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Application of Enhanced Recovery after Surgery Pathways in Patients Undergoing Laparoscopic Cholecystectomy With and Without Common Bile Duct Exploration

A systematic review and meta-analysis

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Abstract:

Many researchers implemented enhanced recovery after surgery (ERAS) pathways for laparoscopic cholecystectomy (LC) and found it effective over conventional care. This review investigates the efficacy and safety of ERAS pathways implemented for LC over conventional practices. We searched PubMed/Medline, SCOPUS, CENTRAL, Ovid, and clinicaltrials.gov using relevant keywords to identify studies in which ERAS pathways in LC were compared with conventional pathways. The primary outcome was length of stay (LOS) from the day of surgery and the secondary outcomes were comparison of pain scores, postoperative nausea/vomiting (PONV), readmissions (within 30-days after surgery), complications (medical and surgical), time to first flatus, and cost. Out of 590 articles identified, 6 studies (n=1489 patients) fulfilled inclusion criteria and were used for qualitative and quantitative analysis. On pooled analysis, the LOS, time to first flatus, PONV, pain scores were significantly less in ERAS group than the conventional one. However, readmission and complications were comparable in both groups.

Keywords: Cholecystectomy, Enhanced recovery After Surgery, Fast-track surgery, Laparoscopy, Meta-analysis, Perioperative care, Systematic review

Introduction:

Laparoscopic cholecystectomy (LC) is a minimally invasive surgical procedure performed in patients with acute or chronic cholecystitis, symptomatic cholelithiasis, biliary dyskinesia, acalculous cholecystitis, gallstone pancreatitis, and gallbladder masses or polyps. Over the years, LC has been established as a safe procedure facilitating early recovery compared to the earlier open cholecystectomies. However, the usual problems with LC are postoperative nausea/vomiting (PONV), acute postoperative pain which can interfere with early discharge process and also contribute to respiratory and cardiovascular events postoperatively. [1] Enhanced Recovery after Surgery (ERAS®) pathways are patient-centred, evidence-based, multidisciplinary team developed pathways for a surgical specialty and facility culture to reduce the patient's surgical stress response, optimize their physiologic function, and facilitate recovery. [2] ERAS pathways involve evidence-based preoperative, intraoperative, postoperative pathways which has demonstrated faster patient recovery, early feeding and mobilization, early discharge from the hospital, and better patient satisfaction. [3,4] The conventional pathway involves the era before ERAS i.e., a pre-operative fasting of 6 hours or more, mandatory bowel preparation, extended postoperative nil by mouth (at times till next day), retaining tubes in situ (nasogastric tube, Foley catheter), not particularly using short acting medications (opioids, muscle relaxants) and intraoperative warming of patients, extended hospital stays, no strict postoperative mobilization policies, opioid-bases postoperative analgesia.

Several researchers investigated the advantages and efficacy of implementing ERAS pathways in patients undergoing LC. [5-11] Various outcomes like length of stay (LOS) in the hospital, pain scores, surgical site infections (SSI), readmission rate, the timing of flatus passage, and adverse effects like PONV were compared in various studies between ERAS pathways and a conventional approach in patients undergoing LC. Although ERAS pathways are being used in many centres will variable compliance, there is no clarity whether the pathways are providing favourable postoperative outcomes and improved patient care. The present systematic review and meta-analysis (SRMA) was conducted to compare the efficacy and advantages of implementing ERAS pathways with conventional pathways in adult patients undergoing LC.

Methods:

Search strategy and criteria:

The protocol for this systematic review was registered with PROSPERO, an international prospective register of systematic reviews with the following registration number: CRD42022358554. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations and the Cochrane Handbook for Systematic Reviews of Interventions were followed for conducting this SRMA (supplementary file 1). [12] The databases searched were PubMed/Medline, the Cochrane Reviews library (CENTRAL), Scopus, Ovid, and clinical trials.gov from the year 2000 till July 2022. The language was restricted to English. The search approach made use of the following keywords: (ERAS OR enhanced recovery after surgery OR fast track surgery) AND (laparoscopic cholecystectomy).

Study selection and data extraction:

Our study covered research comparing ERAS routes with conventional pathways in adult patients undergoing LC, and studies comparing at least two ERAS pathway components with conventional pathways were taken into consideration. Studies that compared only one pathway or lacked a control group were excluded. Case reports, editorials, commentaries, reviews, publications with only abstracts, and all other types of writing like thesis or dissertation were disregarded.

The titles and abstracts were separately reviewed and duplicates were removed by two writers (AN and HHM). The final included studies were chosen after consideration by both writers who also read the complete texts. Any disagreement and any inconsistency were settled by a third author (NB). For studies in which data was not reported in the results or not available in supplementary files, the corresponding author was contacted via email for providing the necessary information to access suitability for analysis. Conference abstracts without sufficient detail regarding study design or data were excluded from analysis.

Two writers gathered pertinent data, including author details, publication dates, sample size, age, sex, and various ERAS route components. Studies that had less than two ERAS outcomes were excluded. The outcomes compared between the ERAS pathways and conventional care pathways were operative time, the timing of oral feeds, LOS (after surgery), readmission (within 30-days of surgery), and complications. The complications

could be surgical (leak, surgical site infection), or medical (fever, sepsis, pneumonia). Any disagreement and inconsistency were settled by a third author (NB).

Methodological quality assessment:

The Revised Cochrane risk-of-bias tool for randomized trials (RoB 2) was used to access the methodologic quality and risk of bias of the included trials. [13] Six categories were taken into consideration for bias assessment: bias due to randomisation, bias due to deviation from intended intervention, bias due to missing data, bias due to outcome measurement, bias due to selection of reported result, and overall bias. The quality of randomized trials was assessed independently by two authors (AN and NB) based on the Jadad score. [14]

Meta-analysis:

After a qualitative review, a quantitative review was performed among the articles which have the quantitative statistical data. All included studies that directly compared outcomes between patients who underwent LC with ERAS protocols and conventional care pathways were included in the quantitative meta-analysis.

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 the accompanying 95% CI was determined using the inverse variance approach. The continuous variables in mean and standard deviation were used for analysis. In case the values were presented as median and interquartile range (IQR), the median can be used as mean and the difference of IQR divided by 1.35 gives the standard deviation. We evaluated the heterogeneity between studies using the I2 statistic which was defined as: 0-40%- might not be important, 30-60%- may represent moderate heterogeneity, 50-90%-may represent significant heterogeneity, 75-100%- considerable heterogeneity. [15] Review Manager version 5.4.1 (Cochrane Collaboration, Software Update, Oxford, UK) was used for analysis. [16] The results were compared with the random effects model and fixed effects model, and the reliability of the combined results was eventually analysed according to the consistency degree of the results. When $P>0.01$ and $I2<50\%$, the fixed effects model was used and when $P<0.01$ and $I2>50\%$, the random effects model was used for meta-analysis. A funnel plot will be constructed to determine if there was a publication bias if there are at least 10 studies included in the meta-analysis.

