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Enhanced recovery after surgery pathways for patients undergoing laparoscopic appendectomy: A systematic review and meta–analysis

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ABSTRACT

Objective: To compare the benefits of enhanced recovery after surgery (ERAS) pathways with traditional pathways for adult patients undergoing laparoscopic appendectomy .

Methods: We looked for publications using the keywords "Enhanced Recovery After Surgery," "Fast-track Surgery," "Laparoscopic Appendectomy," and "Laparoscopic Appendicectomy" in PubMed/Medline, Embase, and the Cochrane library. Operative time, lesser length of stay, oral intake timing, readmission rate, pain/satisfaction levels, readmission rate, and surgical site infections were recorded and analyzed.

Results: A total of 95 articles from registers and 161 articles from databases were identified. Three eligible studies were included. The ERAS pathways had a lesser length of stay [Z=2.06, MD= −1.05, 95% CI=(−2.04, −0.05), P=0.04] and an earlier start to postoperative feeds [Z=6.22, MD= −267.49, 95% CI=(−351.80, −183.19), P<001].

Conclusions: ERAS pathways have a shorter length of stay and earlier postoperative feed initiation for adult patients undergoing laparoscopic appendectomy compared with standard care. Both approaches have similar operative time, surgical site infection incidence, and readmission rate.

Clinical registration: This review is registered with INPLASY202280005.

KEYWORDS: Enhanced recovery after surgery; Fast-track surgery; Laparoscopic appendectomy; Perioperative period

1. Introduction

Appendectomy or appendicectomy is a decisive procedure for a patient with acute appendicitis. Both an open method and a laparoscopic procedure are available for appendectomy[1]. Less bowel handling, less pain, quicker recovery from surgery and return to normal activities, shorter hospital stays, and improved cosmetic results are the benefits of laparoscopic surgery versus open surgery[2]. Laparoscopic appendectomy (LA) is superior to open appendectomy according to numerous studies[3,4].

Enhanced recovery after surgery (ERAS) pathways are patient-centered and evidence-based, the multidisciplinary team developed pathways to reduce the patient's surgical stress response, optimize their physiologic function, and facilitate recovery[5]. Initially,

Significance

This review is to evaluate benefits of enhanced recovery after surgery pathways for patients undergoing laparoscopic appendicectomy. We found that adhering to enhanced recovery after surgery pathways during laparoscopic appendicectomy has lesser length of stay and earlier start to postoperative feeds when compared to conventional pathways. The review emphasizes the importance of implementing enhanced recovery after surgery pathways in patients undergoing laparoscopic appendicectomy.

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ERAS pathways were used for colorectal surgeries. Subsequently, the pathways were validated for many other surgical specialties including emergency surgeries, and pediatric and neonatal surgeries[6-9]. ERAS pathways are also now being practiced in patients undergoing emergency surgeries[10,11]. Implementing ERAS pathways for various surgeries has lesser length of stay (LOS), faster recovery, early mobilization and feeds, lesser cost, and lesser readmission provided the patients are selected appropriately[12,13].

Several studies have demonstrated the beneficial effects of applying ERAS pathways for patients undergoing LA. Various outcomes like operative time, LOS, pain scores, surgical site infections (SSI), readmission rate, the timing of oral feeds and flatus passage, and patient satisfaction scores were compared in various studies between ERAS pathways and conventional approaches[14-18]. The present systematic review and meta-analysis (SRMA) were conducted to compare the efficacy and advantages of implementing ERAS pathways with conventional pathways in adult patients undergoing LA.

2. Methods

2.1. Search strategy and criteria

The protocol for this systematic review was registered with INPLASY, an international prospective register of systematic reviews with the following registration number: INPLASY202280005. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses recommendations and the Cochrane Handbook for Systematic Reviews of Interventions were followed[19]. The databases searched were PubMed/Medline, the Cochrane Reviews library, Embase, and Web of Science from the year 2000 till July 2022. The language was restricted to English.

