851). The meta-analysis results of the random effect model showed no significant difference in operation time between the ERAS group and the control group (combined effect: SMD = −0.07, 95% CI = −0.24 ~ 0.11, p = 0.462).

Intraoperative blood loss

The results regarding the postoperative bleeding volume (mL) were reported in three articles. The random-effects model Meta-analysis showed that the difference in intraoperative bleeding between the ERAS group and the control group was not statistically significant (combined effect: SMD = −1.43, 95% CI = −3.48 ~ 0.63, p = 0.173). There was significant heterogeneity between the literature (I^2 = 98%, $p < 0.0001$). The source of heterogeneity was not found using the sensitivity analysis, indicating that the results were relatively stable.

Postoperative morbidity

The results regarding postoperative morbidity incidence were reported in 12 articles, with low heterogeneity (I^2 = 19%) and good homogeneity. The fixed-effects model meta-analysis indicated a significantly lower rate of postoperative complications in the ERAS group than in the control group (combined effect: OR = 0.22, 95% CI = 0.15 ~ 0.31, $p < 0.0001$). The publication bias analysis results showed that the left and right funnel plots were basically symmetrical, indicating a low risk of publication bias (Fig. 5).

Patient satisfaction

The results regarding patient satisfaction incidence were reported in eight articles, with low heterogeneity (I^2 = 0%) and good homogeneity. The fixed effect model Meta-analysis showed that patient satisfaction was significantly higher in the ERAS group than in the control group (combined effect: OR = 8.11, 95% CI = 4.96 ~ 13.24, $p < 0.0001$).

DISCUSSION

Improving the safety and effectiveness of surgery and accelerating the postoperative rehabilitation in patients have been the goals of modern medicine for a long time. Many original studies show that the ERAS concept has achieved remarkable results in perioperative nursing with its wide application in various surgical fields in China. At present, its application in gynaecological surgery is becoming more and more widely used.

Original research shows that, compared with traditional or conventional nursing measures, the ERAS concept has certain advantages in all perioperative period aspects. However, few studies systematically analyse all original evidence.

Therefore, the present study systematically analyses original evidence of the ERAS concept compared with traditional or conventional surgical concepts in gynaecological surgery in order to provide a solid theoretical basis for the promotion and application of the ERAS concept in the field of gynaecological surgery in China. The results of the present study show that the ERAS concept can effectively improve surgery safety and effectiveness; significantly shorten the length of hospital stay and postoperative ambulation, feeding, exhaust and defecation times; reduce hospitalisation expenses and postoperative morbidity; and improve patient satisfaction.

However, no significant difference was found between the ERAS concept and the conventional or routine concept in terms of operative time and intraoperative blood loss. The research results are consistent with the result of previous systematic analyses [29, 30].

In contrast with traditional or conventional surgical concepts, the ERAS concept emphasises cancelling preoperative bowel preparation and reducing excessive consumption before surgery, thus accelerating patient recovery. In addition, the use of the ERAS concept in postoperative analgesia, early postoperative feeding and ambulation promotes patient recovery.

Studies have shown that effective analgesia can reduce postoperative stress response and intestinal paralysis, which is conducive to postoperative activity and eating habits of patients [31]. Early feeding after surgery plays an important role in patient intestinal function recovery [32]. A systematic evaluation of the effect of early feeding on gastrointestinal function showed that, compared with non-feeding after surgery, early feeding significantly shortened the patient hospitalisation time and gastrointestinal recovery time [33].

The recommendation of the ERAS guideline (2019) in the gynaecology/tumour field was reorganised. It was recommended that patients eat general food six hours before anaesthesia, receive a liquid diet 2 h before anaesthesia, and adopt target-directed liquid therapy during the operation.

An appropriate nutritional status should be maintained after operation, and a routine diet should be carried out within 24 h after operation to promote the rapid recovery of intestinal function and improve the operation quality [34]. The results of a study conducted by Relph et al. showed that the total cost of hospitalisation in the ERAS group decreased by 12.7%, saving approximately GBP 176.15 [35]. Furthermore, a retrospective analysis carried out by Pache et al. [36] found that the average total hospitalisation expenses of patients in the ERAS group saved $4381 compared with the traditional concept group. Thus, the ERAS concept can not only promote postoperative recovery, but also has economic benefits in health economics.