Results:

Results of literature search:

We searched PubMed/Medline, the Cochrane Reviews library (CENTRAL), Scopus, Ovid, and clinical trials.gov for RCTs comparing ERAS pathways with conventional care pathways in patients undergoing LC. We identified 590 articles on searching the above-mentioned databases and registries. After removing duplicates and also articles that were not relevant, we identified 15 articles for scrutiny. A total of 10 studies were considered eligible. From these 4 studies were excluded (study with no control group-1, review articles-1, articles with an active control group-1, unrelated primary and secondary outcomes-1). Finally, we included 6 studies which included 1489 patients for analysis (560 in ERAS group and 929 in control group), [figure 1]. For one study details, the corresponding author was contacted twice requesting for relevant data which was not available in the results but was described in the methodology. As we did not receive any reply from them, we excluded that study from analysis. [17]

Study characteristics:

Out of the 6 studies selected, in 4 studies there were ERAS pathways implemented for LC which was compared with conventional pathways [5-7,10] and in two studies there was ERAS pathway implementation in common bile duct exploration (CBD) done along with LC which was compared to LC with CBD exploration using conventional pathways. [9,11] Therefore, we analyzed the pooled data of all 6 studies initially and then by dividing into two groups: LC with ERAS and LC-CBD exploration with ERAS. [9,11] The study by Kamel et al had 4 groups: LC (lap cholecystectomy-conventional), LE (laparoscopic cholecystectomy- ERAS), OC (open cholecystectomy-conventional), OE (open cholecystectomy- ERAS), with 20 patients in each group and a total sample size of 80. For pooled analysis, we used 40 patients: 20 in LC and 20 in LE. [7] The summary of all the included studies is presented in table 1.

Risk of Bias:

The risk of bias within the trials according to ROB2 is shown in Figure 2. The summary plot of quality assessment is shown in Figure 3. The bias from randomization process was low in 4 studies [5-7,11] and high in two studies. [9,10] Bias due to deviations from intended interventions (allocation concealment) was high in 5 studies [5-7,9,10] and there was no information in one study. [11] Bias arising due to missing outcome data was low in 4 studies [5,6,9,10] and there was

no information in 2 studies. [7,11] Bias in measurement of outcome was low in 3 studies [6,7,9], high in one [5], and not known in two studies. [10,11] Bias arising due to selection of reported result was low in one study [7] and not known in 5 studies. [5,6,9-11] The overall bias was low in two studies [6,7] and high in 4 studies. [5,9-11] The average Modified Jadad score calculated was around 4 which was suggestive of average quality of the studies included for the analysis.

Primary outcomes analysis:

Meta-analysis: LOS

There were 6 studies with available LOS data. [5-6,9-11] There were 560 patients in the ERAS group and 929 patients in the control group. On pooled analysis, the LOS lesser when compared to control that was statistically significant (MD: -31.37 [95% CI: -54.69 to -8.05, P=0.008]. A random effect model was applied ($Tau^2 = 650.63$; $Chi^2 = 650.66$, df = 4 ($P < 0.00001$); $I^2 = 99\%$) which was suggestive of a high level of heterogeneity (figure 3a).

Group 1:

There were 4 studies with available LOS data in subgroup 1. [5-7,10] There were 390 patients in the ERAS group and 609 patients in the control group. On pooled analysis, the LOS was lesser with ERAS group when compared to control that was statistically significant (MD: -13.97 [CI: -20.99 to -6.95], P=0.008]. A random effect model was applied [Heterogeneity: $Tau^2 = 29.79$; $Chi^2 = 9.94$, df = 2 ($P = 0.007$); $I^2 = 80\%$] which was suggestive of a significant heterogeneity (figure 4a).

Group 2:

In group 2, two studies reported LOS. [9-11] There were 170 patients in the ERAS group and 320 patients in the control group. On pooled analysis, the LOS was lesser in the ERAS group when compared to control group [MD: -61.61 (CI: -93.31to -29.90), P=0.0001). A random effect model was applied [Heterogeneity: $Tau^2 = 398.05$; $Chi^2 = 3.18$, df = 1 ($P = 0.07$); $I^2 = 69\%$] which was suggestive of significant heterogeneity (figure 5a).

Secondary outcomes:

Meta-analysis-readmissions:

For readmissions, 5 studies reported the data. [5-7,10,11] There were 412 patients in the ERAS group and 632 patients in the control group. On pooled analysis, the readmission was comparable in both groups [RR: 0.54 (95% CI: 0.23 to 1.27, P=0.16]). A fixed effect model

was applied (Heterogeneity: $Chi^2 = 1.45$, df = 2 (P = 0.48); $I^2 = 0\%$) which was without heterogeneity (figure 3b).

In group 1, for readmissions, 4 studies reported the data. [5-7,10] There were 390 patients in the ERAS group and 609 patients in the control group. On pooled analysis, the readmission was comparable in both groups [RR: 0.54 (CI: 0.23 to 1.27), P=0.16]. A fixed effect model was applied (Heterogeneity: $Chi^2 = 1.45$, df = 2 (P = 0.48); $I^2 = 0\%$) which was without heterogeneity (figure 4b). There were no studies in group 2 which reported readmissions

***Meta-analysis- time to first flatus**:*

The data of time to first flatus was reported by 4 studies. [6,7,9-11] There were 278 patients in the ERAS group and 440 patients in the control group. On pooled analysis, the time to first flatus was much earlier in patients with ERAS implementation than in control group which was statistically significant [MD: -6.56 (95% CI: -10.64 to -2.48, P=0.002)]. A random effect model was applied [Heterogeneity: $Tau^2 = 14.28$; $Chi^2 = 30.73$, df = 3 (P < 0.00001); $I^2 = 90\%$] which was suggestive of significant heterogeneity (figure 3c).

In group 1, the data of time to first flatus was reported by 2 studies. [5,7] There were 278 patients in the ERAS group and 440 patients in the control group. On pooled analysis, the time to first flatus was much earlier in patients with ERAS implementation than in control group which was statistically significant [MD: -3.49 (CI: -6.10 to -0.89), P=0.009]. A random effect model was applied [Heterogeneity: $Chi^2 = 0.70$, df = 1 (P = 0.40); $I^2 = 0\%$] without heterogeneity (figure 4c).