The following keywords were utilized in the search strategy: (ERAS OR enhanced recovery after surgery OR fast track surgery) AND (laparoscopic appendectomy OR laparoscopic appendicectomy). Studies comparing ERAS routes with traditional pathways in adult patients undergoing LA were included in our review and studies comparing at least two elements of ERAS pathways with traditional pathways were considered. Studies without a control group or ones that only compared one pathway were disregarded. Case reports, editorials, commentaries, reviews, articles with only abstracts, and studies involving young patients receiving LA were all disregarded.

2.2. Study selection and data extraction

The titles and abstracts were separately reviewed and duplicates were removed by two writers. The final included studies were chosen after consideration by both writers who also read the complete texts. If there were any discrepancies, the choice was ultimately made through agreement. The RoB-2 technique was used to evaluate the risk of bias among studies[20]. The first two writers independently evaluated the standard of randomized trials using the Jadad score[21]. Two writers gathered pertinent data, including author details, publication dates, sample size, age, sex, and various ERAS route components. The outcomes compared between the ERAS pathways and conventional care pathways were operative time, the timing of oral feeds, LOS, readmission, and SSI.

2.3. Meta-analysis

After a qualitative review, a quantitative review was performed. Studies that directly compared outcomes between LA patients with ERAS protocols and conventional care pathways were included in the quantitative meta-analysis.

2.4. Sensitivity analysis

The results were compared with the random effects model and fixed effects model, and the reliability of the combined results was eventually analyzed according to the consistency degree of the results. When $P>0.01$ and $I^2<50\%$, the fixed effects model was used and when $P<0.01$ and $I^2>50\%$, the random effects model was used for meta-analysis. A funnel plot was constructed to determine if there was a publication bias.

2.5. Statistical analysis

Mantel-Haenszel technique was used to assess dichotomous variables and the risk ratio with the associated 95% confidence interval (*CI*) was determined. For units-unified continuous variables, the mean difference (*MD*) with 95% *CI* was determined using the inverse variance approach. The I^2 value, which was divided into low (25%-49%), moderate (50%-74%), and high (>75%), was used to assess the degree of study heterogeneity. A *P* value of 0.05 or lower was regarded as statistically significant. Review Manager version 5.4.1 (Cochrane Collaboration, Software Update, Oxford, UK) was used for analysis[22].

3. Results

3.1. Search results

A total of 161 articles from the databases and 95 articles from registers were identified. Out of these, 103 duplicate documents were removed, 80 documents were excluded after reading topics and abstracts, and 30 documents were removed for other reasons. Later, after excluding articles, 43 records were retrieved, out of which 22 reports were assessed for eligibility. Out of 22, 3 records were included in the quantitative review. Figure 1 shows the screening process. Table 1 summarizes the included literature.

