Systematic Review and Meta-Analysis

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Enhanced recovery after surgery on multiple clinical outcomes

Umbrella review of systematic reviews and meta-analyses

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Abstract

Background: Previously, many meta-analyses have reported the impact of enhanced recovery after surgery (ERAS) programs on many surgical specialties.

Objectives: To systematically assess the effects of ERAS pathways on multiple clinical outcomes in surgery.

Design: An umbrella review of meta-analyses.

Date sources: PubMed, Embase, Web of Science and the Cochrane Library.

Results: The umbrella review identified 23 meta-analyses of interventional study and observational study. Consistent and robust evidence shown that the ERAS programs can significantly reduce the length of hospital stay (MD: −2.349 days; 95%CI: −2.740 to −1.958) and costs (MD: −$639.064; 95%CI:: −933.850 to −344.278) in all the surgery patients included in the review compared with traditional perioperative care. The ERAS programs would not increase mortality in all surgeries and can even reduce 30-days mortality rate (OR: 0.40; 95%CI: 0.23 to 0.67) in orthopedic surgery. Meanwhile, it also would not increase morbidity except laparoscopic gastric cancer surgery (RR: 1.49; 95%CI: 1.04 to 2.13). Moreover, readmission rate was increased in open gastric cancer surgery (RR: 1.92; 95%CI: 1.00 to 3.67).

Conclusion: The ERAS programs are considered to be safe and efficient in surgery patients. However, precaution is necessary for gastric cancer surgery.

Abbreviations: AMSTAR = a measurement tool to assess systematic reviews, CI = confidence interval, ERAS = enhanced recovery after surgery, GRADE = Grading of Recommendation Assessment, Development and Evaluation, OR = odds ratio, RR = relative ratio.

Keywords: enhanced recovery after surgery, enhanced recovery after surgery, meta-analyses, surgery, umbrella review

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1. Introduction

Enhanced recovery after surgery (ERAS) programs are multidisciplinary, multimodal care pathway aimed to optimize the management of perioperative period, reduce surgical stress response and accelerate patient recovery, which was proposed initially by professor Henrik Kehlet in 1997, also known as fast track surgery (FTS).[1,2] Multidisciplinary means that the successful implementation of ERAS pathways depending on the cooperation of surgeon, anesthetist, physiotherapist, nurse and patient.[1] The ERAS pathways involving in preoperative period, intraoperative period and postoperative period consist of preadmission counseling, nutritional screening/support, medical optimization of chronic disease, no routine use of mechanical bowel preparation, no prolonged fasting, carbohydrate treatment, antibiotic prophylaxis, thrombosis prophylaxis, preanesthetic sedative medication (no routine use), minimally invasive surgical techniques, standardized anesthesia protocol, restrictive use of surgical site drains, remove nasogastric tubes early, avoidance of salt and water overload, maintenance of normal temperature, early intake of oral fluids and solids, early removal of urinary catheters and intravenous fluids, prevention of nausea and vomiting, multimodal approach to opioid-sparing pain control, early mobilization, prepare for early discharge[3,4]

The ERAS pathways were initially trialed in colorectal surgery[1] and then were rapidly introduced in other specialties in the next few years, including liver, gastric, orthopedic, pancreatic, urology, breast, esophageal, bariatric and other surgeries.[2] The majority of studies have reported that the ERAS can reduce the total length of hospital stay (LOS) and cost of hospitalization, improve the quality of life (QOL) and patient satisfaction by reducing the insulin resistance and inflammatory reaction caused by surgery.[5–12] Besides, the secondary outcomes including return of gastrointestinal function, time to first diet, post-operative pain score,[6] operation time,[9,10] blood loss,[7,10] and nutritional status[6] were also improved. The ERAS pathway was originally used for elective surgery, recently, some articles have shown that it is safe and feasible in emergency surgery.[13,14] After two decades of development, more and more publications have been published to study the safety and effectiveness of the ERAS program in surgical patients, and many guidelines or consensus have been reached for multiple surgical sub-specialties.[15–19]

Considering the superiority of the ERAS programs, it has been widely used in many surgical specialties worldwide.[20] However, is this beneficial to all surgery? Obviously, it is not clear yet. For example, in some studies, the morbidity and readmission would be increased with the ERAS programs for gastric cancer surgery.[21,22] It is necessary to determine the effects of ERAS on the multiple clinical outcomes of different procedures. Therefore, we systematically investigated the evidence of ERAS in clinical outcomes and conducted the umbrella review to determine the pros and cons of ERAS for all procedures.

2. Methods

2.1. Umbrella review methods

An umbrella review is the review of existing systematic reviews and/or meta-analyses, which can provide important information that can be used by decision makers in healthcare to systematically understand a topic area.[23] We conducted an umbrella review to evaluate the impact of enhanced recovery after surgery (ERAS) for all kinds of surgical patients. The article did not require ethical approval because it was a systematic review and did not involve patients.

2.2. Literature search

We systematically searched the PubMed, Embase, Web of Science and Cochrane Library from the inception to March 21, 2019, to identify systematic review and meta-analyses of observational studies and randomized controlled trials (RCTs) which examined the effects of ERAS on clinical outcomes for surgery people. We used the following search strategy: ("enhanced recovery*" OR "fast tract*" OR "ERAS") and ("systematic review*" OR "meta-analys*"), and the terms were truncated for all fields, which following the SIGN guidance recommended search terms for systematic reviews and meta-analyses.[24] We also searched the reference lists of eligible articles and relevant clinical guidelines. Two researchers reviewed the identified records independently and screened eligible studies by a three step parallel reviews of title, abstract and full text based on the predefined inclusion and exclusion criteria. Disagreements were settled by consensus or discussion with a third researcher.

2.3. Eligibility criteria

The included criteria were:

(1) the article was a systematic review and meta-analyses or a meta-analyses of both RCTs and observational studies;
(2) evaluated the effects of enhanced recovery after surgery program for surgical patients;
(3) reported effect sizes-odds ratio (OR), relative risk (RR), or hazard ratio (HR) for qualitative outcomes and mean difference (MD) or standardized mean differences (SMD) for quantitative outcomes;
(4) the ERAS protocols must be used in ERAS/FT group;
(5) the meta-analyses investigated the effects of ERAS compared with conventional care;
(6) the article must be published in English.

Systematic reviews without meta-analyses were ruled out. The meta-analyses emphasized just one protocol of the ERAS program (such as early oral feeding or early mobilization on postoperative) was excluded. If full text was unavailable, the article was excluded as well.

2.4. Data extraction

Data was extracted using a double-extraction method from each eligible study by the two investigators. We extracted data of each eligible reference and recorded the first author, year, journal of publication, and the type of surgery. Then we extracted the number of studies included in meta-analyses, study design(s) (case-control, cohort, or randomized controlled trial), the number of participants, the range of ERAS protocols in the articles and the study outcomes (length of hospital stay, mortality, complication and so on). In addition, we abstracted data from the meta-analyses of observational studies or randomized controlled trials, included metric (odds ratio, risk ratio, mean differences, standard mean difference, weighted mean difference), the summary estimates and related 95% confidence interval (CI), heterogeneity (I^2) and type of effect model used in the meta-analysis (fixed or random), publication bias was recorded as well. If possible, we also extracted the populations as well as the country where the study was conducted. When the article reported more than one outcome, we recorded each outcome respectively. When there was more than one paper reported the same outcomes, we would choose the updated one. If any discrepancies could not be resolved by consensus, the third researcher involved in and made the final decision.