In group 2, two studies reported time to first flatus. [9,11] There were 170 patients in ERAS group and 320 patients in control group. On pooled analysis, the time to first flatus was much early in ERAS group when compared to control group patients [MD: -8.60 (CI: -16.94to -0.250, P=0.04]. A random effect model was applied [Heterogeneity: $Tau^2 = 35.10$; $Chi^2 = 30.33$, df = 1 (P < 0.00001); $I^2 = 97\%$] which was suggestive of considerable heterogeneity (figure 5b).

Meta-analysis-PONV:

The data of PONV was reported by 3 studies. [5,7,9] There were 256 patients in ERAS group and 418 patients in the control group. On pooled analysis, the number of PONV events were

found to be considerably less in the ERAS group when compared to the control group which was statistically significant [RR: 0.36 (95% CI: 0.23 to 0.56, P<0.00001)]. A fixed effect model was applied (Heterogeneity: $Chi^2 = 0.03$, df = 2 (P = 0.98); $I^2 = 0\%$) which was without heterogeneity (figure 3d).

In group 1, the data of PONV was reported by 2 studies. [5,7] There were 108 patients in ERAS group and 121 patients in the control group. On pooled analysis, the number of PONV events were found to be considerably less in the ERAS group when compared to the control group which was statistically significant [RR: 0.26 (CI: 0.13 to 0.50), P<0.001]. A fixed effect model was applied [Heterogeneity: $Chi^2 = 0.02$, df = 1 (P = 0.90); $I^2 = 0\%$] without heterogeneity (figure 4d). The studies in group 2 did not report PONV.

Meta-analysis: pain scores:

The comparison of postoperative pain scores was reported by two studies. [5,7] There were 108 patients in ERAS group and 121 patients in control group. On pooled analysis, the pain scores were lesser in ERAS group of patients than in the control group [MD: -0.93 (95% CI: -1.33 to -0.54, P<0.00001)]. A fixed effect model was used [Heterogeneity: $Chi^2 = 0.80$, df = 1 (P = 0.37); $I^2 = 0\%$] which was without heterogeneity (figure 3e).

In group 1, the comparison of postoperative pain scores was reported by two studies. [5,7] There were 108 patients in ERAS group and 121 patients in control group. On pooled analysis, the pain scores were lesser in ERAS group of patients than in the control group [MD: -1.07 [-1.46, -0.67, P<0.00001]. A fixed effect model was used [Heterogeneity: $Chi^2 = 0.79$, df = 1 (P = 0.38); $I^2 = 0\%$] which was without heterogeneity (figure 4e).

The studies in group 2 did not report pain scores.

Meta-analysis: complications:

The data of postoperative complications was reported in 5 studies. [5-7,9,10] There were 530 patients in ERAS group and 906 patients in the control group. Pooled analysis revealed that the complications were comparable in both the groups [RR: 0.73 (95% CI: 0.46 to 1.17, P=0.19)]. A fixed effect model was used [Heterogeneity: $Chi^2 = 1.91$, df = 4 (P = 0.75); $I^2 = 0\%$] which was without heterogeneity (figure 3f).

In group 1, the data of postoperative complications was reported in 4 studies. [5-7,10] There were 382 patients in ERAS group and 609 patients in the control group. Pooled analysis revealed that the complications were comparable in both the groups [RR: 0.69 (CI: 0.39 to 1.20), P=0.19]. A fixed effect model was used [Heterogeneity: $Chi^2 = 1.85$, df = 3(P = 0.60); I^2 = 0%] which was without heterogeneity (figure 4f). The studies in group 2 did not report any complications.

Discussion:

This systematic review and meta-analysis demonstrate the advantages of implementation of ERAS pathways in patients undergoing LC. Adhering strictly to ERAS protocols can have a reduced LOS after LC, early time to first flatus post-surgery, lesser PONV, and better pain scores in the postoperative period without CBD exploration and reduced LOS and early time to first flatus with CBD exploration. This could lead to better patient satisfaction, lesser cost of treatment and hospitalization, and early initiation of oral diet. However, the pooled analysis did not find any significant decrease in the rate of postoperative complications and readmissions after the discharge. To the best of our knowledge, this is the first SRMA comparing the perioperative outcomes following LC with implementation of ERAS pathways with conventional pathways.

Several researchers applied ERAS pathways to various laparoscopic abdominal surgeries successfully. In a systematic review conducted by Li et al were they analysed articles from January 1990 to October 2017, the authors identified 34 comparative studies (15 randomized controlled studies and 19 non-randomized controlled studies) and analysed a data involving 3615 patients (1749-ERAS group, 1866-control group). [18] On analysing the pooled data, they concluded that ERAS is safe, effective and when combined with laparoscopic surgery leads to a faster postoperative recovery without increasing readmission rate and perioperative mortality. In another SRMA conducted by Ni et al, the authors analysed the efficacy and safety of ERAS implementation in laparoscopic digestive system surgery. [19] The authors identified 25 randomized controlled trials which comprised of 2219 patients. On pooled analysis, they concluded that ERAS implementation led to faster postoperative rehabilitation, shorter LOS, and lesser postoperative complication rates.

In the website of ERAS society, there are no specific guidelines for LC per se. However, many researchers adhered to the key pathways of ERAS and conducted several studies that

compared postoperative outcomes when ERAS was implemented versus conventional pathways. In a prospective, randomized non-blinded clinical trial in patients undergoing LC for acute cholecystitis, Nechay et al compared outcomes of LC in patients with ERAS and conventional pathways (88 patients in ERAS group and 101 patients in conventional pathways. [5] The authors concluded that implementation of ERAS pathways improved postoperative recovery and reduced LOS in patients undergoing LC, without increasing the rate of complications or re-admissions. Akhtar et al randomised 150 patients undergoing LC (75 in ERAS group and 75 in conventional pathways). [6] On analysis, the authors concluded that implementation of ERAS pathways led to reduced LOS, lesser cost of treatment, with comparable recovery scores on discharge, day 3, and day 10. Kamel et al compared perioperative outcomes in patients undergoing LC with ERAS pathways and traditional care pathways. [7] They concluded that patients in ERAS pathways had a lesser LOS, lesser complications, and lower rate of readmissions. In another study by Yu et al, authors enrolled 200 patients undergoing LC into two groups: 100 in fast-track group with continuous postoperative care and 100 in routine care group. [8] They compared surgical stress levels, postoperative recovery (time to first exhaust, time to first meal, time to first getting out of bed, LOS), complications, SF-36 scores after discharge, and overall satisfaction in both groups. On analysis, the authors concluded that with fast-track pathways there was overall reduced level of surgical stress, accelerated recovery process, reduced complications, improved quality of life of patients significantly, and greater satisfaction. Zhang et al published a retrospective, cohort study involving 445 patient undergoing LC with common bile duct exploration with ERAS pathways and conventional pathways. [9] They compared stress response index, postoperative complication rate, and postoperative rehabilitation between 2 groups. On analysis, the authors concluded that incorporating ERAS pathways led to lesser complications, early rehabilitation, and reduced stress response. Demouron et al conducted a study in patients with acute calculous cholecystitis undergoing LC and analysed patients following ERAS and conventional pathways (209 in ERAS and 414 in conventional pathways). [10] Although ERAS pathways had a lesser LOS, the morbidity rate, mortality rate, readmission rate, and reoperation rate were comparable. Wang et al randomized 45 patients undergoing LC (23 in conventional pathways and 22 in ERAS pathways). [11] On analysis they concluded that times to ambulation, time of first flatus passage, and LOS were significantly shorter with ERAS pathways.

