

Cover sheet

Title

Early versus delayed laparoscopic cholecystectomy for biliary colic

Reviewers

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Dates

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Contribution of reviewers

KS Gurusamy wrote the review and assessed the trials for inclusion and extracted data on included trials. K Samraj is the co-author for the review and independently assessed the trials for inclusion and extracted data on included trials. BR Davidson critically commented on the review and provided advice

for improving the review.

Internal sources of support

None

External sources of support

None

What's new

Dates

Date review re-formatted: //

Date new studies sought but none found: //

Date new studies found but not yet included/excluded: //

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Text of review

Synopsis

Early laparoscopic cholecystectomy for biliary colic decreases morbidity during the waiting period, conversion to open cholecystectomy, operating time, and hospital stay

Biliary colic is one of the commonest indications for key-hole removal of gallbladder (laparoscopic cholecystectomy), which is performed electively after several months of waiting. However, patients can develop life threatening complications while waiting for surgery. In this review including one randomised clinical trial, we found that patients suffered life threatening complications and 35% required emergency hospital admissions for complications related to gallstones. More people required open operations; and the operating time and hospital stay was more in the elective surgery group. Further randomised clinical trials are urgently necessary.

Abstract

Background

About 10% to 15% of the adult western population have gallstones Between 1% and 4% become

symptomatic in a year. Laparoscopic cholecystectomy ('key-hole removal of gallbladder') is now the preferred method of treatment for symptomatic gallstones. Biliary colic is one of the commonest indications for operation, which is performed electively after several months of waiting. However, patients can develop life threatening complications while waiting for surgery.

Objectives

To assess the clinical effectiveness of early laparoscopic cholecystectomy for patients with biliary colic.

Search strategy

We searched *The Cochrane Hepato-Biliary Group Controlled Trials Register*, *The Cochrane Central Register of Controlled Trials* in *The Cochrane Library*, *MEDLINE*, *EMBASE*, and *Science Citation Index Expanded* until March 2007.

Selection criteria

We included all randomised clinical trials comparing early laparoscopic cholecystectomy (< 2 weeks after onset of symptoms) and delayed laparoscopic cholecystectomy (> 6 weeks after onset of symptoms).

Data collection & analysis

We collected the data on the characteristics, methodological quality, morbidity during waiting period, surgical morbidity, operating time, and hospital stay from each trial. We intended to analyse the data with both the fixed-effect and the random-effects model using RevMan Analysis. For each outcome we calculated the relative risk (RR) or weighted mean difference (WMD) with 95% confidence intervals (CI) based on intention-to-treat analysis.

Main results

Only one trial including 75 patients, who were randomised to early laparoscopic cholecystectomy (< 24 hours of diagnosis) (n = 35) and delayed laparoscopic cholecystectomy (placed on waiting list with a mean waiting period of 4.2 months) (n = 40) qualified for this review. This trial was of high risk of bias. During the waiting period in the delayed group, the complications that the patients suffered included acute severe pancreatitis resulting in mortality (1), empyema of gallbladder (1), gallbladder perforation (1), acute cholecystitis (2), cholangitis (2), obstructive jaundice (2), and recurrent biliary colic requiring hospital visits (5). There was a statistically significant lower rate of conversion to open cholecystectomy in the early group (0%) than the delayed group (8/40 or 20%) (RR 0.08, 95% CI 0.01 to 1.38). There was a statistically significant lower operating time (minutes) and hospital stay (days) in the early group than the delayed group (WMD -14.80, 95% CI -18.02 to -11.58 and -1.25, 95% CI -2.05 to -0.45 respectively). 14 patients (35%) required 18 hospital admissions for symptoms related to gallstones during the mean waiting period of 4.2 months in the delayed group. This is equivalent to 11 admissions per 100 persons per month.

Reviewers' conclusions

- (1) Based on evidence from one trial, it appears that early laparoscopic cholecystectomy decreases the morbidity during the waiting period for elective laparoscopic cholecystectomy, decreases the conversion to open cholecystectomy, decreases operating time, and decreases hospital stay.
- (2) Further randomised clinical trials are necessary urgently.