2.5. Evaluation of quality and grading of evidence

We used the assessment of multiple systematic reviews (AMSTAR) tool to assess the methodological quality of each involved meta-analysis. The AMSTAR was a reliable and valid measurement tool to assess the quality of systematic review and meta-analyses,[25] which was made of 11 items including a priori design, study selection and data extraction, the literature search, gray literature, the list of included and excluded studies, study characteristics, critical appraisal, formulation of conclusions, the combination of study results, publication bias, and conflicts of interest.[26] The Grading of Recommendations Assessment, Development, and Evaluation (GRADE)[27] system was used to access the quality of evidence for included articles. The GRADE assorted the quality of evidence into four categories: "high", "moderate", "low", and "very low".[28] The quality of Evidence based on RCTs or observational studies can be decreased or increased according to the study design, risk of bias, imprecision, inconsistency, indirectness, and magnitude of effect.[27]

2.6. Data analysis

We extracted the outcomes of ERAS on all of the surgery patients from the identified systematic review and meta-analyses, and we recorded the summary estimates and 95% CI of each related outcomes, which was calculated by both fixed and inverse variance random effects methods, if the heterogeneity existed ($I^2 > 50\%$) between the studies, we used the random effects methods, otherwise, a fixed effects method was used. We extracted the I^2 metric and Egger test to measure the heterogeneity and publication bias if they were available.[29,30] And if the number of studies included in the meta-analyses was more than ten, we would calculate the publication bias through Egger regression test with the original detailed data was obtainable. A $P < .1$ for Egger regression test was regarded as statistically significant publication bias. We did not reanalyze the other data or primary studied included in the meta-analyses.

3. Results

3.1. Characteristics of meta-analyses

A total of 804 publications were revealed in the systematic research, including 276 publications by PubMed, 367 publications by Web of Science, 116 publications by Embase and 45 publications by the Cochrane Library. After removing duplicates, a total of 581 articles were rested. Based on the title, abstract and full text, 55 meta-analyses were included in the umbrella review which applying our inclusion criteria. The detailed selection process was shown in Figure 1.

All of the 55 articles investigated the impact of ERAS/FTS on clinical outcomes compared with conventional care mode involved in colorectal surgery (n=13),[3,31–42] liver surgery (n=7),[43–49] gastric surgery (n=7),[22,50–55] orthopedic surgery (n=3),[56–58] bariatric surgery (n=3),[59–61] urology surgery (n=3),[62–64] breast surgery (n=3),[65–67] esophageal surgery (n=3),[68–70] pancreatic surgery (n=3)[71–73] and other surgeries (n=10)[4,74–82] including gynecologic surgery,[74] abdominal aortic aneurysm repair surgery,[76] lung surgery[77] and vascular operations.[79] The most clinical results were measured in the meta-analyses are length of hospital stay (LOS)/post-operative hospital stay (PLOS) (n=47), cost (n=16), mortality (n=30), morbidity (n=54), readmission (n=42), reoperation (n=8) and other secondary outcomes. All the meta-analyses reported the ERAS/FTS pathways were used in observational groups and 37 of 55 specifically pointed out the number of protocols in the pathways and the range of ERAS elements applied in the articles was from 2 to 22. Full version information was available in Supplemental Table 1, http://links.lww.com/MD/E467. And we included the latest 23 meta-analyses to analyze.

In the latest meta-analysis, ERAS pathways can significantly reduce the morbidity (RR: 0.620; 0.545 to 0.704),[4] LOS (MD:−2.349; −2.740 to −1.958),[4] hospital cost (MD: −639.06; −933.85 to −344.28),[4] and shorten the time to first flatus (MD: −13.119; −17.980 to −8.257)[4] for surgery patients, while have no impacts on mortality and readmissions.[4] However, the results were different among diverse surgical specialties.

3.2. ERAS on colorectal cancer

Consistent evidence indicated that the ERAS pathways can significantly reduce the LOS, PLOS, morbidity and enhance the recovery of bowel functions. Morbidity was decreased by 34% compared with conventional care (RR: 0.66; 0.54 to 0.80).[3] And the reduction in LOS were 2.6 days (−3.2 to −2.0),[3] PLOS were 2.0 days (−2.52 to −1.48),[37] cost were $1003.790 (−1872.567 to −135.012),[4] time to first flatus and defecation were shortened by 1 day as well.[42] Similar results were found in laparoscopic surgery.[37] In addition, inflammatory response indicators were attenuated with the ERAS pathways, C-reactive protein (CRP), Interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) levels on POD 3 to POD 5 were reduced significantly.[37] Results were shown in Table 1.

3.3. ERAS on orthopedic surgery

Evidence shown that the mortality and morbidity of orthopedic surgery have been significantly reduced by 60% and 30% (RR: 0.40, 0.23 to 0.67; 0.70, 0.64 to 0.78; respectively).[57] Moreover, meta-analyses indicated that a decrease in LOS of 2.03 (−2.64 to −1.42)[56] days, PLOS of 0.85 (−1.24 to −0.45)[58] days in those patients treated with ERAS pathways for joint arthroplasty. Most importantly, Oswestry Disability Index and transfusion rate were decreased as well, but not for readmission.[57] The detailed results were shown in Table 2.

3.4. ERAS on gastric surgery

Compared with traditional care, LOS was significantly reduced by 2.47 days (WMD: 2.47, 3.06 to −1.89),[22] PLOS were decreased 1.85 (−2.35 to −1.35)[52] and 2.65 (−4.01 to −1.29)[53] days both in open and laparoscopic approach. The cost,[52] time to first flatus[54] and inflammatory response[22] were also reduced. However, the readmission was increased (RR: 1.95; 95%CI: 1.03 to 3.67).[22] Mortality and morbidity were comparable between ERAS and traditional pathways. The detailed results were shown in Table 3.

3.5. ERAS on other surgeries

The data indicated that ERAS pathways can significantly reduce LOS and PLOS compared with traditional care. And the reduction of LOS were 3.75 days (−5.13 to −2.36) in cystectomy;[64] 3.55 days (−4.42 to −2.69) in esophageal cancer surgery;[69] 3.5 days (−5.8 to −1.4) in vascular operations;[79] 3.17 days (−3.99 to −2.35) in liver surgery;[49] 3.05 days (−4.87 to −1.23) in abdominal gynecologic surgery,[74] and 1.58 days (−1.99 to −1.18) in breast reconstruction.[66] There are also some articles shown the reduction of PLOS, in pancreatic surgery, it was shorter 4.45 days (−5.99 to −2.91)[72] than traditional groups, 4.17 days (−5.72 to −2.61) in pancreaticoduodenectomy[73] and 2.72 days (−3.86 to −1.57) in hepatectomy.[44] Meta-analysis shown a significant reduction in the total cost of hospital for upper gastrointestinal surgery,[81] liver surgery[47] and non-colorectal surgery[82] compared with control groups. ERAS pathways can reduce the rate of morbidity in bariatric,[59] cystectomy,[64] liver surgery,[47] lung cancer surgery[77] and pancreatic surgery.[72] The detailed information was shown in the Supplement Table 1, http://links.lww.com/MD/E467.