There are still several limitations to this study:

1. The heterogeneity of research and analysis is high. Considering that the heterogeneity is derived from research carried out by different institutions, there may be no unified standard in surgical skills and data recording; this can easily lead to bias.
2. It was difficult to implement the blind method in patients and testers included in the

study due to disease and surgical method types.

CONCLUSIONS

In summary, the application of the ERAS concept in gynaecological surgery is safe and effective. However, there are still certain limitations to this study, and a large number of large-samples, high-quality and multi-centre RCTs are required to verify the application effect of the ERAS concept in the field of gynaecology.

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Table 1. Basic characteristics of included literature

Author	Year	Sample size		Age		Disease	Modus operandi
		ERAS group	Control group	ERAS group	Control group		
Lian	20	46	46	31.	32.5	Canc	Microtra

Guomei	20			48 ± 6.95	1 ± 6.84	er	uma
Zhao Wei	2019	40	40	50.24 ± 1.36	50.24 ± 1.36	Cancer	NR
Yue Fengxian	2018	85	85	39.72 ± 3.10	40.25 ± 3.06	NR	Laparoscope
Cai Bin	2020	100	100	50.14 ± 6.43	50.36 ± 6.29	Cancer	Laparoscope
Xu Jun	2020	53	53	45.37 ± 10.26	44.91 ± 11.22	NR	NR
Gong Guifang	2019	100	100	30.91 ± 2.51	30.88 ± 2.46	Cancer	Laparoscope
Wang Jinmei	2019	64	64	18–60	18–60	NR	Laparoscope
Fang Lingling	2021	60	60	34.8 ± 2.4	35.5 ± 2.2	NR	Laparoscope
Zhou Jingjing	2020	75	75	50.34 ± 4.34	49.89 ± 5.03	Cancer	Microtrauma
LV juping	2021	79	79	51.6 ± 10.7	50.2 ± 12.4	NR	Microtrauma
Liu Lanlan	2020	30	30	52.2 ± 5.7	52.5 ± 5.8	NR	Laparoscope
Chen Dongluan	2020	48	48	45.32 ± 4.97	44.69 ± 4.36	NR	Laparoscope
Yu Yamin	2020	80	80	34.3 ± 4.8	33.6 ± 5.1	NR	Laparoscope
Wang Jing	2018	82	83	47.15 ± 11.43	45.00 ± 10.81	NR	Laparoscope
Jing Wang	2018	52	52	44.07 ± 9.97	42.13 ± 10.12	NR	Laparoscope
Cheng Chuanxi	2017	83	83	43.63 ± 9.02	44.84 ± 8.88	NR	NR

Xiao Lihong	2019	51	51	42.69 ± 7.85	42.17 ± 7.69	NR	Pelvic surgery
Chu Boliang	2020	54	57	37.74 ± 11.45	38.98 ± 13.10	Tumour	Laparoscope
Huang Zhujuan	2012	53	53	37.5 ± 8.5	37.5 ± 8.5	NR	NR
Fan Yinghong	2019	50	50	55.7 ± 12.5	55.9 ± 12.6	Cancer	NR
Zhang Qun	2019	42	42	36 ± 8.5	36 ± 8.8	NR	Laparoscope
Zhi Binlin	2014	100	100	NR	NR	NR	NR
GUI Lingli	2017	55	55	43.5 ± 6.6	43.1 ± 6.5	NR	NR
Qiu Huajuan	2019	150	150	43.7 ± 10.4	42.9 ± 10.1	NR	NR

Table 2. Quality evaluation of 24 studies included in the analysis

Author	Year	Random sequence	Blind grouping	Blinding researchers and subjects	Blinding the evaluation	Integrity of outcome data	Results of selective reporting	Other sources of bias
Lian Guomei	2020	Unknown risks	Unknown risks	Low risks	Low risks	Low risks	Low risks	Unknown risks
Zhao Wei	2019	Unknown risks	Unknown risks	Unknown risks	High risks	Low risks	Low risks	Low risks
Yue Fengxian	2018	Low risks	Unknown risks	High risks	High risks	Low risks	Unknown risks	Unknown risks
Cai Bin	2020	Low risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Low risks
Xu Jun	2020	Unknown risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Unknown risks
Gong Guifang	2019	Low risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Low risks
Wang Jinmei	2019	Unknown risks	High risks	High risks	Unknown risks	Low risks	Unknown risks	Unknown risks
Fang Lingling	2021	Unknown risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Unknown risks
Zhou Jingjing	2020	Unknown risks	Unknown risks	Unknown risks	High risks	Low risks	Low risks	Unknown risks