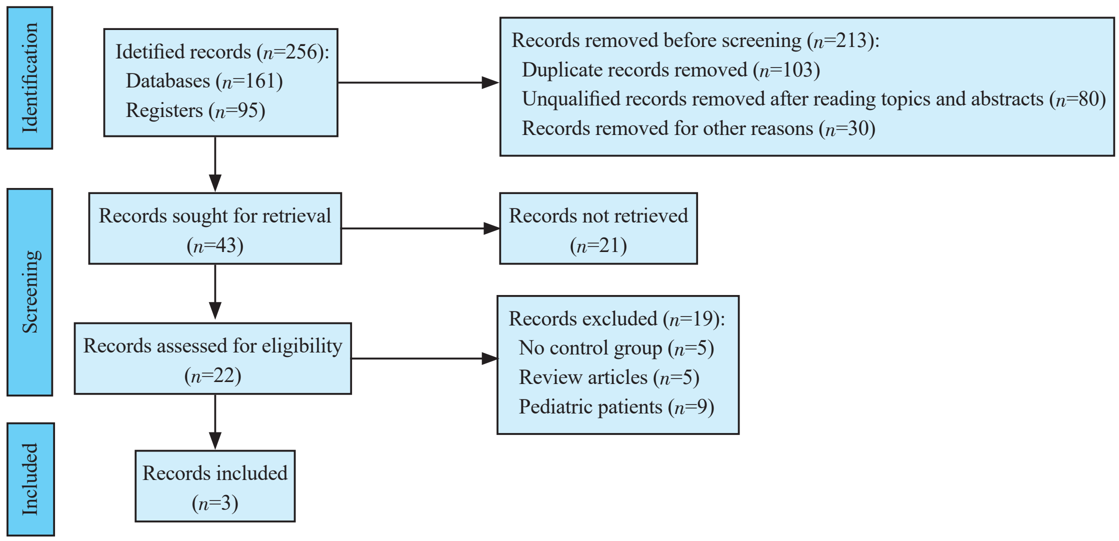

Figure 1. Flowchart of study.

Table 1. Basic characteristics of the included studies.

Author	Year	Country	Study duration	Number of patients		Ref
				ERAS	Conventional	
Trejo-Avila *et al*	2019	Mexico	January 1, 2016 to May 30, 2017	50	58	[15]
Neechay *et al*	2021	Russia	June 2016 and December 2017	50	54	[16]
Núñez-Venzor *et al*	2021	Mexico	April 1,2019 to December 31, 2019	19	19	[14]

3.2. Risk of bias evaluation

The risk of bias within the trials according to RoB-2[21] is shown in Figure 2. The bias from the randomization process, due to deviation from intended intervention, due to missing data, and bias in the selections were low in all 3 studies. However, there was no information on bias due to outcome measurement in two studies[14,15]. The Jadad score was 6 for all the 3 studies, which were suggestive of good quality.

3.3. Operative time

There were 3 studies with available operative time data[14-16]. A fixed effects model was applied (Heterogeneity: Chi^2=0.68, *df*=2, *P*=0.71, I^2=0%). The operative time was less in the ERAS group than in the control group, but the difference was not significant [*Z*=1.85, *MD*= −4.99, 95% *CI*=(−10.26, 0.29), *P*=0.06] (Figure 3).

3.4. LOS

There were 3 studies with available LOS data[14-16]. A random effects model was applied (Heterogeneity: Tau^2=0.50, Chi^2=7.92, *df*=2, *P*=0.02, I^2=75%). The LOS was significantly less in the ERAS group than in the control group [*Z*=2.06, *MD*= −1.05, 95% *CI*=(−2.04, −0.05), *P*=0.04] (Figure 4).

3.5. SSI

There were 3 studies with available SSI data[14-16]. A random effects model was applied (Heterogeneity: Tau^2=2.06, Chi^2=4.61, *df*=2, *P*=0.10, I^2=57%). No significant reduction in SSI was found in the ERAS group when compared to the control group [*Z*=0.31, *RR*=0.71, 95% *CI*=(0.08, 6.16), *P*=0.76] (Figure 5).

3.6. Time of starting oral feed

There were 3 studies with available starting oral feeds data[14-16]. A fixed effects model was applied (Heterogeneity: Tau^2=0.00; Chi^2=0.43, *df*=2, *P*=0.80, I^2=0%). The timing of starting oral feeds was much earlier in the ERAS group than in the control group [*Z*=6.22, *MD*= −267.49, 95% *CI*=(−351.80, −183.19], *P*<0.01) (Figure 6).

3.7. Readmission

There were 2 studies with available readmission after surgery data[15,16]. A fixed effect model was applied (Heterogeneity: Tau^2=0.00; Chi^2=0.10, *df*=1, *P*=0.75, I^2=0%). No significant change in readmission after surgery was noted in the ERAS group when compared to the control group [*Z*=0.33, *RR*=0.81, 95% *CI*=(0.23, 2.87), *P*=0.74] (Figure 7).