Background

About 10% to 15% of the adult western population have gallstones ([Jørgensen 1987](#); [NIH 1992](#); [Muhrbeck 1995](#); [Halldestam 2004](#)). Between 1% and 4% become symptomatic in a year ([NIH 1992](#); [Halldestam 2004](#)). More than half a million cholecystectomies (removal of gallbladder) are performed per year in the United States alone ([NIH 1992](#)). Regional differences exist in the cholecystectomy rates ([Mjäländ 1998](#)). Laparoscopic ('key-hole') cholecystectomy, which was introduced in 1987, is now the preferred method of cholecystectomy ([NIH 1992](#); [Fullarton 1994](#); [Bakken 2004](#); [Keus 2006](#)) and is advised only for symptomatic gallstones ([NIH 1992](#)).

Biliary colic (pain due to gallstones) is one of the symptoms related to gallstones and is the one of the commonest indications for surgery in patients with gallstones ([Somasekar 2002](#)). In countries like United Kingdom, where the health care is funded by the government, the patients with biliary colic are put on waiting list and operated electively several months after the diagnosis. However, patients may develop complications of gallstones including pancreatitis (which can be life-threatening), cholangitis, choledocholithiasis, and recurrent attacks of cholecystitis while waiting for surgery ([Rutledge 2000](#); [Lawrentschuk 2003](#); [Vetthus 2003](#)). Studies have shown that laparoscopic cholecystectomy done for biliary colic has a lower conversion rate and morbidity rate than that performed after an attack of cholecystitis ([Glasgow 2000](#); [Peng 2005](#)).

While there are theoretical advantages in the adoption of a policy of early laparoscopic cholecystectomy, additional resources have to be allocated to achieve this policy. This includes urgent referral of all patients with suspected gallstones (as the cause for right upper abdominal pain) for an ultrasound which may increase the workload of the radiologist. Once diagnosed as having gallstones, these patients have to be scheduled for an early operation, which may put a strain on the resources available (such as surgeon's time, operation theatre time, funds).

In spite of this strain on the resources, if early laparoscopic cholecystectomy for biliary colic is clinically effective in preventing the serious complications of gallstones; decrease the morbidity associated with laparoscopic cholecystectomy; and can reduce the number of work days lost due to symptoms related to gallstones and its complications, early laparoscopic cholecystectomy can be recommended for biliary colic.

We have not been able to identify any systematic reviews or meta-analyses assessing the clinical effectiveness of early laparoscopic cholecystectomy for biliary colic.

Objectives

To assess the clinical effectiveness of early laparoscopic cholecystectomy for patients with biliary colic.

Criteria for considering studies for this review

Types of studies

We considered all randomised clinical trials, which compare early and delayed laparoscopic cholecystectomy in patients with biliary colic (irrespective of language, blinding, publication status, or sample size).

Quasi-randomised trials (where the method of allocating participants to a treatment are not strictly random, for example, date of birth, hospital record number, alternation) were excluded.

Types of participants

Patients with biliary colic eligible to undergo laparoscopic cholecystectomy.

Types of interventions

We included only trials comparing early versus delayed laparoscopic cholecystectomy (irrespective of the size and the number of ports or abdominal lift or open or closed method of induction of pneumoperitoneum). Early laparoscopic cholecystectomy was defined as laparoscopic cholecystectomy performed within two weeks of onset of biliary colic. Delayed laparoscopic cholecystectomy was defined as laparoscopic cholecystectomy, which was intended to be performed after six weeks of onset of biliary colic.

Types of outcome measures

- (1) Mortality at maximal follow-up (mortality due to any cause; mortality due to complications of gallstones; mortality related to surgery).
- (2) Morbidity.
 - (a) Complications (pancreatitis, recurrent episodes of cholecystitis, obstructive jaundice).
 - (b) Surgery related morbidity (bile duct injury, bile leak, reoperation rate, infection, bleeding).
- (3) Conversion to open cholecystectomy.
- (4) Operating time.
- (5) Hospital stay (post-operative stay; total hospital stay including admissions for treatment of recurrent symptoms).
- (6) Number of visits to general practitioner or emergency department for symptoms.
- (7) Number of work days lost (return to work after surgery; total number of days lost due to surgery, recurrent symptoms, and complications).

Search strategy for identification of studies

We searched *The Cochrane Hepato-Biliary Group Controlled Trials Register*, the *Cochrane Central Register of Controlled Trials (CENTRAL)* in *The Cochrane Library*, *MEDLINE*, *EMBASE*, and *Science Citation Index Expanded* ([Royle 2003](#)). We have given the search strategies in [Table 01](#) with the time span for the searches.