LV juping	2021	Low risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Low risks
Liu Lanlan	2020	Low risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Low risks
Chen Dongluan	2020	Unknown risks	Unknown risks	High risks	Unknown risks	Low risks	Low risks	Unknown risks
Yu Yamin	2020	Low risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Low risks
Wang Jing	2018	Unknown risks	Unknown risks	Unknown risks	High risks	Low risks	Low risks	Unknown risks
Jing Wang	2018	Low risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Low risks
Cheng Chuanxi	2017	Unknown risks	High risks	Unknown risks	Unknown risks	Low risks	Unknown risks	High risks
Xiao Lihong	2019	Unknown risks	High risks	Unknown risks	Unknown risks	Low risks	Low risks	Unknown risks
Chu Boliang	2020	Unknown risks	High risks	Unknown risks	Unknown risks	Low risks	Low risks	Unknown risks
Huang Zhujuan	2012	Low risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Low risks
Fan Yinghong	2019	Low risks	Unknown risks	Unknown risks	Unknown risks	Low risks	Low risks	Low risks
Zhang Qun	2019	Unknown risks	Unknown risks	Unknown risks	High risks	Low risks	Low risks	Unknown risks
Zhi Binlin	2014	Unknown risks	Unknown risks	Unknown risks	High risks	Low risks	Low risks	Unknown risks
GUI Lingli	2017	Unknown risks	Unknown risks	Unknown risks	High risks	Low risks	Low risks	Unknown risks
Qiu Huajuan	2019	Unknown risks	Unknown risks	High risks	High risks	Low risks	Low risks	Unknown risks