3.6. Heterogeneity of included outcomes

Among the 146 outcomes of 23 meta-analyses, about 15.0% did not report the value of I^2, and we did not conduct the I^2 statistic

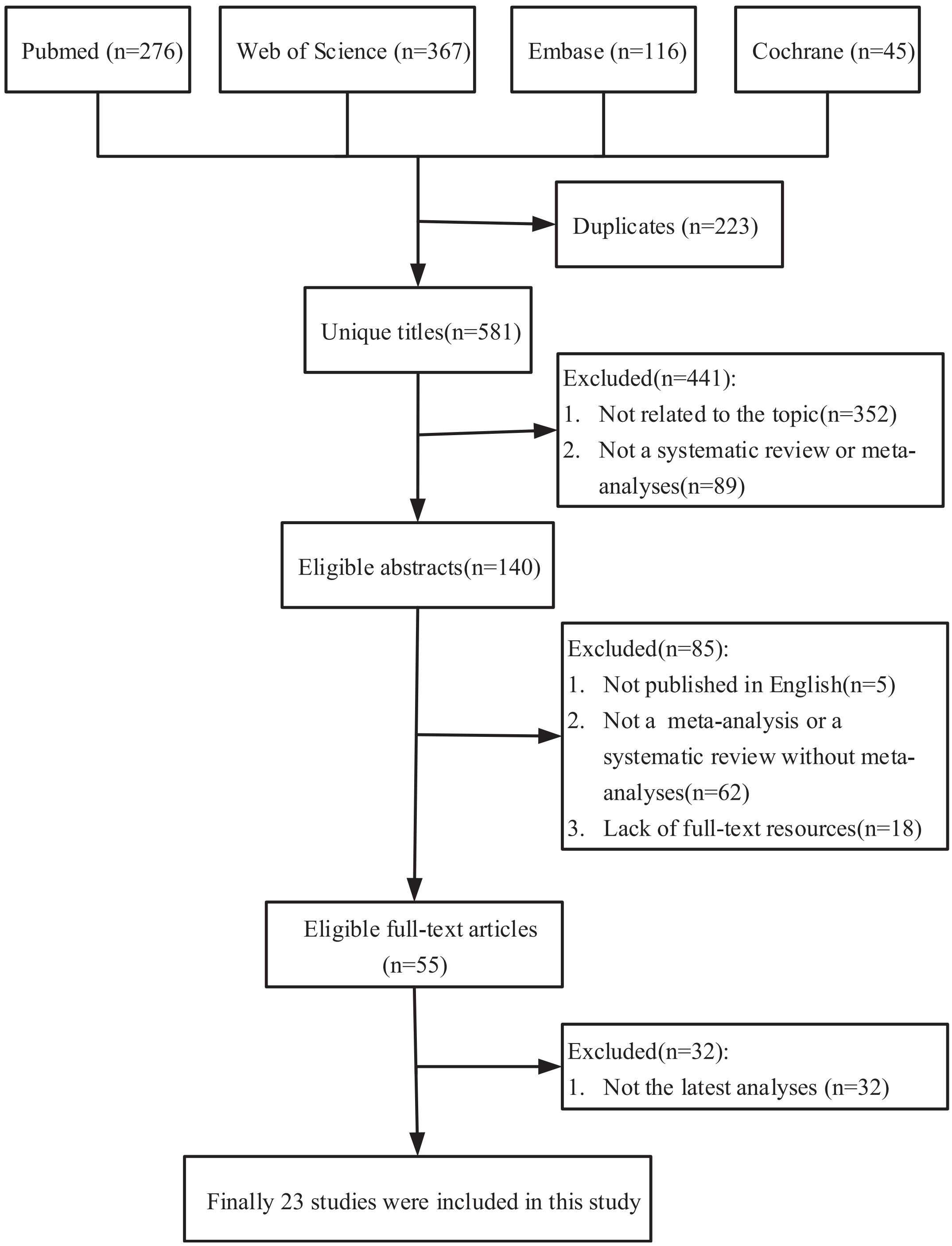

Figure 1. Flowchart of process of selection.

for assessment of heterogeneity because of the lack of available data. For the other outcomes, 35.0% had low heterogeneity with $I^2 < 25\%$, and 26.7% had very high heterogeneity, with $I^2 > 75\%$. About 23.3% had moderate-to-high heterogeneity with I^2 range from 25% to 75%. The heterogeneity in the individual studies included meta-analyses was affected by many factors such as the participation, type of surgery, duration of follow-up, the number of ERAS protocols used in the study and the endpoints of ERAS in each primary study.

3.7. Publication bias of included outcomes

Of the total of 146 outcomes, about 41.8% did not report the publication bias, and we did not conduct the Egger regression test for these outcomes because the data were unavailable or the study was too small. For the remaining outcomes with assessment of publication bias, 20.5% were evaluated with Egger regression test and 37.7% were evaluated with funnel plots. In Egger's regression test, 22 of those reported the P value, 18 outcomes with the $P > .1$, 4 outcomes with the $P < .1$, and 8 outcomes were

Table 1

The effect of ERAS programs on outcomes for colorectal surgery.