Udayasankar et al randomized 50 patients undergoing elective LC into two equal groups (25 patients in each group) and compared postoperative recovery with ERAS pathways and the conventional approach. [20] On analysis they concluded that patients in ERAS group had reduced anxiety, hunger, thirst, fatigue and an enhanced overall perioperative comfort in patients undergoing LC when compared to conventional care. Yeh et al retrospectively reviewed a data of 250 paediatric patients who underwent LC with and without ERAS implementation. [21] The authors concluded on analysis that ERAS implementation facilitated single day discharge with lesser complications without readmissions or emergency department visits. All these studies have highlighted the advantages of ERAS pathway implementation for LC over conventional care.

There were several limitations in this SRMA. Since prospective RCTs were few, overall sample size was small, and outcomes were inconsistent. In group 2 studies, only LOS and time to first flatus were reported. Therefore, there was no uniformity in the reporting of outcomes in both the groups. Many essential components of ERAS pathways especially the preoperative pathways which involves optimization of the medical conditions and intraoperative pathways which included anaesthesia management (multimodal analgesia, PONV, fluid management, intraoperative warming) were not reported and compared in several studies. There was heterogeneity in quantitative analysis of several variables which could be explained due to different study designs, variable sample size, and inconsistent reporting and analysis of data.

Conclusions:

Implementation of ERAS pathways in patients undergoing LC can facilitate lesser LOS in hospital after surgery, better pain scores, early bowel activity, and lesser PONV when compared to patients undergoing LC only using conventional perioperative pathways with lesser LOS and early time to first flatus in patients undergoing LC with CBD exploration. Further well-designed studies need to conducted to compare various preoperative and intraoperative pathways including postoperative opioid consumption which has not been addressed in previous studies.

Authors' Contribution

AN contributed in the concepts, design, definition of intellectual content, literature review, manuscript preparation, manuscript review, statistical analysis. HHMA contributed in the

concepts, design, definition of intellectual content, literature review. NB contributed in the concepts, design, manuscript review. MR contributed in the literature review, manuscript editing, manuscript review. PWH contributed in the concepts, design, manuscript review. All authors approved the final version of the manuscript.

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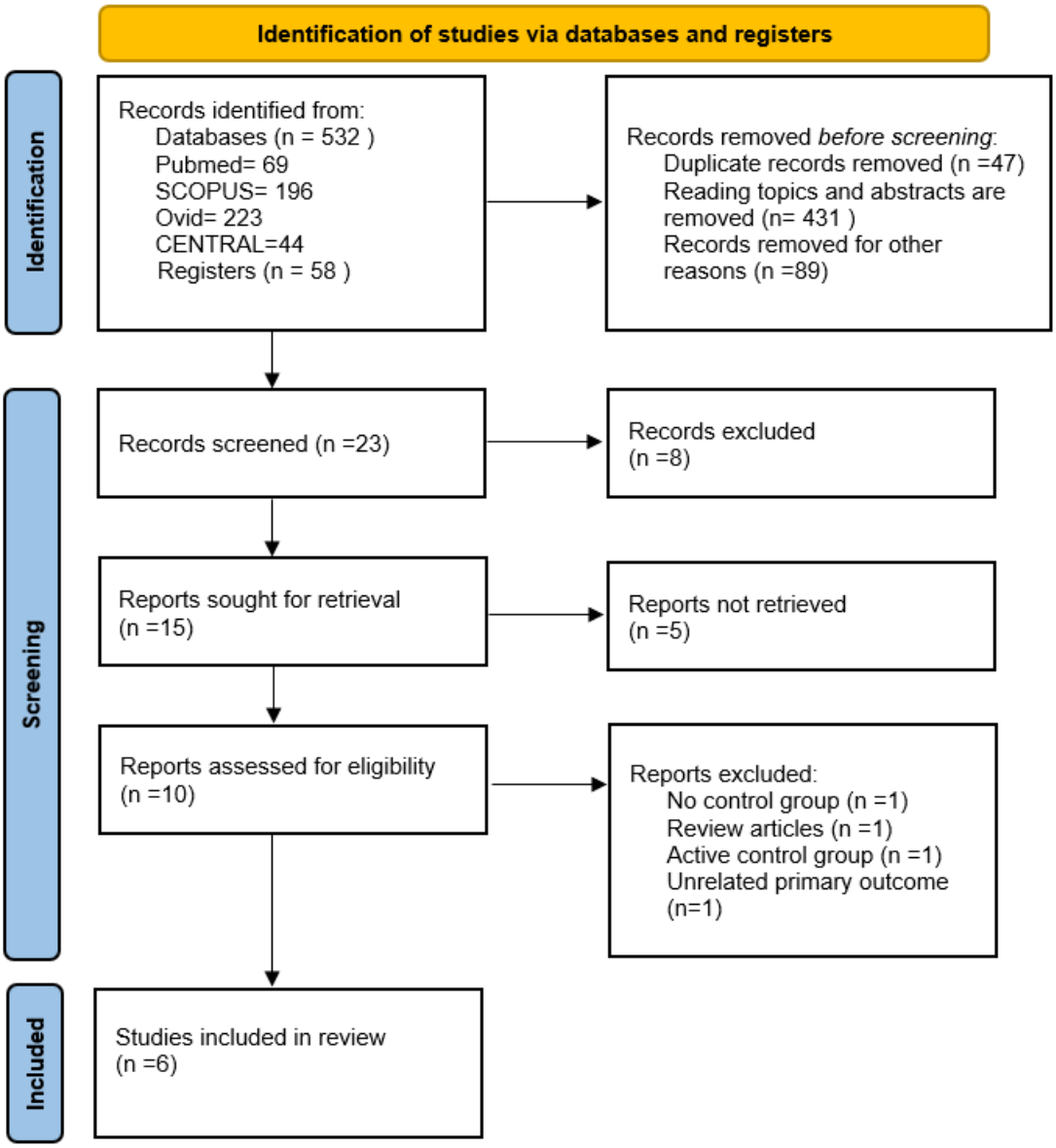