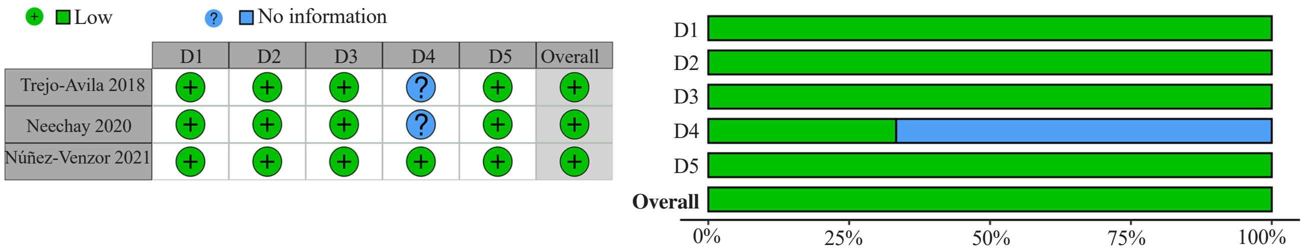

Figure 2. Risk of bias. D1: bias arising from the randomization process; D2: bias due to deviations from intended intervention; D3: bias due to missing outcome data; D4: bias in measurement of the outcome; D5: bias in selection of the reported result.

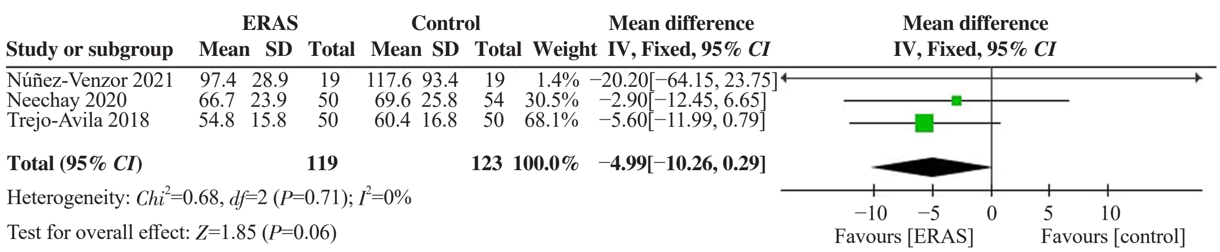

Figure 3. Operative time with ERAS pathways versus conventional pathways.

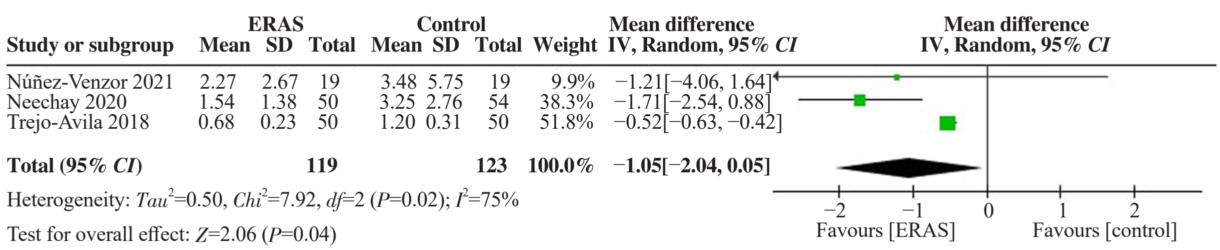

Figure 4. Length of stay with ERAS pathways versus conventional pathways.

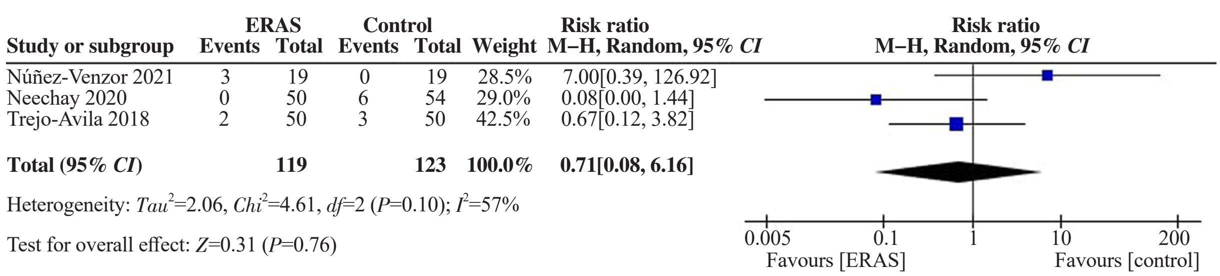

Figure 5. Surgical site infection with ERAS pathways versus conventional pathways.

