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SYSTEMATIC REVIEW AND META-ANALYSIS COMPARING EARLY VERSUS DELAYED LAPAROSCOPIC CHOLECYSTECTOMY FOR ACUTE CHOLECYSTITIS

General Surgery

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ABSTRACT

Background: Debate continues regarding the treatment outcomes of early laparoscopic cholecystectomy compared with delayed laparoscopic cholecystectomy for acute cholecystitis. **Aim:** This study was conducted to assess the differences in patient outcomes of early cholecystectomy Vs delayed cholecystectomy in terms of its safety and effectiveness. **Methodology:** The online databases were systematically searched for randomised control trials investigating the effectiveness of early laparoscopic cholecystectomy compared with delayed laparoscopic cholecystectomy for acute cholecystitis. **Results:** 16 studies with a total of 1625 patients were included .Early laparoscopic cholecystectomy was associated with higher patient satisfaction quality of life, lower hospital costs, fewer work days lost, lower risk of wound infections. There were no significant differences between the two groups in mortality, bile duct injury, bile leakage, conversion to open cholecystectomy or overall complications. **Conclusion:** For patients with acute cholecystitis, Early laparoscopic cholecystectomy appears as safe and effective as Delayed laparoscopic cholecystectomy. Early laparoscopic cholecystectomy might be associated with lower hospital costs, fewer work days lost and greater patient satisfaction.

KEYWORDS

INTRODUCTION

Cholelithiasis is the most common disease of gallbladder and biliary tree affecting 10 to 15% of the population.Acute cholecystitis is the result of blockage of cystic duct that does not resolve leading to inflammation with edema and subserosal haemorrhage. Approximately 1-2% per year will develop symptoms requiring cholecystectomy. The optimal timing for laparoscopic cholecystectomy in the treatment of acute cholecystitis remains controversial. Previous reports suggested that early laparoscopic surgery for acute cholecystitis was associated with increased complication rates, prolonged operation times and increased conversion rates[1-9]. As a consequence, initial conservative management with subsequent elective laparoscopic cholecystectomy became accepted practice[10-12]. Delayed cholecystectomy potentially increases the chances of further gallstone-related complications and thus further hospital admissions. Recent evaluation has indicated early laparoscopic surgery to be a safe option in acute cholecystitis, although conversion to open rates may be higher[13-19]. This meta analysis was therefore conducted to compare the safety and efficacy of Early laparoscopic cholecystectomy versus Delayed laparoscopic cholecystectomy for patients with acute cholecystitis.

METHODS

The study was designed in accordance with the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions[20] as well as the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting meta-analyses[21].

The PubMed, Embase, Cochrane Library and Web of Science databases were searched. The electronic searches were performed using medical subject headings and the appropriate corresponding terms including 'cholecystitis' and 'cholecystectomy'.The searches were limited to human subjects and articles published in English.The references of relevant reviews and included studies were also checked manually to identify additional potentially eligible studies.

Study Selection

Published RCTs meeting the following criteria were included: adult patients with acute cholecystitis; Early laparoscopic cholecystectomy performed within 7 days of the onset of symptoms; Delayed laparoscopic cholecystectomy performed at least 1 week after initial conservative treatment; and reporting one or more of the outcomes described below.

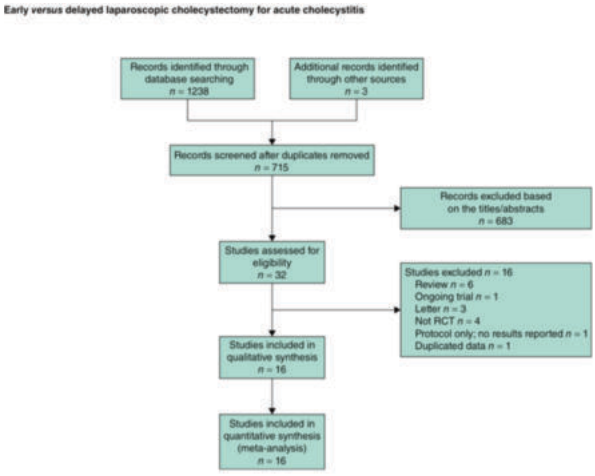


Fig. 1 PRISMA flow diagram showing selection of articles for meta-analysis. RCT, randomized clinical trial

Data Extraction And Outcome Measures

The following information was extracted from each study: first author, year of publication, number of patients, patient characteristics, study design, definition of Early laparoscopic cholecystectomy and Delayed laparoscopic cholecystectomy , and outcomes.