Figure 1: PRISMA flow diagram

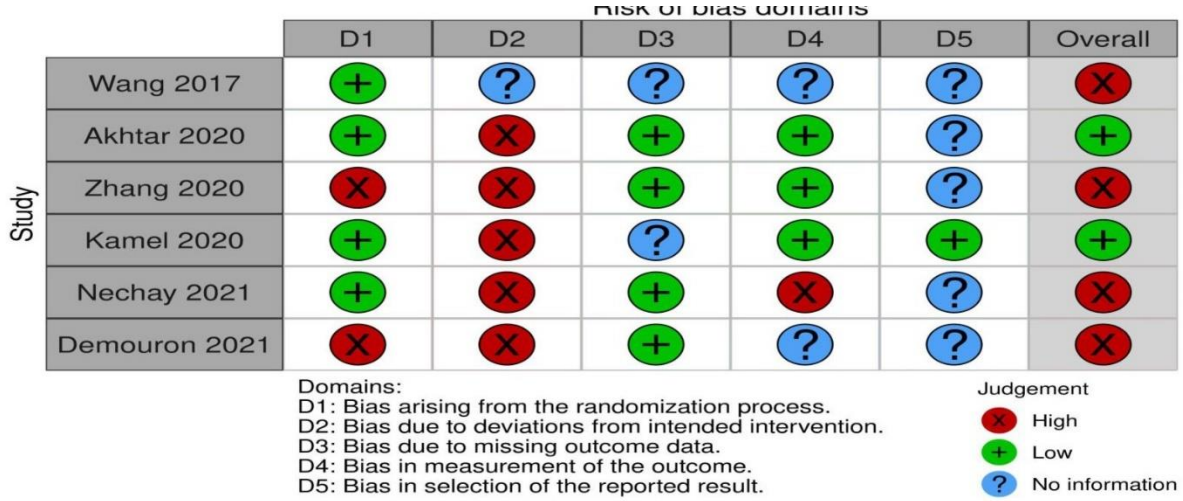


Figure 2a

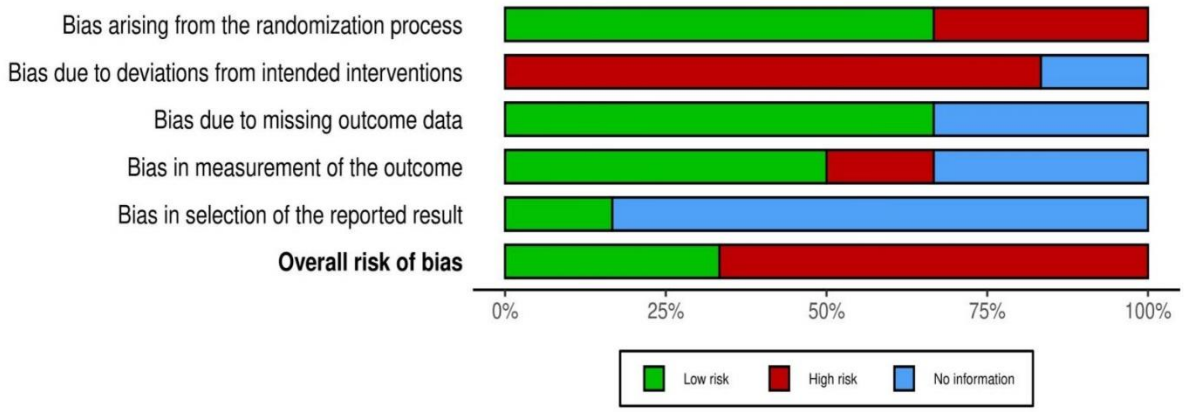


Figure 2b

Figure 2: Risk of bias assessment. **A**: Traffic light plot showing risk of bias within the trials. **B**: Summary plot showing quality assessment for each included study.

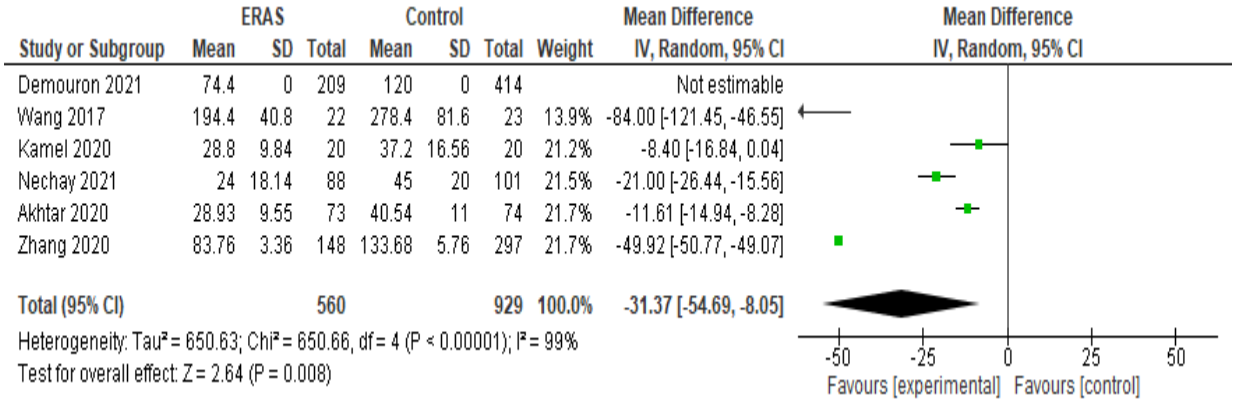


Figure 3a: Forest plot of comparison of LOS between ERAS group and conventional group