First author	Year	Outcomes	Population	No. of studies in MA	Type of studies in MA	Participants in MA	Metric of MA	Effects mode	Effect size (95% CI)	I^2 (%)	Publication bias	ERAS Elements
Greer, N.L	2018	Morbidity	NR	19	16 RCT,3 CCT	2919	RR	REM	0.66 (0.54 to 0.80)	53.0	NR	4 to 18
Greer, N.L	2018	Mortality	NR	22	18 RCT, 4 CCT	3255	OR	FEM	1.79 (0.81 to 3.95)	4.0	NR	4 to 18
Greer, N.L	2018	Readmissions	NR	19	18 RCT, 1 CCT	2515	RR	REM	1.10 (0.81 to 1.50)	0.0	NR	4 to 18
Greer, N.L	2018	Surgical site infection	NR	17	15 RCT, 2 CCT	2880	RR	REM	0.75 (0.52 to 1.07)	0.0	NR	4 to 18
Greer, N.L	2018	LOS	NR	24	20 RCT,4 CCT	3787	MD	REM	−2.6 (−3.2 to −2.0)	92.0	NR	4 to 18
Ni, X.F	2019	CRP POD1	Asia, Europe	3	3 RCT	190	WMD	REM	−24.72 (−49.64 to 0.19)	98.5	NR	13
Ni, X.F	2019	CRP POD3	Asia, Europe	2	2 RCT	220	WMD	REM	−25.98 (−47.05 to −4.91)	96.4	NR	13
Ni, X.F	2019	CRP POD5	Asia, Europe	2	2 RCT	220	WMD	REM	−30.34 (−53.96 to −6.72)	96.9	NR	13
Ni, X.F	2019	IL-6 POD 1	Asia, Europe	2	2 RCT	220	WMD	REM	−26.45 (−42.57 to −10.34)	93.2	NR	13
Ni, X.F	2019	IL-6 POD 3	Asia, Europe	2	2 RCT	220	WMD	FEM	−24.21 (−27.31 to −21.10)	0.0	NR	13
Ni, X.F	2019	IL-6 POD 5	Asia, Europe	2	2 RCT	220	WMD	REM	−18.33 (−25.00 to −11.65)	84.7	NR	13
Ni, X.F	2019	Morbidity	Asia, Europe	13	13 RCT	1298	RR	REM	0.59 (0.40 to 0.86)	56.6	NR	13
Ni, X.F	2019	Mortality	Asia, Europe	5	5 RCT	NR	RR	FEM	0.89 (0.34 to 2.38)	0.0	NR	13
Ni, X.F	2019	PLOS	Asia, Europe	12	12 RCT	1256	WMD	REM	−2.00 (−2.52 to −1.48)	95.3	0.14	13
Ni, X.F	2019	Readmissions	Asia, Europe	5	5 RCT	NR	RR	FEM	0.65 (0.35 to 1.20)	0.0	NR	13
Ni, X.F	2019	Time to first defecation	Asia, Europe	7	7 RCT	678	WMD	REM	−32.93 (−45.36 to −20.50)	95.6	NR	13
Ni, X.F	2019	Time to first flatus	Asia, Europe	9	9 RCT	1071	WMD	REM	−12.18 (−16.69 to −7.67)	91.7	NR	13
Zhuang, C.L	2013	General complications	NR	12	12 RCT	1807	RR	FEM	0.68 (0.56 to 0.82)	15.0	0.05	8 to 15
Zhuang, C.L	2013	LOS	NR	7	8 RCT	855	MD	REM	−2.39 (−3.70 to −1.09)	85.0	0.91	8 to 15
Zhuang, C.L	2013	Morbidity	NR	13	13 RCT	1910	RR	FEM	0.71 (0.58 to 0.86)	65.0	0.02	8 to 15
Zhuang, C.L	2013	Mortality	NR	9	9 RCT	1562	RR	FEM	1.02 (0.40 to2.57)	0.0	0.32	8 to 15
Zhuang, C.L	2013	PLOS	NR	12	12 RCT	1740	MD	REM	−2.44 (−3.06 to −1.83)	88.0	0.04	8 to 15
Zhuang, C.L	2013	Readmissions	NR	13	13 RCT	1235	RR	FEM	0.93 (0.56 to 1.54)	0.0	0.54	8 to 15
Zhuang, C.L	2013	Surgical complications	NR	12	12 RCT	1807	RR	FEM	0.90 (0.75 to 1.09)	4.0	0.005	8 to 15
Zhuang, C.L	2013	Time to first defecation	NR	6	6 RCT	1351	WMD	REM	−1.12 (−1.37 to −0.87)	85.0	0.24	8 to 15
Zhuang, C.L	2013	Time to first flatus	NR	6	6 RCT	1355	WMD	REM	−1.02 (−1.36 to −0.67)	98.0	0.55	8 to 15

CCT = clinical control trial, CI = confidence interval, ERAS = enhanced recovery after surgery, FEM = fixed effects model, LOS = length of hospital stay, MA = meta-analysis, MD = mean difference, NR = not report, OR = odds ratio, PLOS = postoperative length of hospital stay, RCT = randomized control trial, REM = random effects model, RR = relative risk, SMD = standardized mean differences, WMD = weighted mean differences.

reported as no publication bias. In funnel plots, 7 outcomes were reported had high risk of publication bias, 11 outcomes were reported had low risk of publication bias and 37 outcomes were reported as no publication bias. The statistical evidences of publication bias were shown in LOS and mortality for gastric cancer surgery, and mortality and post-operative paralytic ileus for cystectomy with ERAS pathway.

3.8. Results of AMSTAR and GRADE assessment

In the 23 meta-analyses, the median AMSTAR score was 8.5 out of 11 (range 6.0–10.5, interquartile range 7.5–9). Studies that did not assess heterogeneity and publication bias were marked as lower scores. After assessing the quality of evidences with the GRADE, about 28.8% were rated as "very low", 47.2% were rated as "low" and 24.0% rated as "moderate", none was rated as "high" quality. As for the "low" and "very low" quality of evidences, most of them had a risk of publication bias, inconsistency or imprecision. Table 4 shows detailed information about AMSTAR score and GRADE evaluation.

4. Discussion

4.1. Main findings and interpretation in light of evidence

We identified 23 meta-analyses in our umbrella review to systematically evaluate the impacts of ERAS programs on clinical outcomes for all surgery. We summarized the existing evidence of ERAS in various operations and then drawn a conclusion. As the result shown that ERAS is beneficial to all surgery, which can

Table 2

The effect of ERAS programs on outcomes for orthopedic surgery.

First author	Year	Outcomes	Population	No. of studies in MA	Type of studies in MA	Participants in MA	Metric of MA	Effects mode	Effect size (95% CI)	I^2 (%)	Publication bias	ERAS elements
Deng, Q.F	2018	LOS	NR	15	9 RCT,6 CS	9209	MD	REM	−2.03 (−2.64 to −1.42)	98.0	>0.05	NR
Deng, Q.F	2018	Morbidity	NR	8	6 RCT,2 CS	8474	RR	FEM	0.74 (0.62 to 0.87)	0.0	>0.05	NR
Deng, Q.F	2018	Mortality	NR	4	4 CS	8169	RR	FEM	0.48 (0.27 to 0.85)	10.0	>0.05	NR
Deng, Q.F	2018	Postoperative ROM	NR	4	2 CS, 2 CCS	178	MD	REM	7.53 (−2.16 to 17.23)	58.0	>0.05	NR
Deng, Q.F	2018	Readmission	NR	6	3 RCT,3 CS	3039	RR	REM	0.86 (0.56 to 1.30)	55.0	>0.05	NR
Deng, Q.F	2018	Transfusion	NR	4	2 RCT,2 CS	4978	RR	FEM	0.43 (0.37 to 0.51)	28.0	>0.05	NR
Hu, Z.C	2019	Morbidity	North America, Europe, Asia	11	11 CS	13611	OR	FEM	0.70 (0.64 to 0.78)	0.0	NA	8
Hu, Z.C	2019	Mortality	North America, Europe, Asia	7	7 CS	13715	OR	FEM	0.40 (0.23 to 0.67)	0.0	None	8
Hu, Z.C	2019	ODI	North America, Europe, Asia	2	1 CS	101	WMD	FEM	−7.86 (−10.15 to −5.58)	0.0	None	8
Hu, Z.C	2019	Readmission	North America, Europe, Asia	6	6 CS	11432	OR	FEM	1.06 (0.92 to 1.22)	45.0	None	8
Zhu,S.B	2017	Morbidity	US, Australia, Germany	7	RCT, CCT	7789	OR	FEM	0.77 (0.61 to 0.98)	0.0	NR	11 to 22
Zhu,S.B	2017	PLOS	Europe, Asia, Americ	7	RCT, CCT	8346	SMD	REM	−0.85 (−1.24 to −0.45)	99.0	NR	11 to 22
Zhu,S.B	2017	Readmission	US, Australia, New Zealand	5	RCT, CCT	6430	OR	FEM	0.84 (0.65 to 1.08)	34.0	NR	11 to 22

CCT = clinical control trial, CI = confidence interval, CS = cohort study, ERAS = enhanced recovery after surgery, FEM = fixed effects model, LOS = length of hospital stay, MA = meta-analysis, MD = mean difference, NR = not report, ODI = Oswestry disability index, OR = odds ratio, PLOS = postoperative length of hospital stay, RCT = randomized control trial, REM = random effects model, ROM = range of motion, RR = relative risk, SMD = standardized mean differences, WMD = weighted mean differences.