As there were overall less than 5 studies included in the meta-analysis, a funnel plot to assess publication bias was not plotted.

4. Discussion

The operational time, LOS, and timing of commencing oral feeds following surgery in the ERAS group were all shorter than the traditional pathways group, according to this SRMA, while the incidence of SSI and the rate of readmission were comparable. Zhang *et al*. previously conducted a meta-analysis in which they contrasted ERAS routes with traditional pathways in children undergoing LA (age 3-18 years)[23], with rehabilitation, postoperative stay, and rate of readmission and reoperation as primary outcomes. In our meta-analysis, we included adult patients only (older than 18 years).

Acute appendicitis is a frequent cause of acute abdomen, necessitating either an open or a laparoscopic appendectomy. With a mortality rate of 0.09% to 0.24% or 1%-4% in industrialized and underdeveloped nations, respectively, it is a safe surgery[24]. Professor Henrik Kehlet first proposed the idea of ERAS or fast-track operations for colorectal procedures back in the 1990s[25]. Preoperative, intraoperative, and postoperative elements of the

Study or subgroup	ERAS Mean	ERAS SD	ERAS Total	Control Mean	Control SD	Control Total	Weight	Mean difference IV, Fixed, 95% *CI*
Núñez-Venzor 2021	367.4	230.3	19	696.3	393.3	19	16.9%	−328.90[−533.81, −123.99]
Neechay 2020	541.8	366.6	50	805.2	422.4	54	30.9%	−263.40[−415.12, −111.68]
Trejo-Avila 2018	110.0	113.0	50	360.0	405.6	50	52.2%	−250.00[−366.69, −133.31]
Total (95% *CI*)			**119**			**123**	**100.0%**	**−267.49[−351.80, −183.19]**

Heterogeneity: Tau^2=0.00, Chi^2=0.43, df=2 (P=0.80); I^2=0%

Test for overall effect: Z=6.22 (P<0.001)

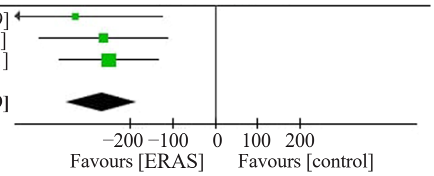

Figure 6. Initiation of orals after surgery with ERAS pathways versus conventional pathways.

Study or subgroup	ERAS Events	ERAS Total	Control Events	Control Total	Weight	Risk ratio M–H, Fixed, 95% *CI*
Núñez-Venzor 2021	2	19	2	19	47.0%	1.00[0.16, 6.38]
Trejo-Avila 2018	2	50	3	50	53.0%	0.67[0.12, 3.82]
Total (95% *CI*)		**69**		**69**	**100.0%**	**0.81[0.23, 2.87]**

Heterogeneity: Tau^2=0.00, Chi^2=0.10, df=1 (P=0.75); I^2=0%

Test for overall effect: Z=0.33 (P=0.74)

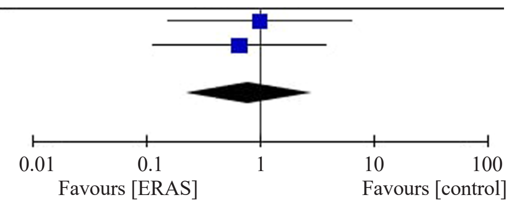

Figure 7. Readmission after surgery with ERAS pathways versus conventional pathways.