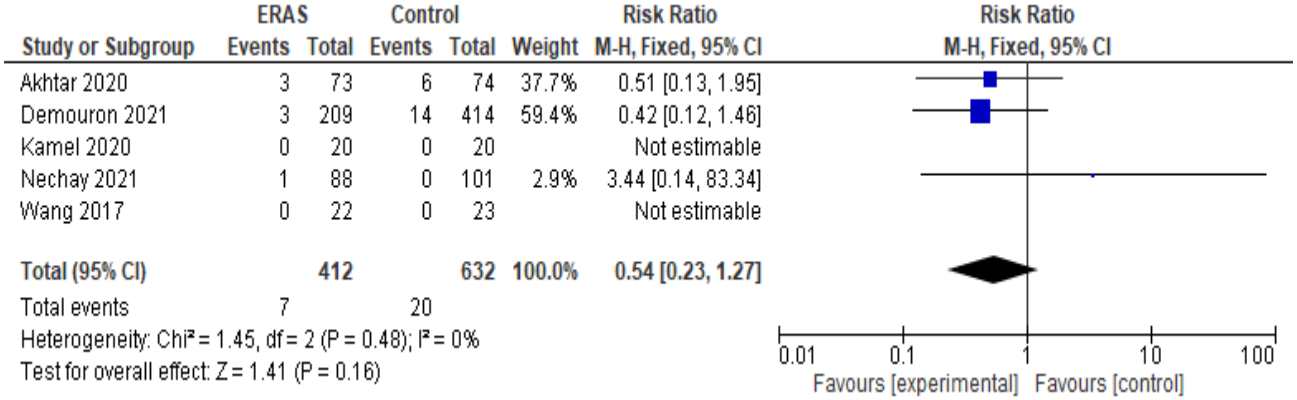


Figure 3b: Forest plot of comparison of readmissions between ERAS group and conventional group

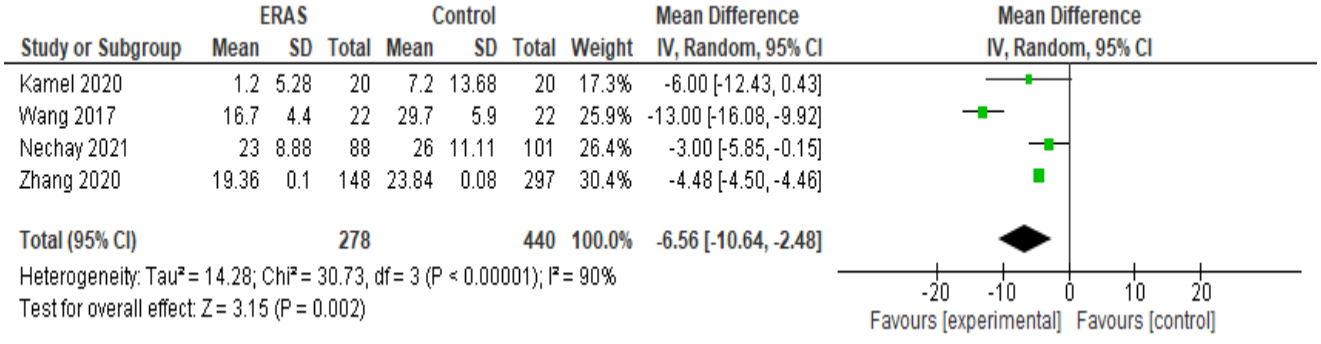
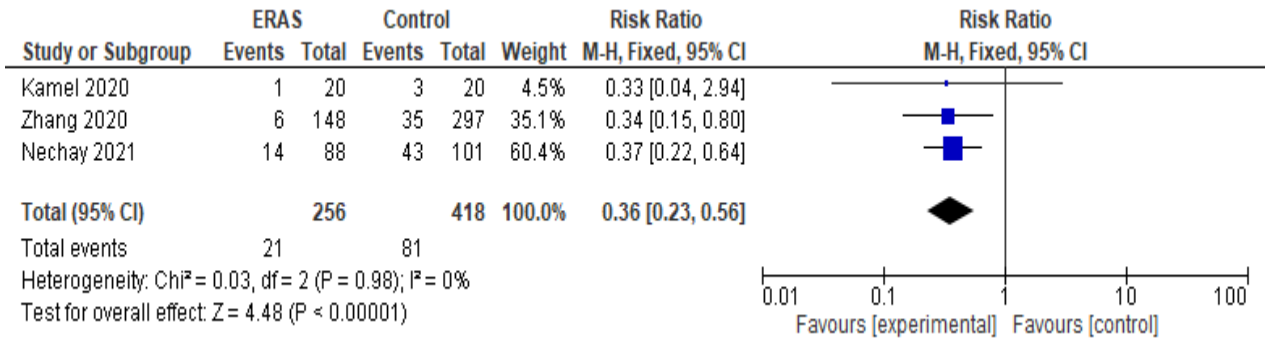


Figure 3c: Forest plot of comparison of time of first flatus between ERAS group and conventional group

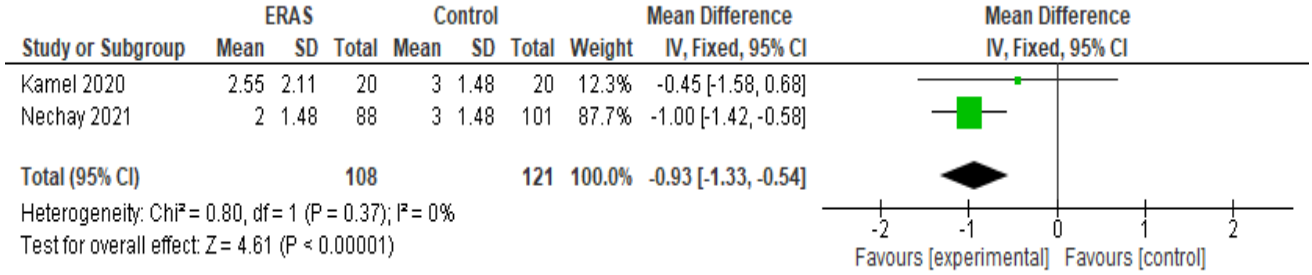


480

481 **Figure 3d:** Forest plot of comparison of PONV between ERAS group and conventional

482 group

483

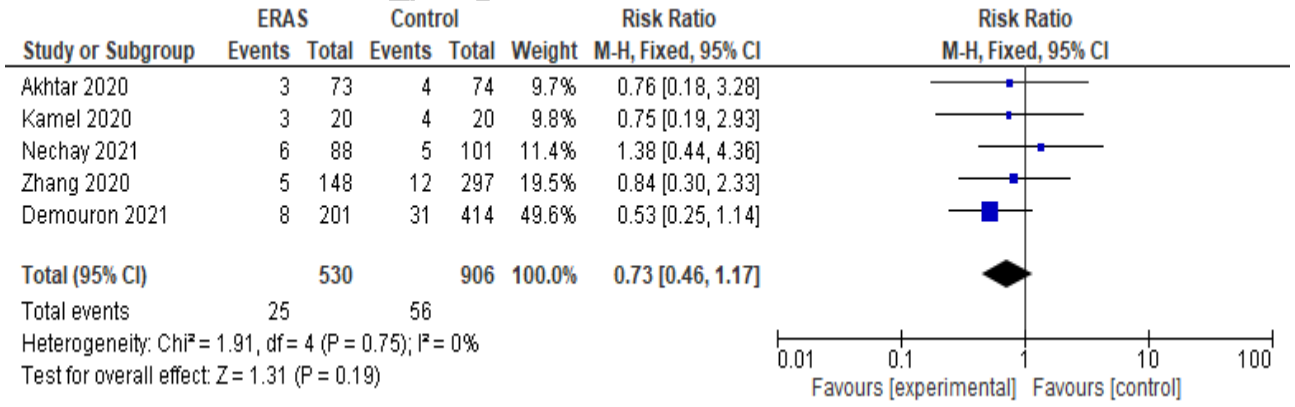


484

485 **Figure 3e:** Forest plot of comparison of 24-hrs pain score between ERAS group and