Table 3

The effect of ERAS programs on outcomes for gastric surgery.

First author	Year	Outcomes	Population	No. of studies in MA	Type of studies in MA	Participants in MA	Metric of MA	Effects mode	Effect size (95% CI)	I2 (%)	Publication bias	ERAS Elements
Beamish	2015	LOS	NR	13	8 RCT,5 CS	1561	SMD	REM	−1.10 (−1.56 to −0.65)	93.0	NR	NR
Beamish	2015	Morbidity	NR	13	8 RCT,5 CS	1596	OR	FEM	0.83 (0.65 to 1.06)	31.0	NR	NR
Beamish	2015	Readmission	NR	9	3 RCT,6 CS	1347	OR	FEM	1.67 (0.88 to 3.19)	0.0	NR	NR
Ding, J	2017	Blood loss	NR	6	6 RCT	635	WMD	FEM	−1.80 (−7.71 to 4.12)	9.0	NR	11.3
Ding, J	2017	Cost	NR	6	6 RCT	NR	SMD	REM	−0.94 (−1.40 to −0.48)	87.0	NR	11.3
Ding, J	2017	CRP	NR	5	5 RCT	282	WMD	REM	−19.46 (−21.74 to −17.18)	73.0	NR	11.3
Ding, J	2017	Duration of foley catheter	NR	2	2 RCT	107	SMD	REM	−1.30 (−3.30 to 0.70)	95.0	NR	11.3
Ding, J	2017	IL-6	NR	3	3 RCT	197	WMD	FEM	−32.16 (-33.86 to −30.46)	95.0	NR	11.3
Ding, J	2017	Morbidity	NR	8	8 RCT	801	OR	REM	1.31 (0.76 to 2.27)	71.0	NR	11.3
Ding, J	2017	Operation time	NR	6	6 RCT	635	WMD	FEM	−2.88 (−6.21 to 0.46)	0.0	NR	11.3
Ding, J	2017	PLOS	NR	8	8 RCT	801	WMD	REM	−1.85 (12.35 to −1.35)	86.0	NR	11.3
Ding, J	2017	Readmission	NR	6	6 RCT	635	OR	FEM	3.42 (1.43 to 8.21)	0.0	NR	11.3
Ding, J	2017	Time to first flatus	NR	7	7 RCT	740	WMD	REM	−17.04 (−23.64 to −10.43)	81.0	NR	11.3
Li, M.Z	2018	Cost	NR	3	3 RCT	127	WMD	REM	−523.43 (−799.79 to −247.06)	64.0	NR	NR
Li, M.Z	2018	Morbidity	NR	6	6 RCT	400	OR	FEM	1.57 (0.82 to 2.98)	0.0	NR	NR
Li, M.Z	2018	PLOS	NR	5	5 RCT	359	WMD	REM	−2.65 (− 4.01 to −1.29)	91.0	NR	NR
Li, M.Z	2018	Time to first flatus	NR	3	3 RCT	149	WMD	REM	−17.72 (−39.46 to −4.02)	90.0	NR	NR
Li, Z.Y	2017	Ambulation time	China,Korea	2	2 RCT	188	WMD	REM	−0.97 (−2.27 to 0.33)	61.0	NR	NR
Li, Z.Y	2017	Cost	China	3	3 RCT	127	WMD	REM	−4.72 (−6.88 to −2.55)	72.0	NR	NR
Li, Z.Y	2017	Morbidity	China,Korea	5	5 RCT	315	OR	REM	0.63 (0.37 to 1.09)	43.0	NR	NR
Li, Z.Y	2017	PLOS	China,Korea	4	4 RCT	274	WMD	REM	−2.169 (−3.05 to −1.26)	65.0	NR	NR
Li, Z.Y	2017	Readmission	China,Korea	2	2 RCT	105	OR	none	3.14 (0.12 to 81.35)	0.0	NR	NR
Li, Z.Y	2017	Time to first flatus	China,Korea	4	4 RCT	154	WMD	REM	−9.78 (−13.75 to −5.81)	0.0	NR	NR
Li, Z.Y	2017	Time to start diet	China,Korea	2	2 RCT	188	WMD	REM	−1.30 (−2.87 to 0.26)	97.0	NR	NR
Wee,I.J.Y	2019	Cost	NR	13	NR	1358	WMD	REM	−4.40 (−5.58 to −3.21)	83.0	0.157	9.7
Wee,I.J.Y	2019	CRP POD1	NR	8	NR	NR	WMD	NR	−11.46 (−28.26 to −5.34)	NR	NR	9.7
Wee,I.J.Y	2019	CRP POD3/4	NR	8	NR	NR	WMD	NR	−2.05 (−28.32 to −15.78)	NR	NR	9.7
Wee,I.J.Y	2019	CRP POD7	NR	6	NR	NR	WMD	NR	−18.14 (−24.21 to −12.07)	NR	NR	9.7
Wee,I.J.Y	2019	IL-6 POD 1	NR	5	NR	NR	WMD	NR	−1.57 (−2.39 to −075)	NR	NR	9.7
Wee,I.J.Y	2019	IL-6 POD 3/4	NR	4	NR	NR	WMD	NR	−1.02 (−2.00 to −0.04)	NR	NR	9.7
Wee,I.J.Y	2019	IL-6 POD 7	NR	2	NR	NR	WMD	NR	−4.29 (−8.99 to 0.40)	NR	NR	9.7
Wee,I.J.Y	2019	LOS	NR	22	13 RCT,8 CS	2469	WMD	REM	−2.47 (3.06 to −1.89)	91.0	0.047	9.7
Wee,I.J.Y	2019	Morbidity	NR	17	12 RCT,4 CS	4348	RR	REM	0.96 (0.75 to 1.23)	45.0	0.083	9.7
Wee,I.J.Y	2019	Mortality	NR	12	NR	1313	RR	NR	0.58 (0.06 to 6.10)	NR	NR	9.7
Wee,I.J.Y	2019	Readmission	NR	9	NR	1273	RR	REM	1.95 (1.03 to 3.67)	0.0	0.288	9.7
Wee,I.J.Y	2019	Time to return of function	NR	14	NR	1643	WMD	REM	−0.70 (−1.02 to −0.37)	93.0	0.903	9.7
Wee,I.J.Y	2019	TNFα POD1	NR	4	NR	NR	WMD	NR	−0.49 (−1.20 to 0.23)	NR	NR	9.7
Wee,I.J.Y	2019	TNFα POD3/4	NR	3	NR	NR	WMD	NR	−0.36 (−0.61 to -0.11)	NR	NR	9.7

CC = cohort study, CI = confidence interval, CRP = C-reactive protein, ERAS = enhanced recovery after surgery, FEM = fixed effects model, IL-6 = Interleukin-6, INF-a = tumor necrosis factor-a, LOS = length of hospital stay, MA = meta-analysis, MD = mean difference, NR = not report, OR = odds ratio, PLOS = postoperative length of hospital stay, POD = postoperative day, RCT = randomized control trial, REM = random effects model, RR = relative risk, SMD = standardized mean differences, WMD = weighted mean differences.

reduce LOS and cost without increasing morbidity, mortality or readmission for colorectal, liver, gastric, orthopedic, bariatric, urology, breast, esophageal, pancreatic, gynecologic, lung, abdominal aortic aneurysm repair surgery and vascular operations. What is more, the complication rates were reduced in pancreatic surgery, colorectal surgery, cystectomy, lung cancer surgery, liver surgery and bariatric surgery. While in gastric surgery, the morbidity and readmission rates were increased when compared with conventional care.