The outcomes were duration of operation, length of hospital stay, wound infection, bile duct injury, bile leakage, conversion to open surgery, overall complications and mortality, cost-effectiveness (hospital cost and number of work days lost) and quality of life. Hospital stay in the delayed group comprised the combined length of stay for the admission at presentation and readmission for Delayed laparoscopic cholecystectomy . Extracted data were entered into a pre-generated standard Microsoft® Excel file.The risk of bias appraised by the Cochrane risk of bias tool[22].

Statistical Analysis

Relative risks (RRs) with 95 per cent Confidence Interval were

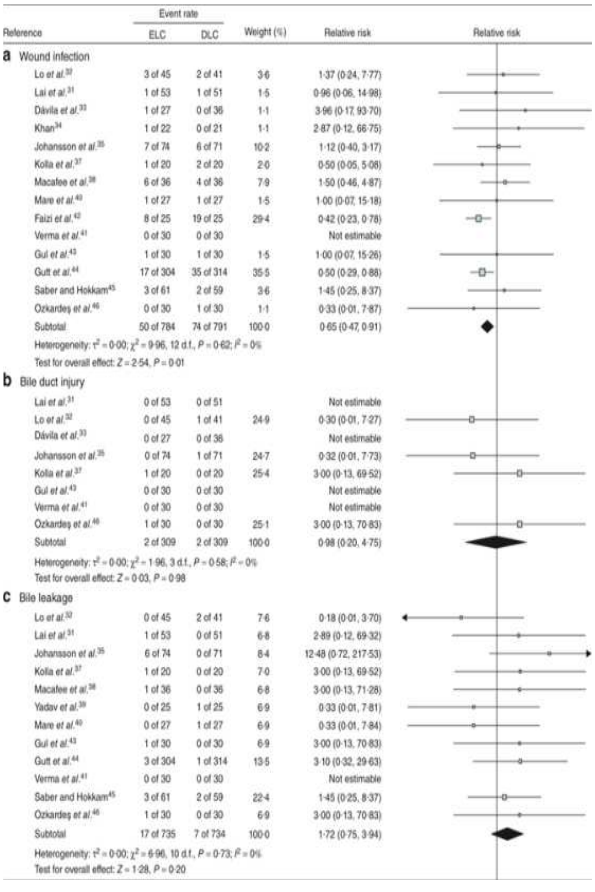
estimated for dichotomous outcomes and mean differences (MDs) with 95 per cent Confidence Interval for continuous outcomes. When mean values were not available for continuous data, median values were used for evaluation[23].The results were considered statistically significant at the P < 0·050 level if the 95 per cent Confidence Interval did not include 1·00. A random-effects model was used regardless of heterogeneity. Heterogeneity was reported using the I^2 statistics ; a value of 0 per cent indicated no heterogeneity and over 50 per cent indicated significant heterogeneity. Results were considered as statistically significant if P < 0·050. Funnel plots were created to determine the presence of publication bias[24]. All statistical analyses were done using RevMan 5.3 .

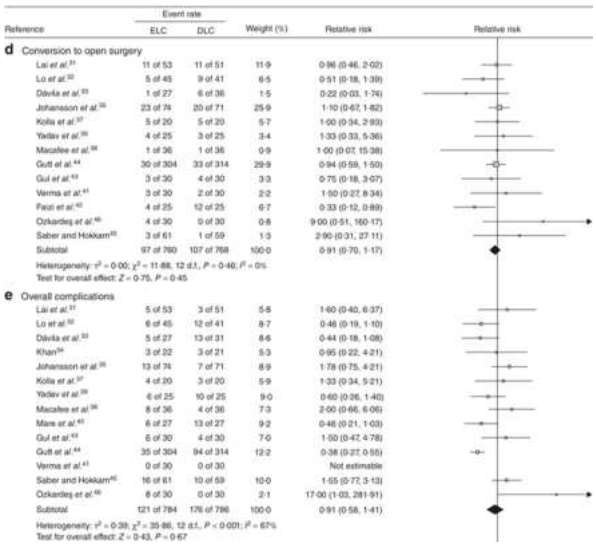
Table 1 Characteristics of randomized clinical trials included in the meta-analysis