486 conventional group

487



488

489 **Figure 3f:** Forest plot of comparison of LOS between ERAS group and conventional group

490

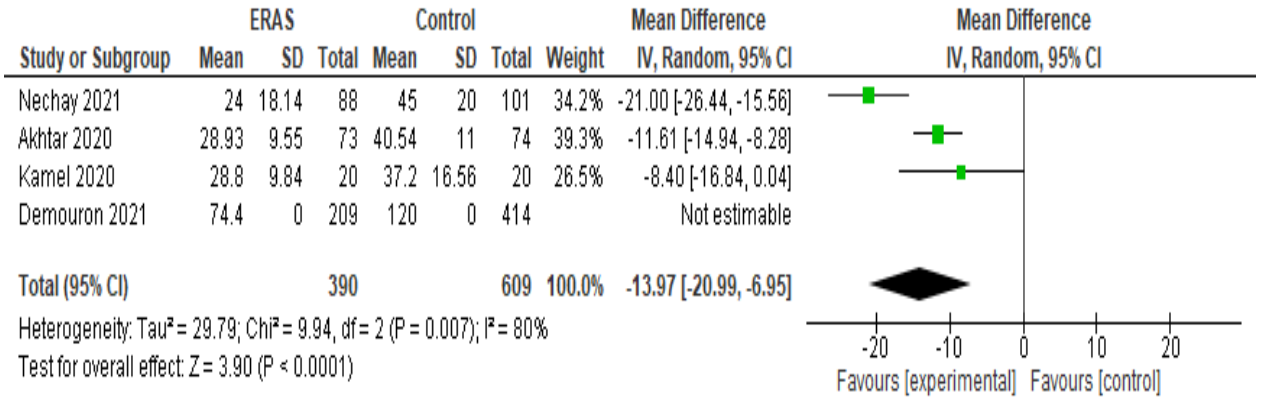


Figure 4a: Forest plot of comparison of LOS between ERAS group and conventional group (group 1)

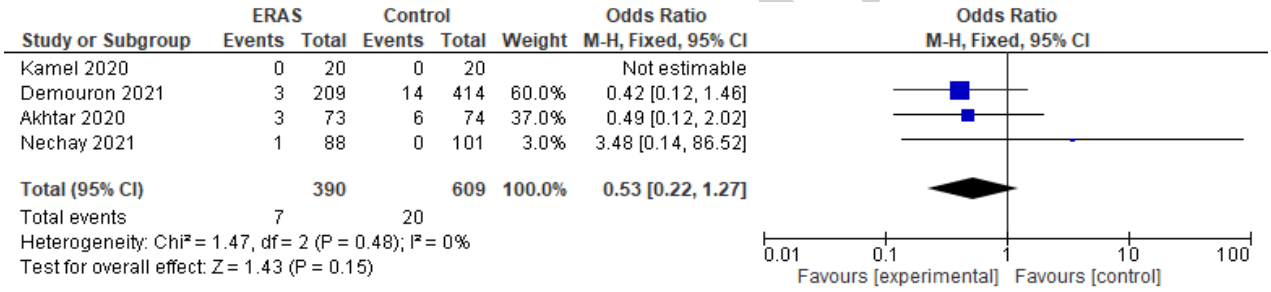


Figure 4b: Forest plot of comparison of readmissions between ERAS group and conventional group (group 1)

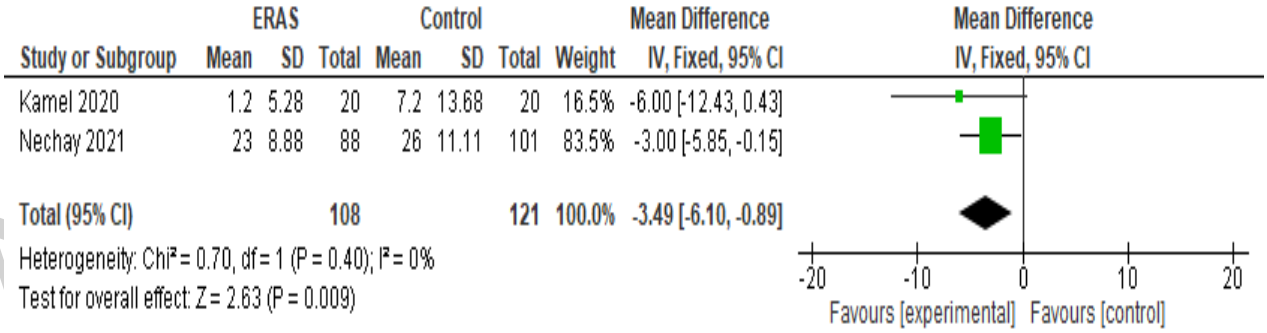
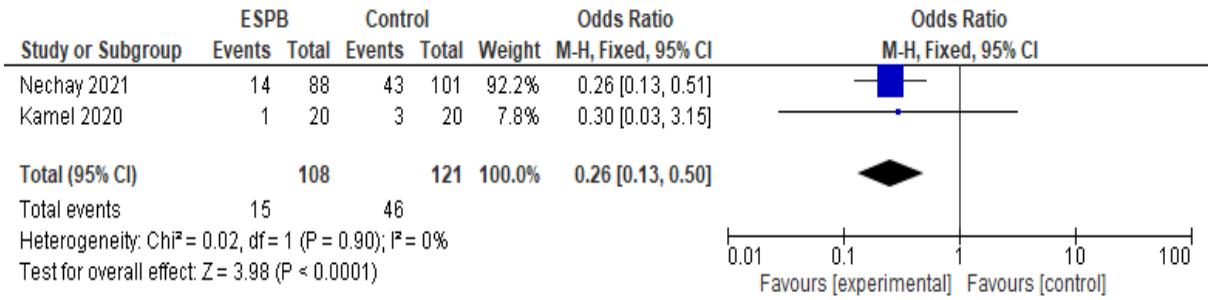