ERAS pathways have been described. ERAS pathways can improve patient recovery, increase patient satisfaction, enable an early return to normal activity, including nutrition, and speed up hospital discharge. Preoperative counseling, preoperative nutrition, treatment of comorbidities, avoiding perioperative fasting, carbohydrate loading up to 2 hours before surgery, avoidance of premedication, thromboprophylaxis if indicated, no/selective bowel preparation, and antibiotic prophylaxis are the preoperative elements. Use of short-acting medications, regional anesthesia/epidural analgesia as required, multimodal analgesia, postoperative nausea and vomiting prophylaxis, intraoperative patient warming, no drains, and prudent intravenous (*i.v.*) fluid use belong to intraoperative components. Multimodal analgesia, early removal of drains and tubes, postoperative nausea/vomiting management, early oral food, early mobilization, avoiding excessive *i.v.* fluids, and audit of procedures and results belong to postoperative components[26-28].

4.1. Operative time

ERAS pathways involve the use of short-acting agents, multimodal analgesia, and intraoperative warming which facilitates smooth recovery. This could result in a lesser operative time provided the operative time involves the time when a patient is extubated and not when the last stitch is placed. In this SRMA, the operative time in the ERAS group was similar to that in the control group [Z=1.85, MD= −4.99, 95% CI=(−10.26, 0.29), P=0.06].

4.2. LOS

Implementation of ERAS pathways reduced LOS in various surgeries. A cohort study by Dunkman *et al*. demonstrated that with ERAS implementation for radical cystectomy, the median LOS of conventional pathways was 10 (8, 18) d compared to ERAS pathways 7 (6, 11) d (P<0.001)[29].

In a single, tertiary center experience in Korea by Kim *et al*., the postoperative hospital stay was significantly shorter with ERAS pathways [(18.0±12.4) d] *vs*. conventional pathways [(24.5±14.4) d], regardless of complications[30]. The 90-day readmission rates, however, were comparable between the two groups (9.1% *vs*. 8.5%, P=0.785). For patients having liver procedures, Noba *et al*. did an SRMA of 6 randomized controlled trials and 21 cohort studies with 3 739 patients (1 777 in the ERAS group and 1 962 in the standard treatment group)[31]. In the ERAS group, the overall LOS was decreased by 2.22 d [MD=2.22, 95% CI=(1.68, 2.77), P<0.001] compared to the patients in the conventional pathways.

The results of this SRMA show that LOS was significantly less in the ERAS group than in the control group [Z=2.06, MD= −1.05, 95% CI=(−2.04, −0.05), P=0.04]. The essential components of ERAS pathways like multimodal analgesia, early mobilization, opioid-sparing analgesia, and early oral feeds facilitate lesser LOS, early discharge, and cost-effective patient care.

4.3. Timing of postoperative oral feeds

Although early initiation of oral feeds is an essential component of ERAS, there is a wide disparity among clinicians in adopting the practice. This is commonly seen in abdominal surgeries, especially bower surgeries. In a nationwide survey conducted in China by Huang *et al*., which received 5 370 responses, the authors concluded that postoperative early start of oral intake was highly variable among gastrointestinal, hepatopancreatic biliary, and even non-abdominal surgeries[32].

An open-labeled randomized controlled trial by Yi *et al*. demonstrated that with preoperative carbohydrate loading and postoperative early initiation of oral feeding[33], there was shorter LOS [(78.13±33.05) h *vs.* (99.49±22.54) h]; a lower readmission rate within one month (6% *vs.* 16%); lower weight loss [(−0.3±2.3) kg *vs.* (−2.1±2.3) kg)]; a lower C-reactive protein-albumin ratio [(0.3±1.2) *vs.* (1.1±2.6)]; preserved muscle mass [(0.4±1.7) kg *vs.* (−0.7±2.6) kg]; and better handgrip strength[(0.6±4.3) kg *vs.* (−1.9±4.7) kg] when compared to control group.

In this meta-analysis, the timing of starting oral feeds was much earlier in the ERAS group than in the control group (Z=6.22, MD= −267.49, 95% CI=(−351.80, −183.19), P<0.01]. This indicates that by strictly adhering to ERAS pathways, patients can be started on orals earlier which will facilitate faster recovery and also provide better patient satisfaction.