We used the AMSTAR to assess the methodological quality of included meta-analyses, and GRADE to assess the quality of outcomes in each study. In the most recent 23 meta-analyses with 146 outcomes, about 60.9% of the meta-analyses had an AMSTAR score of more than 8, and 76.0% of the outcomes were graded as "low" or "very low". The high AMSTAR score of meta-analyses did not related to high quality of outcomes in each meta-analysis, because there were many factors could decrease the GRADE classification such as heterogeneity or some outcomes were derived from subgroup which had a smaller study and participants and would reduce the quality of evidence. Although there were many RCTs, ERAS program as an intervention, it is impossible to achieve blinding.

All meta-analyses included in the umbrella review indicated that ERAS pathways can significantly reduce the LOS and hospital cost for all surgery patients. As a stressor, surgery can arouse the changes of the neurohormonal system and inflammation responses resulting in major trauma to the human body.[37] The purpose of ERAS pathways is to reduce the surgical stress which can cause organ dysfunction and prioperative morbidity that result in the subsequent need for hospitalization.[11] With the multimodal measures, operations are completed in the condition of pain-free and stress-free.[83] Early removal of the drainage tubes and multimodal analgesia including epidural analgesia, local anesthetic and patient controlled analgesia (PCA) would enable patient early mobilization, which can avoid post-operative complications such as intestinal obstruction; early oral nutrition can reduce catabolism, limit loss of muscle function and postoperative fatigue and accelerate the recovery of the gastrointestinal function; all of those measurements would enhance the recovery of surgery patients,[20,83] therefore, the LOS were significantly reduced and the hospital cost were lessened as well.

In the mid-1990s, the multimodal interventions have been used for colonic surgery, and reduced LOS by 2 to 3 days under standard discharge criteria.[84] With several decades' development, the incidence of complications has been reduced by 30% to 50%, and similar reductions in LOS.[85,86] The effects of ERAS pathways on colorectal surgery are safe, effective and conclusive, which has been confirmed by multi-institutional and multinational studies, and has been widely spread worldwide.[11] From

Table 4

Results of AMSTAR and GRADE.

Type of surgery	Author	Year	Outcomes	AMSTAR	Grade
AAA repair surgery	Gurgel, S. J. T. et al	2014	Mortality	7.0	Very low
AAA repair surgery	Gurgel, S. J. T. et al	2014	Morbidity	7.0	Very low
Bariatric surgery	Ahmed Ola S, et al	2018	LOS	6.0	Low
Bariatric surgery	Ahmed Ola S, et al	2018	Morbidity	6.0	Low
Bariatric surgery	Ahmed Ola S, et al	2018	Operative time	6.0	Low
Bariatric surgery	Ahmed Ola S, et al	2018	Cost	6.0	Low
Breast surgery	Offodile. et al	2019	LOS	7.5	Very low
Breast surgery	Offodile. et al	2019	Major complications	7.5	Very low
Breast surgery	Offodile. et al	2019	Readmissions	7.5	Very low
Breast surgery	Offodile. et al	2019	Post-operative hematomas	7.5	Very low
Breast surgery	Offodile. et al	2019	Post-operative infections	7.5	Very low
Colorectal surgery	Greer, N. L. et al	2018	LOS	7.0	Very low
Colorectal surgery	Greer, N. L. et al	2018	Morbidity	7.0	Low
Colorectal surgery	Greer, N. L. et al	2018	Mortality	7.0	Moderate
Colorectal surgery	Greer, N. L. et al	2018	Readmissions	7.0	Low
Colorectal surgery	Greer, N. L. et al	2018	Surgical site infection	7.0	Low
Colorectal surgery	Zhuang, C. L. et al	2013	PLOS	8.5	Low
Colorectal surgery	Zhuang, C. L. et al	2013	LOS	8.5	Moderate
Colorectal surgery	Zhuang, C. L. et al	2013	Readmissions	8.5	Moderate
Colorectal surgery	Zhuang, C. L. et al	2013	Morbidity	8.5	Low
Colorectal surgery	Zhuang, C. L. et al	2013	General complications	8.5	Low
Colorectal surgery	Zhuang, C. L. et al	2013	Surgical complications	8.5	Low
Colorectal surgery	Zhuang, C. L. et al	2013	Mortality	8.5	Low
Colorectal surgery	Zhuang, C. L. et al	2013	Time to first flatus	8.5	Moderate
Colorectal surgery	Zhuang, C. L. et al	2013	Time to first defecation	8.5	Moderate
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	PLOS	9.0	Moderate
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	Time to first flatus	9.0	Moderate
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	Time to first defecation	9.0	Moderate
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	Morbidity	9.0	Moderate
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	Readmissions	9.0	Low
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	Mortality	9.0	Low
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	IL-6 POD 1	9.0	Low
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	IL-6 POD 3	9.0	Low
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	IL-6 POD 5	9.0	Low
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	CRP POD1	9.0	Low
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	CRP POD3	9.0	Low
Colorectal surgery-lap	Ni, Xiaofei. et al	2019	CRP POD5	9.0	Low
Cystectomy	Xiao, J. et al	2019	Operation time	8.5	Low
Cystectomy	Xiao, J. et al	2019	Blood loss	8.5	Low
Cystectomy	Xiao, J. et al	2019	No. of lymph nodes removed	8.5	Low
Cystectomy	Xiao, J. et al	2019	Time to first flatus	8.5	Low
Cystectomy	Xiao, J. et al	2019	Time to regular diet	8.5	Moderate
Cystectomy	Xiao, J. et al	2019	LOS	8.5	Low
Cystectomy	Xiao, J. et al	2019	Mortality	8.5	Low
Cystectomy	Xiao, J. et al	2019	Readmission rates	8.5	Low
Cystectomy	Xiao, J. et al	2019	Reoperations	8.5	Low
Cystectomy	Xiao, J. et al	2019	Morbidity	8.5	Low
Cystectomy	Xiao, J. et al	2019	Paralytic ileus	8.5	Low
Cystectomy	Xiao, J. et al	2019	Cardiovascular complication	8.5	Very low
Cystectomy	Xiao, J. et al	2019	Wound dehiscence	8.5	Very low
Gastrectomy	Ding, Jie. et al	2017	Blood loss	10.0	Moderate
Gastrectomy	Ding, Jie. et al	2017	Operation time	10.0	Moderate
Gastrectomy	Ding, Jie. et al	2017	PLOS	10.0	Low
Gastrectomy	Ding, Jie. et al	2017	Cost	10.0	Low
Gastrectomy	Ding, Jie. et al	2017	Time to first flatus	10.0	Moderate
Gastrectomy	Ding, Jie. et al	2017	Duration of foley catheter	10.0	Low
Gastrectomy	Ding, Jie. et al	2017	CRP	10.0	Low
Gastrectomy	Ding, Jie. et al	2017	IL-6	10.0	Moderate
Gastrectomy	Ding, Jie. et al	2017	Readmissions	10.0	Moderate
Gastrectomy	Ding, Jie. et al	2017	Morbidity	10.0	Low
Gastrectomy-Lap	Li, Zhengyan. et al	2017	PLOS	8.5	Low
Gastrectomy-Lap	Li, Zhengyan. et al	2017	Cost	8.5	Very low

(*continued*)

Table 4
(continued).