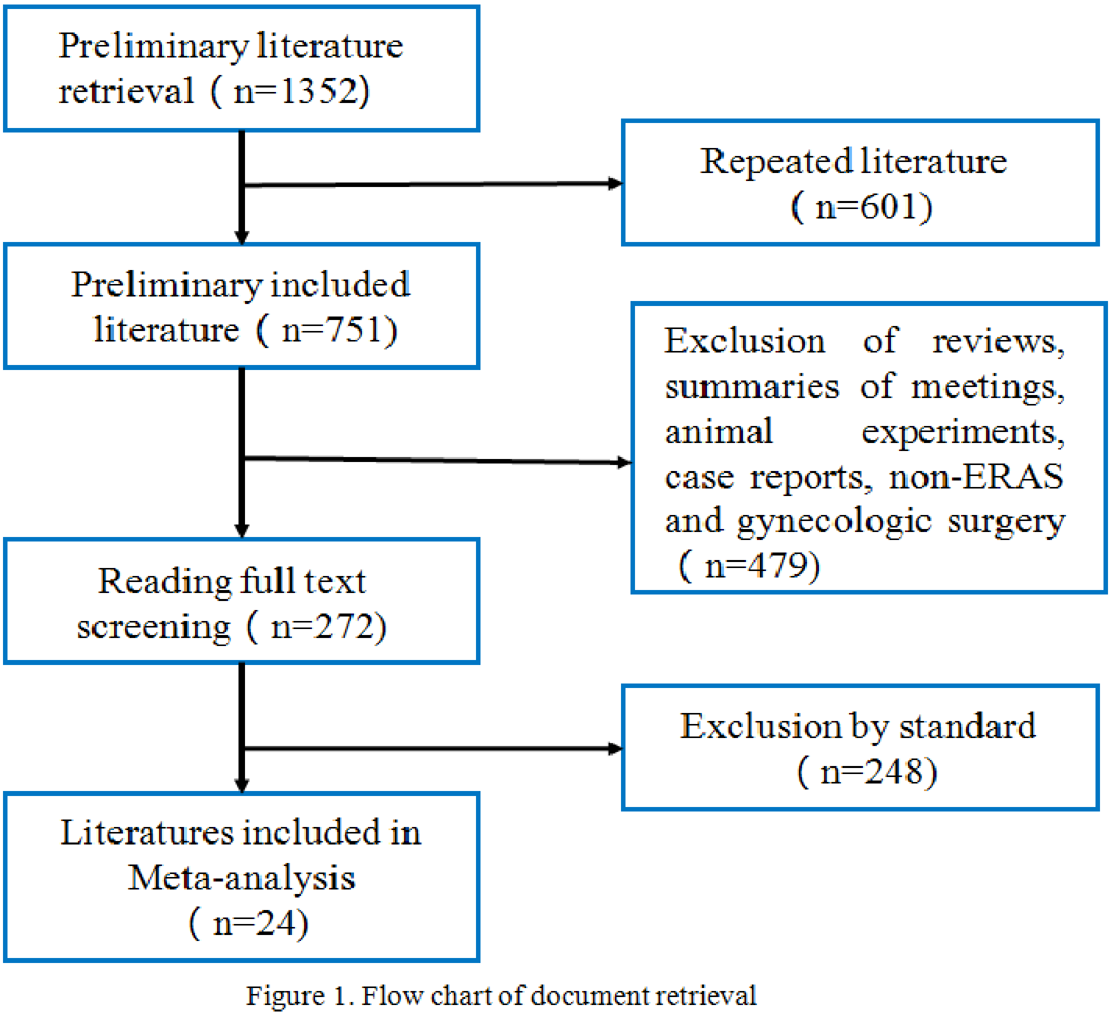

Figure 1. Flow chart of document retrieval

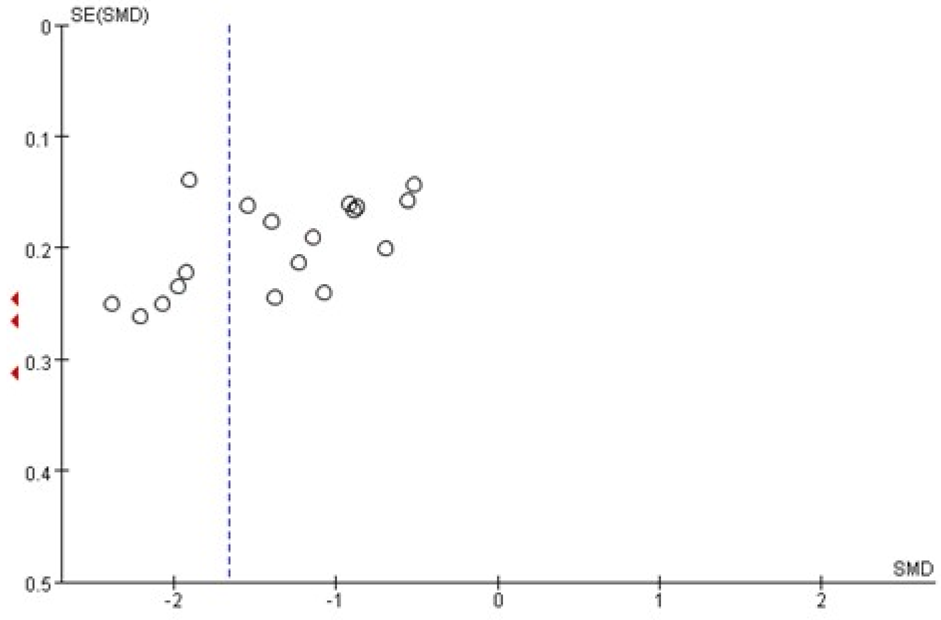

Figure 2. The funnel plot of LOS (d)

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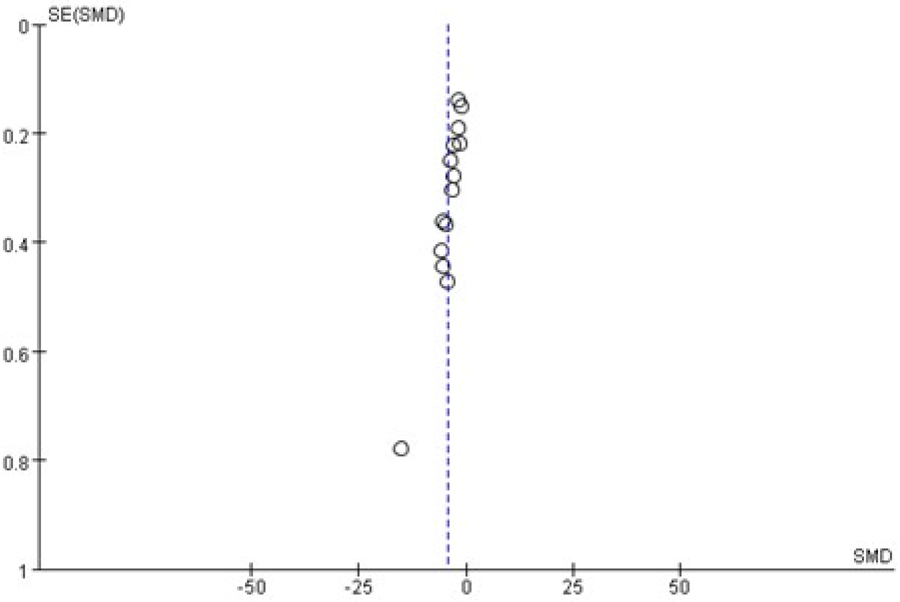