4.4. Readmission after surgery

Adherence to ERAS pathways, according to its proponents, not only speeds up hospital discharge and early recovery but also lowers the rate of readmission, which, however, is not supported by numerous SRMA. In a meta-analysis of randomized controlled trials encompassing 6 RCTs of major open colorectal procedures, Vardhan *et al*. concluded that while LOS and complication rates were lower when using ERAS pathways, difference in overall readmission rates were not statistically significant[34].

Nelson *et al*. concluded that although LOS and complication rates were lower with ERAS implementation, the 30-day readmission rate was comparable with either pathway in a quality improvement study comparing pre-post-ERAS cohorts for colorectal, liver, pancreas, gynecologic oncology, and radical cystectomy across 9 sites in Canada[35]. Our SRMA discovered that there was no significant difference in readmission after surgery between the ERAS group and the control group [RR=0.81, 95% CI=(0.23, 2.87), P=0.74].

4.5. SSI

Prophylactic antibiotic use, early oral feeding, intraoperative warming, and maintaining a high FiO_2 throughout surgery are all ERAS components that, in theory, should lessen the likelihood of SSI.

The incidence of SSI among patients having colonic operations using ERAS and traditional methods was compared by Gronier *et al*[36]. They discovered that ERAS routes (with more than 70% compliance) didn't significantly lower SSI [OR=0.94, 95% CI=(0.46, 1.92), P=0.86]. This might be due to many patient-related factors, such as smoking history, the necessity of the operation, and open operations, which lead to higher rates of SSI than a minimal access strategy. In the SRMA by Zhang *et al*. where they performed an SRMA of ERAS *vs.* conventional pathways in children undergoing LA, they concluded that the incidence of SSI was not less in the ERAS group when compared to the conventional group [OR=0.56, 95% CI= (0.29, 1.08), P=0.08][23]. Our meta-analysis also showed no significant reduction in SSI in the ERAS group when compared to the control group [(Z=0.31, RR=0.71, 95% CI=(0.08, 6.16), P=0.76]. During the review, some papers that mentioned LA and ERAS in the title and keywords were disregarded since a control group was not present. In the study by Ruiz-Tovar *et al*., the researchers studied 850 participants in a prospective observational study[17]. A total of 770 patients had ERAS implemented (90.6%), but there was no control group in this study. As a result, the analysis did not take into account when analyzing readmission, SSI, LOS, and time to first feed. In an ERAS procedure, Kim *et al*. evaluated the perioperative results between a single-incision laparoscopic appendectomy and a 3-port conventional laparoscopic appendectomy[18]. Although groups involved ERAS protocol and there was no control group, this study was not included in the analysis, either.

There were several limitations in this SRMA. Since prospective RCTs are few, overall sample size was small, and outcomes were inconsistent. Many essential components of ERAS pathways especially the intraoperative pathways were not compared.

5. Conclusion

The findings of this meta-analysis demonstrate that there is a decrease in LOS, an earlier start to postoperative feeds, and a shorter operating time in adult patients having LA when ERAS pathways are used instead of traditional care. However, the rates of readmission and SSI were similar for both pathways. The preoperative pathways of ERAS can not be applied for LA as it is an emergency or urgent surgery. Therefore pathways, such as the scheduling of antibiotics, premedication, and cost-effectiveness, were, however, frequently lacking in research. The availability of postoperative pain scores for comparison between the two groups was also inconsistent, which is a crucial factor in determining if ERAS is more effective than the traditional one. This SRMA concludes that adhering to ERAS components is indeed beneficial for better outcomes like lesser LOS, early feeds, and faster surgeries. However, further RCTs comparing ERAS *vs.* conventional pathways should include more ERAS components.

Conflict of interest statement

The authors declare no conflict of interest.

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Authors' contributions

A.N.: Concept, design, definition of intellectual content, literature search, data acquisition, data analysis, statistical analysis, manuscript preparation, manuscript review; H.H.M.Al-A.: Definition of intellectual content, literature search, data acquisition, manuscript review; O.A.I.: Definition of intellectual content, literature search, manuscript review; P.W.H.: Concept, manuscript editing, definition of intellectual content; A.N.: Guarantor.

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