We also searched the references of the identified trials to identify further relevant trials.

Methods of the review

Trial selection and extraction of data

KSG and KS, independently of each other, identified the trials for inclusion. KSG and KS also intended to list the excluded studies with the reasons for the exclusion. BRD adjudicated any differences in opinion.

Both authors independently extracted the following data.

- (1) Year and language of publication.
- (2) Country.
- (3) Year of conduct of the trial.
- (4) Inclusion and exclusion criteria.
- (5) Sample size.
- (6) Population characteristics such as age and sex ratio.
- (7) Timing of early and delayed intervention.
- (8) Outcomes (mentioned above).
- (9) Methodological quality (described below).
- (10) Sample size calculation.
- (11) Intention-to-treat analysis.

Any unclear or missing information was sought by contacting the authors of the individual trials. If there was any doubt whether the trials shared the same patients - completely or partially (by identifying common authors and centres), we intended to contact the authors of the trials to clarify whether the trial report had been duplicated.

We resolved any differences in opinion through discussion. BRD adjudicated any differences in opinion.

Assessment of methodological quality

We assessed the methodological quality of the trials independently, without masking of the trial names. We followed the instructions given in *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2006](#)) and the *Cochrane Hepato-Biliary Group Module* ([Gluud 2006](#)). Due to the risk of biased overestimation of intervention effects in randomised trials with inadequate methodological quality ([Schulz 1995](#); [Moher 1998](#); [Kjaergard 2001](#)), we looked at the influence of methodological quality of the trials on the results by evaluating the reported randomisation and follow-up procedures in each trial. If information was not available in the published trial, we contacted the authors in order to assess the trials correctly. We assessed generation of allocation sequence, allocation concealment, blinding, and follow-up.

Generation of the allocation sequence

- Adequate, if the allocation sequence was generated by a computer or random number table.

Drawing of lots, tossing of a coin, shuffling of cards, or throwing dice will be considered as adequate if a person who was not otherwise involved in the recruitment of participants performed the procedure.

- Unclear, if the trial was described as randomised, but the method used for the allocation sequence generation was not described.
- Inadequate, if a system involving dates, names, or admittance numbers were used for the allocation of patients. These studies are known as quasi-randomised and were excluded from the review.

Allocation concealment

- Adequate, if the allocation of patients involved a central independent unit, on-site locked computer, or sealed envelopes.
- Unclear, if the trial was described as randomised, but the method used to conceal the allocation was not described.
- Inadequate, if the allocation sequence was known to the investigators who assigned participants. Such studies were excluded.

Blinding

We expected that there would be no double-blind trials. However, we recorded whether any of the outcomes were assessed by a blinded observer or blinded assessor.

Follow-up

- Adequate, if the numbers and reasons for dropouts and withdrawals in all intervention groups were described or if it was specified that there were no dropouts or withdrawals.
- Unclear, if the report gave the impression that there had been no dropouts or withdrawals, but this was not specifically stated.
- Inadequate, if the number or reasons for dropouts and withdrawals were not described.

Statistical methods

We performed the meta-analyses according to the recommendations of The Cochrane Collaboration ([Higgins 2006](#)) and the Cochrane Hepato-Biliary Group Module ([Gluud 2006](#)) using the software package RevMan 4.2 ([RevMan 2003](#)). For dichotomous variables, we calculated the relative risk (RR) with 95% confidence interval. For continuous variables, we calculated the weighted mean difference (WMD) with 95% confidence interval. We used a random-effects model ([DerSimonian 1986](#)) and a fixed-effect model ([DeMets 1987](#)). In case of discrepancy between the two models, we intended to report both results; otherwise we intended to report only the results from the fixed-effect model. Heterogeneity was explored by chi-squared test with significance set at P value 0.10, and the quantity of heterogeneity was measured by I^2 ([Higgins 2002](#)).

We adopted the 'available-case analysis' ([Higgins 2006](#)). The analysis was performed on an intention-to-treat basis ([Newell 1992](#)). In case we found 'zero-event' trials in statistically significant outcomes, we intended to perform a sensitivity analysis with and without empirical continuity correction factors as suggested by Sweeting et al ([Sweeting 2004](#)). We have also reported the risk difference.

Subgroup analysis

We intended to perform a subgroup analyses of trials with adequate methodology (defined as adequate allocation concealment, assessor blinding, and adequate follow-up).