Figure 3. The funnel plots of postoperative ambulation time

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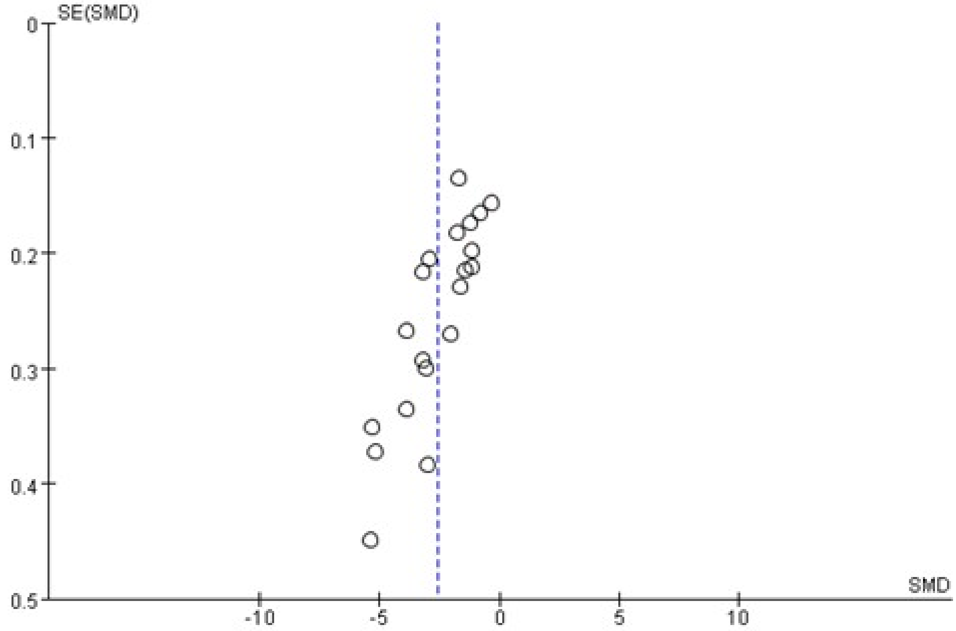

Figure 4. The funnel plots of postoperative exhaust time

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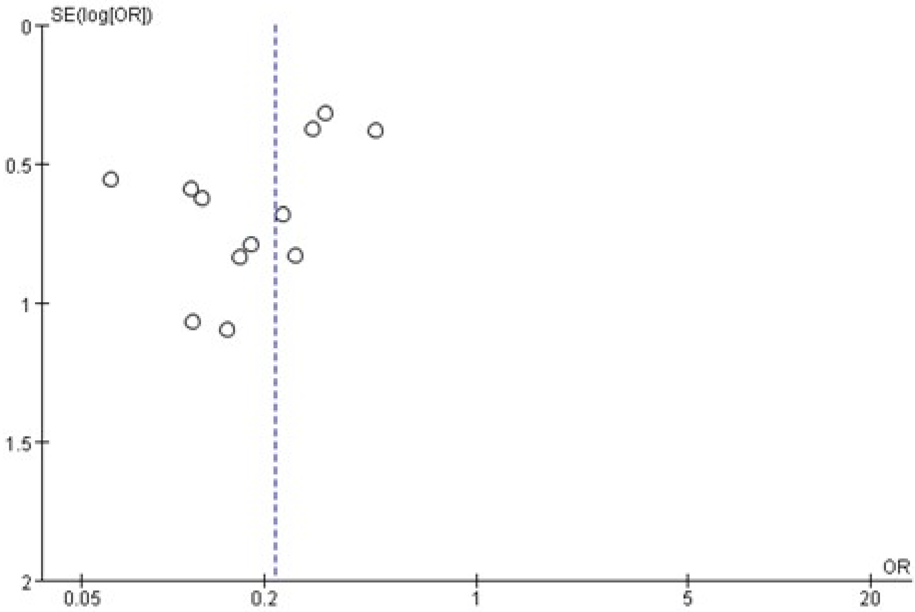

Figure 5. The funnel plots of postoperative morbidity

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