Type of surgery	Author	Year	Outcomes	AMSTAR	Grade
Gastrectomy-Lap	Li, Zhengyan. et al	2017	Morbidity	8.5	Moderate
Gastrectomy-Lap	Li, Zhengyan. et al	2017	Readmissions	8.5	Low
Gastrectomy-Lap	Li, Zhengyan. et al	2017	Time to first flatus	8.5	Very low
Gastrectomy-Lap	Li, Zhengyan. et al	2017	Ambulation time	8.5	Very low
Gastrectomy-Lap	Li, Zhengyan. et al	2017	Time to start diet	8.5	Very low
Gastrectomy-Lap	Li, M. Z. et al	2018	PLOS	10.0	Moderate
Gastrectomy-Lap	Li, M. Z. et al	2018	Time to first flatus	10.0	Moderate
Gastrectomy-Lap	Li, M. Z. et al	2018	Cost	10.0	Moderate
Gastrectomy-Lap	Li, M. Z. et al	2018	Morbidity	10.0	Low
Gastric cancer	Beamish. et al	2015	LOS	8.5	Very low
Gastric cancer	Beamish. et al	2015	Morbidity	8.5	Low
Gastric cancer	Beamish. et al	2015	Readmissions	8.5	Low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	LOS	8.5	Low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	Morbidity	8.5	Low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	Readmissions	8.5	Low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	Time to return function	8.5	Moderate
Gastric cancer surgery	Wee, I. J. Y. et al	2019	Cost	8.5	Moderate
Gastric cancer surgery	Wee, I. J. Y. et al	2019	Mortality	8.5	Very low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	CRP POD1	8.5	Very low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	CRP POD3/4	8.5	Very low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	CRP POD7	8.5	Very low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	IL-6 POD 1	8.5	Very low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	IL-6 POD 3/4	8.5	Very low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	IL-6 POD 7	8.5	Very low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	TNFα POD1	8.5	Very low
Gastric cancer surgery	Wee, I. J. Y. et al	2019	TNFα POD3/4	8.5	Very low
Gynecologic surgery	de Groot, J. J. et al	2016	LOS	8.0	Low
Gynecologic surgery	de Groot, J. J. et al	2016	Morbidity	8.0	Low
Gynecologic surgery	de Groot, J. J. et al	2016	Readmissions	8.0	Low
Joint arthroplasty	Deng, Q. F. et al	2018	Mortality	9.5	Moderate
Joint arthroplasty	Deng, Q. F. et al	2018	Postoperative transfusions	9.5	Low
Joint arthroplasty	Deng, Q. F. et al	2018	Postoperative ROM	9.5	Low
Joint arthroplasty	Deng, Q. F. et al	2018	Readmissions	9.5	Low
Joint arthroplasty	Deng, Q. F. et al	2018	Morbidity	9.5	Moderate
Joint arthroplasty	Deng, Q. F. et al	2018	LOS	9.5	Low
Liver resection	Wang, Cheng. et al	2017	Morbidity	9.0	Low
Liver resection	Wang, Cheng. et al	2017	LOS	9.0	Low
Liver resection	Wang, Cheng. et al	2017	Readmissions	9.0	Very low
Liver resection	Wang, Cheng. et al	2017	Mortality	9.0	Very low
Liver resection	Wang, Cheng. et al	2017	Time to bowel function recovery	9.0	Low
Liver resection	Wang, Cheng. et al	2017	cost	9.0	Low
Liver resection	Wang, Cheng. et al	2017	blood loss	9.0	Very low
Liver resection	Wang, Cheng. et al	2017	Transfusion Rate	9.0	Very low
Liver resection	Zhao, Yiyang. et al	2017	LOS	7.5	Moderate
Liver resection	Zhao, Yiyang. et al	2017	Time to first flatus	7.5	Low
Liver resection	Zhao, Yiyang. et al	2017	Morbidity	7.5	Low
Lung cancer	Li, S. et al	2017	Morbidity	10.5	Moderate
Lung cancer	Li, S. et al	2017	Mortality	10.5	Low
Lung cancer	Li, S. et al	2017	Pulmonary complications	10.5	Moderate
Lung cancer	Li, S. et al	2017	Surgical complications	10.5	Moderate
Lung cancer	Li, S. et al	2017	Cardiovascular complications	10.5	Low
Noncolorectal surgery	Visioni, Anthony. et al	2018	LOS	8.0	Moderate
Noncolorectal surgery	Visioni, Anthony. et al	2018	Morbidity	8.0	Low
Noncolorectal surgery	Visioni, Anthony. et al	2018	Readmissions	8.0	Low
Noncolorectal surgery	Visioni, Anthony. et al	2018	Time to first flatus	8.0	Moderate
Noncolorectal surgery	Visioni, Anthony. et al	2018	Cost	8.0	Moderate
Orthopedic surgery	Hu, Z. C. et al	2019	Morbidity	9.5	Very low
Orthopedic surgery	Hu, Z. C. et al	2019	Readmissions	9.5	Very low
Orthopedic surgery	Hu, Z. C. et al	2019	Mortality	9.5	Very low
Orthopedic surgery	Hu, Z. C. et al	2019	ODI	9.5	Very low
Pancreatic surgery	Ji, H. B. et al	2018	Pancreatic fistula	9.0	Low
Pancreatic surgery	Ji, H. B. et al	2018	DGE	9.0	Low

(*continued*)

Table 4
(continued).

Type of surgery	Author	Year	Outcomes	AMSTAR	Grade
Pancreatic surgery	Ji, H. B. et al	2018	Morbidity	9.0	Low
Pancreatic surgery	Ji, H. B. et al	2018	Abdominal infection	9.0	Low
Pancreatic surgery	Ji, H. B. et al	2018	PLOS	9.0	Moderate
Pancreatic surgery	Ji, H. B. et al	2018	Mortality	9.0	Moderate
Pancreatic surgery	Ji, H. B. et al	2018	Readmissions	9.0	Moderate
Pancreatic surgery	Ji, H. B. et al	2018	Reoperation	9.0	Moderate
Surgery	Lau, C. S. et al	2017	LOS	7.0	Low
Surgery	Lau, C. S. et al	2017	Readmissions	7.0	Very low
Surgery	Lau, C. S. et al	2017	Cost	7.0	Very low
Surgery	Lau, C. S. et al	2017	Morbidity	7.0	Very low
Surgery	Lau, C. S. et al	2017	Time to first flatus	7.0	Very low
Surgery	Lau, C. S. et al	2017	Mortality	7.0	Very low
UGI surgery	Siotos, C. et al	2018	Morbidity	7.5	Low
UGI surgery	Siotos, C. et al	2018	Morbidity for gastrectomy	7.5	Low
UGI surgery	Siotos, C. et al	2018	Mortality	7.5	Low
UGI surgery	Siotos, C. et al	2018	Time to first flatus	7.5	Very low
UGI surgery	Siotos, C. et al	2018	PLOS	7.5	Low
UGI surgery	Siotos, C. et al	2018	Reoperations	7.5	Very low
UGI surgery	Siotos, C. et al	2018	Readmissions	7.5	Very low
UGI surgery	Siotos, C. et al	2018	Cost	7.5	Very low
Vascular operations	McGinigle, K. L. et al	2019	Time to regular diet	6.0	Very low
Vascular operations	McGinigle, K. L. et al	2019	LOS	6.0	Moderate