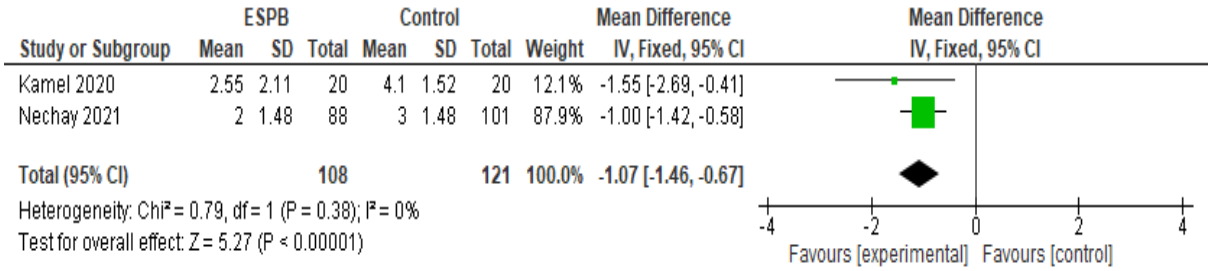
Figure 4c: Forest plot of comparison of time of first flatus between ERAS group and conventional group (group 1)



503

504 **Figure 4d:** Forest plot of comparison of PONV between ERAS group and conventional
505 group (group 1)

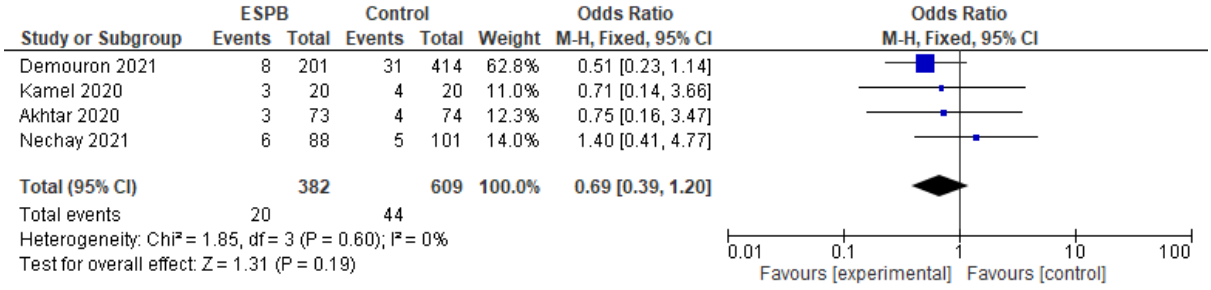
506



507

508 **Figure 4e:** Forest plot of comparison of pain scores between ERAS group and conventional
509 group (group 1)

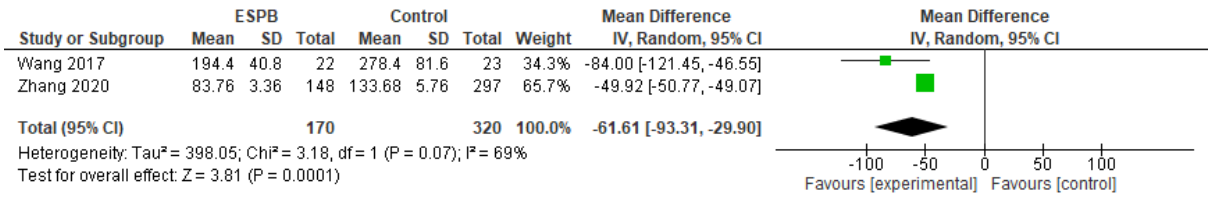
510



511

512 **Figure 4f:** Forest plot of comparison of complications between ERAS group and
513 conventional group (group 1)

514



515

Figure 5a: Forest plot of comparison of LOS between ERAS group and conventional group (group 2)

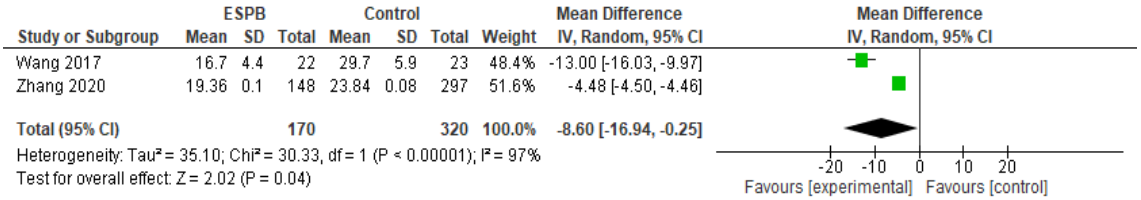


Figure 5b: Forest plot of comparison of time to first flatus between ERAS group and conventional group (group 2)

Table 1:

Authors/year	Country	Type of study	Number of patients	Primary outcome	Secondary outcome	Conclusions
Wang et al/ 2017	China	Randomized-controlled trial	45 (22-fast track, 23-conventional)	Clinical indicators between both groups	Postoperative comfort	Fast tracking improves patient satisfaction, postoperative quality of life without increases in complications
Akhtar et al/ 2020	Pakistan	Randomised-controlled trial	147 (73-ERAS group, 74-conventional group)	LOS hospital and cost of hospitalization	Opioid use, surgical recovery scores	reduction in LOS and total cost although there were similar post discharge recovery scores

Zhang et al/ 2020	China	Retrospective cohort study	445(148 in ERAS group and 297 in traditional group)	Comparison of stress response, postoperative complications and rehabilitation	Demography	Use of ERAS reduces the stress Response, postoperative complications, and accelerates postoperative rehabilitation
Kamel et al/ 2021	Egypt	Randomized-controlled trial	80 (40 in each group)	LOS (hospital and ICU)	Postoperative pain score, Passage of first flatus, postoperative nausea	There was decrease in postoperative hospitalisation with lower complications and little chance of readmission.
Nechay et al/ 2021	Russia	Randomized prospective non-blinded controlled trial	189(88-ERAS, 101-control)	LOS postoperative	Readmission, postoperative pain, peristalsis recovery	There was improved postoperative recovery and reduced hospital stay in

						patients with ERAS without increasing the rate of complications or re-admissions
Demouron et al/ 2021	France	2 step multicentre study: 1st – feasibility study, 2nd-case control study	209-ERAS, 414-conventional	LOS	Morbidity rate, readmission and reoperation rate	ERAS implementation for LC is feasible, effective, and safe for patients.

525 *LOS: length of stay, ERAS: enhanced recovery after surgery, LC: laparoscopic*
526 *cholecystectomy, ICU: intensive care unit*