Reference	Country	No. of patients (ELC/DLC)	Mean age (years)	Men (%)	Definition of ELC	Definition of DLC	Article type
Lai et al.[31] (1998)	China	104 (53/51)	55·9	56·5	Within 24 h of randomization	6–8 weeks after acute episode subsided	Full text
Lo et al.[32] (1998)	China	86 (45/41)	58·4	55	As soon as possible within 72 h of admission	Following 8–12 weeks of discharge after conservative treatment	Full text
Dávila et al.[33] (1999)	Spain	63 (27/36)	56	29	Within 4 days of diagnosis	2 months later	Full text
Khan[34] (2002)	Pakistan	43 (22/21)	57·4	35	Within 7 days of onset	2–4 months after acute episode subsided	Full text
Johansson et al.[35,36] (2003, 2004)	Sweden	145 (74/71)	56·3	40	Within 48 h after randomization but no later than 7 days after onset of symptoms	Following 6–8 weeks of discharge after conservative treatment	Full text
Kolla et al.[37] (2004)	India	40 (20/20)	40·1	20	Within 24 h of randomization	6–12 weeks after acute inflammation subsided	Full text
Macafee et al.[38] (2009)	UK	72 (36/36)	52·5	35	Within 72 h of recruitment	Following 3 months of discharge after conservative treatment	Full text
Yadav et al.[39] (2009)	Nepal	50 (25/25)	41·5	24	As soon as possible	Following 6–8 weeks of discharge after complete relief of symptoms	Full text
Mare et al.[40] (2012)	Switzerland	54 (27/27)	n.r.	n.r.	Immediately after diagnosis	At least 6 weeks after initial diagnosis	Abstract
Verma et al.[41] (2013)	India	60 (30/30)	32·3	10	Within 72 h of onset of symptoms	After 6–8 weeks	Full text
Faizi et al.[42] (2013)	Pakistan	50 (25/25)	41·5	48	Within 72 h of onset of symptoms	At least 5 weeks after acute inflammation resolved	Full text
Gul et al.[43] (2013)	India	60 (30/30)	39·1	20	Within 72 h of admission	Following 8–12 weeks of discharge as soon as acute attack subsided	Full text
Gutt et al.[44] (2013)	Germany	618 (304/314)	56·2	41·3	Within 24 h of hospital admission	On days 7–45	Full text
Saber and Hokkam[45] (2014)	Egypt	120 (61/59)	n.r.	n.r.	Within 72 h of admission	Following 6–8 weeks of discharge after complete relief of symptoms	Full text
Ozkardeş et al.[46] (2014)	Turkey	60 (30/30)	58·7	38	Within 24 h of admission	Following 6–8 weeks of discharge after conservative treatment	Full text

Trial Sequential Analysis

The trial sequential monitoring boundary can be applied to meta-analysis to determine whether the P value is small enough to show the anticipated effect and whether the trial should be terminated early[25-28].The analyses were done with trial sequential analysis version 0.9 beta[29,30] .





RESULTS

The selection of articles for meta-analysis is summarized in Fig. 1. A total of 16 studies[31-46] with a total of 1625 patients (Early laparoscopic cholecystectomy 809, Delayed laparoscopic cholecystectomy 816) were included in the meta-analysis. Study characteristics are presented in Table 1. The sample size ranged from 40 to 618. The trial by Gutt et al.[44] was a multicentre study. All other studies were from a single centre.

Outcomes

Pooled results showed that Early laparoscopic cholecystectomy was associated with a significantly increased duration of operation (95 per cent Confidence Interval 4·57 to 17·67) min; P < 0·001) (I^2 = 30 per cent), but reduced length of hospital stay (MD −3·38 (−4·23 to −2·52) days; P < 0·001) (I^2= 76 per cent). For duration of operation and hospital stay, the accumulative Z-curve crossed the trial sequential analysis boundary, which suggested that the differences were unlikely to result from chance and further studies are unlikely to change the conclusion. Compared with Delayed laparoscopic cholecystectomy , Early laparoscopic cholecystectomy was associated with a lower risk of wound infection (RR 0·65, 95 per cent Confidence Interval 0·47 to 0·91; P = 0·01) (I^2 = 0 per cent), whereas there was no significant difference in bile duct injury or other complications .Only Gutt *et* al[44] provided data on mortality, which was 0·3 per cent in both groups (Early laparoscopic cholecystectomy ,1 of 304; Delayed laparoscopic cholecystectomy ,1 of 314).