AAA = abdominal aortic aneurysm, AMSTAR = a measurement tool to assess systematic reviews, CRP = C-reactive protein, DGE = delayed gastric emptying, ERAS = enhanced recovery after surgery, GRADE = Grading of Recommendations Assessment, Development, and Evaluation, IL-6 = Interleukin-6, INF-a = tumor necrosis factor-a, LOS = length of hospital stay, NR = not report, ODI = Oswestry disability index, PLOS = postoperative length of hospital stay, POD = postoperative day, ROM = range of motion, UGI = upper gastrointestinal.

now on, more than 20 countries have put the ERAS pathways into use.[87] In addition, many countries have published the local guidelines of ERAS.[15,88,89] Therefore, implementation of ERAS programs has been a common way to deal with patients with colorectal surgery.

The ERAS programs were most beneficial to orthopedic surgery[56,57] including total hip arthroplasty (THA),[90] total knee arthroplasty (TKA)[12,56] and spinal surgery.[91,92] The ERAS can reduce the LOS, cost, and blood loss,[12,90,93–95] and can also decrease the rates of morbidity, mortality and readmission.[90,93–95] In THA and TKA, the prevalence of complications was 24.5% in ERAS group whilst 36.9% in the traditional group ($P=.039$).[94] In addition, the rate of readmission for THAs performed under the ERAS pathway was almost one-third of that of traditional care.[90] What is more, the 30-days and 90-days mortality were reduced both in THA and TKA,[93,95] and the reduction is 0.5% to 0.1% ($P=.02$), 0.8% to 0.2%, ($P=.01$) respectively.[93] The reason was that the ERAS programs can decrease the post-operative myocardial infarction (MI). In the study including 6000 consecutive procedures, the 30-day rate of MI was reduced from 0.9% in the conventional group to 0.4% in ERAS group.[95] Although the ERAS group had a higher prevalence of co-morbidities such as hypertension, ischemic heart disease, chronic obstructive pulmonary disease (COPD) and type-2 diabetes, cardiac ischemic events were lesser in the postoperative compared with traditional group.[95] In the latest paper, the morbidity was also reduced in the TKA for patients older than 65 years[94] but the mortality was similar in the control group. So the ERAS pathways are safe and effective in orthopedic surgery.

In gastric cancer surgery, ERAS programs would increase the readmission rates in open surgery.[22] Karran et al[96] conducted a study and shown that the readmission rates were 8.0% in the ERAS group while 0 in the control group of gastric cancer open surgery. Another study also found that the readmission was 19% in ERAS and 5% in the traditional group for elderly gastric cancer open surgery.[21] The reason of readmission is postoperative complications including nausea and vomiting, gastric retention, intestinal obstruction,[21] anastomotic stricture,[97] dysphagia, intra-abdominal collection, pleural effusion, urinary retention, spinal cord compression, post-operative pain and pancreatic pseudocyst.[96] The most importantly reason is perhaps that the majority of gastric cancer patients are elderly, they often are malnourished, have co-morbidities and low physiological reserve compared to other cancer patients, thus, they are more susceptive to post-operative complications and delayed convalescence resulting in higher readmission. Bu et al[21] surveyed the effects of ERAS in elderly patients (>75 years) with gastric cancer and found that the incidence of 30-day readmission and several other complications, including nausea, vomiting, stomach retention and intestinal obstruction, were significantly increased in the ERAS group. Subgroup analysis found that there was no significant difference in readmission (RR: 2.17, 95%CI: 0.77–6.14) if excluding the elderly patients.[55] In addition, with the significant reduction in LOS undergoing ERAS, the late complications did not happen or discover during the stay in hospital, such as intestinal obstruction, anastomotic stricture, which would be detected after discharge and become the cause of readmission.[97] All of those reasons would result in the higher readmission for gastric cancer surgery. Therefore, while focusing on the clinical effects, the cost-effectiveness of ERAS for gastrectomy is an important area for future assessment. And the best ERAS protocol for gastrectomy may need further discussion.

Laparoscopic approach had the preference of rapid recovery, low morbidity, and decreased length of stay due to the less invasiveness and pain,[83,98] maybe combining ERAS with laparoscopic surgery was superior to the conventional prioperative care with laparoscopic surgery for gastric cancer. However, there was a higher morbidity in the laparoscopic gastric cancer surgery with ERAS programs in this umbrella review. And there was inconsistent evidence. Hu et al[99] evaluated the safety and effectiveness of ERAS combined with laparoscopic gastrectomy for gastric cancer found that there were 12 post-operative complications in ERAS group while 8 in the control group. As for elderly patient, morbidity in ERAS group was 11 while in control group was 6.[100] But in another two RCTs, morbidity was similar between ERAS and traditional groups.[97,101] The same result was found in a meta-analysis, which included 6 RCTs aimed to compare fast-track recovery with conventional recovery strategies in laparoscopic radical gastrectomy.[53] Maybe there were other reasons for the result in this umbrella review, for instance, heterogeneity and publication bias of the included studies. Whether morbidity with the ERAS pathways would be increased need further study in high quality studies.

4.2. Strengths and limitations

There was several strength in this study. This umbrella review systematically evaluated the effects of ERAS pathway in multiple clinical outcomes for all kinds of surgeries included the latest evidence in each surgical specialty. And we found that the ERAS programs were not beneficial to all the surgeries, for example, readmission and morbidity would be increased for gastric cancer surgery, so precaution is necessary for gastric cancer surgery with ERAS programs. However, there were also many limitations in this umbrella review. First, only the study published in English was included, other studies would be ignored. Secondly, the conclusion depended on the meta-analyses, some individual studies which have been missed might have minor influence on our findings, because the meta-analyses we selected was the most recent one with the highest number of studies included. Thirdly, a number of meta-analyses put emphasis on gastrointestinal surgery, just a few studies involved in the thoracic or vascular surgery. Fourthly, compliance or ERAS components used in each study were different, which would have an impact on the effectiveness of ERAS. Fifthly, in these publications included in meta-analyses, many of data derived from cohort studies rather RCT, and even in RCT, blindness is impossible due to the nature of intervention,[75] and maybe the study populations were small or highly selected result in lacking external validity.[102] Finally, it was uncertain whether the evidence-based experience of colorectal surgery can be fully used in other operations.[21,102]

5. Conclusions

In a conclusion, the ERAS programs are safe, feasible and efficient in most surgeries, especially for orthopedic surgery. However, it is necessary to take measures to prevent adverse events when adopting ERAS pathways for gastric cancer surgery especially in older patients. And more RCT is needed to justify the feasibility and effectiveness for those patients.

Author contributions

Yong Zhou, and Ka Li conceived and designed the study; Zhang Xingxia, Jie Yang Xinrong Chen collected the data; Zhang Xingxia, Xinrong Chen and Liang Du analyzied and interpreted the data; Zhang Xingxia wrote the manuscript; Yong Zhou provided critical revisions; and all authors approved the final version of the manuscript.

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