Hospital Costs And Work Days Lost

Three studies included hospital costs. Gutt *et al.*[44] demonstrated that total hospital cost was significantly lower in the Early laparoscopic cholecystectomy group which was in agreement with the findings of Ozkardes *et al.*[46]. Macafee et al.[38] reported similar costs for both groups. Lo et al.[32,] Khan et al. [34,] and Gutt et al. [44] included data for work days lost. Early laparoscopic cholecystectomy was associated with fewer work days lost than Delayed laparoscopic cholecystectomy

Patient Satisfaction And Quality Of Life

The overall rate of satisfaction was higher for patients who underwent Early laparoscopic cholecystectomy than for those in the Delayed laparoscopic cholecystectomy group. . Macafee et al.[38] reported significantly lower visual analogue scale scores in the
Early laparoscopic cholecystectomy group compared with the Delayed laparoscopic cholecystectomy group, but both treatments resulted in rapid recovery.

DISCUSSION

The present study suggests that Early laparoscopic cholecystectomy is associated with a lower risk of wound infection, shorter hospital stay, better cost-effectiveness, and higher patient satisfaction and quality of life. Of the three RCTs that reported costs, two suggested that ELC could lower the healthcare cost, whereas Macafee *et al.*[38] found no difference between ELC and DLC. However recent observational studies that analysed actual hospital costs and some cost–utility studies have confirmed that Early laparoscopic cholecystectomy could significantly reduce expenditure and should be the preferred strategy

from this perspective. One of the most consistent findings in this meta-analysis concerned work days lost. On average participants in the Delayed laparoscopic cholecystectomy group lost 11 more days from work than those who underwent Early laparoscopic cholecystectomy , mainly because of the two separate hospital admissions. Early laparoscopic cholecystectomy thus contributes to an earlier return to work and provides maximal economic gain.

Even though different methodologies were used to estimate quality of life and patient satisfaction, the conclusions were consistent. Patients treated with Delayed laparoscopic cholecystectomy were found to experience recurrent gastrointestinal symptoms frequently, take anti-inflammatory drugs, and may have unresolved or recurrent cholecystitis before the delayed operation. There was an increased risk in younger patients and this was associated with decreased quality of life, reinforcing the value of Early laparoscopic cholecystectomy .

The risk of wound infection was lower in the Early Laparoscopic cholecystectomy group. A retrospective study also found that the risk of post- operative infections increased with the length of delay to surgery. Bile duct injury is the most feared complication of laparoscopic cholecystectomy, and may lead to morbidity and reinterventions. The trial sequential analysis indicated that additional RCTs would still be subject to limited data and only large-scale population-based studies may address this unresolved issue. Recently, a study with sufficient power to detect the difference in bile duct injury showed a significantly lower rate of bile duct injuries for Early laparoscopic cholecystectomy compared with Delayed laparoscopic cholecystectomy (0·3 versus 0·5 per cent; RR 0·53, 95 per cent Confidence Interval 0·31 to 0·90; P = 0·025).

This meta-analysis has several limitations. First, limited data were available on costs of Early laparoscopic cholecystectomy and Delayed laparoscopic cholecystectomy, and quality of life after Early laparoscopic cholecystectomy versus Delayed laparoscopic cholecystectomy has not been well studied. Second, several trials in this review had high risks of bias, and the benefits and harms of Early laparoscopic cholecystectomy or Delayed laparoscopic cholecystectomy may have been overestimated. Third, substantial heterogeneity across studies was observed. The heterogeneity for duration of operation can perhaps be explained by the technical advances in recent years, different surgical practice between hospitals and/or differences in level of surgical expertise. Heterogeneity of hospital stay and work days lost was also observed. Finally, 11 of the 16 eligible RCTs included in the meta-analysis had relatively modest sample sizes (fewer than 100 patients), and overestimation of the treatment effect is more likely than in larger studies.

CONCLUSION

Early laparoscopic cholecystectomy is safe and effective as compared with Delayed laparoscopic cholecystectomy .There were no differences in terms of mortality ,bile duct injury, bile leakage ,conversion to open cholecystectomy or overall complications. Early laparoscopic cholecystectomy appears to be associated with lower hospital costs, fewer work days lost and greater patient satisfaction.

Ethical approval was taken from the local institutional ethical committee on 08/09/2023, 56/CSI/2023.

Conflict Of Interest
None declared

Source Of Funding
Nil

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