Funnel plot

We intended to use a funnel plot to explore bias ([Egger 1997](#); [Macaskill 2001](#)). We intended to use asymmetry in funnel plot of trial size against treatment effect to assess this bias. We also intended to perform the linear regression approach described by Egger et al ([Egger 1997](#)) to determine the funnel plot asymmetry.

Description of studies

We identified a total of 799 references through electronic searches of *The Cochrane Hepato-Biliary Group Controlled Trials Register* and *The Cochrane Central Register of Controlled Trials in The Cochrane Library* (n =138), *MEDLINE* (n = 235), *EMBASE* (n =325), and *Science Citation Index Expanded* (n = 101). We excluded 188 duplicates and 510 clearly irrelevant references through reading abstracts. One reference was retrieved for further assessment. No reference was identified through scanning reference list of the identified randomised trial. The reference retrieved for further assessment met the inclusion criteria. So, we did not list any reference in the 'Characteristics of excluded studies'. The reference retrieved was a completed randomised trial involving 75 patients and could provide data for the analyses ([Salman 2005](#)). Details about the sample size, patient characteristics; the inclusion and exclusion criteria used in the trials; and the methodological quality of the trial are shown in the table 'Characteristics of included studies'.

Participants

A total of 75 participants who had biliary colic were randomised in the only trial ([Salman 2005](#)) to early laparoscopic surgery (< 24 hours of diagnosis) (n = 35) or to delayed laparoscopic cholecystectomy (waiting list for elective surgery; mean waiting time 4.2 months) (n = 40). Of the 75 patients, 7 patients in the early group and 5 patients in the delayed group were excluded after randomisation and the demographic details were not available for these 12 patients. The percentage of females and the mean age of the remaining participants in this trial were 65.1% and 43 years respectively.

Intervention

Early laparoscopic surgery (< 24 hours of diagnosis)

Controls

Delayed laparoscopic cholecystectomy (waiting list for elective surgery; mean waiting time 4.2 months)

Outcome measures

The main outcome measures reported were mortality, morbidity during the waiting period, surgical morbidity, conversion to open cholecystectomy, operating time, hospital stay, number of visits to emergency department, and number of hospital admissions during waiting period.

Methodological quality of included studies

The included trial had adequate generation of allocation of sequence. The allocation concealment was unclear and blinding was not performed. The follow-up was adequate. There were no sample size calculations or intention-to-treat analysis in this report. Because of the unclear allocation concealment,

this trial was considered to have high risk of bias.

Results

The summary measures used were relative risk (RR) and weighted mean difference (WMD). The 95% confidence intervals (95% CI) are also stated.

Mortality at maximal follow-up

The only case of mortality occurred in a patient belonging to the delayed group due to acute severe pancreatitis. Although the difference is not statistically significant, this is an avoidable cause of death.

Morbidity

Complications during waiting period

During the waiting period, the complications that the patients suffered included pancreatitis (1), empyema of gallbladder (1), gallbladder perforation (1), acute cholecystitis (2), cholangitis (2), obstructive jaundice (2), and recurrent biliary colic requiring hospital visits (5). All of these occurred in the delayed group as all the patients were operated within 24 hours in the early group.

Surgery related morbidity

There was no morbidity related to surgery in either group.

Conversion to open cholecystectomy

There was a statistically significant lower rate of conversion to open cholecystectomy in the early group (0%) than the delayed group (8/40 or 20%) (RR 0.08, 95% CI 0.01 to 1.38).

Operating time (minutes)

There was a statistically significant lower operating time in the early group than the delayed group (WMD -14.80, 95% CI -18.02 to -11.58).

Hospital stay (days)

There was a statistically significant lower hospital stay in the early group than the delayed group (WMD -1.25, 95% CI -2.05 to -0.45).

Number of visits to general practitioner or emergency department for symptoms

14 patients (35%) required hospital admission for symptoms related to gallstones during the mean waiting period of 4.2 months in the delayed group. Four of these patients required hospital admissions twice before they underwent surgery. This is equivalent to 11 admissions per 100 persons per month.

Number of work days lost

This outcome was not reported by the included trial.

Variations in statistical analysis

Since there was only one trial, we did not compare the results of fixed-effect and random-effects model. A calculation of risk difference did not change the results.

Subgroup analysis

Since there was only one trial, we could not perform a sub-group analysis.

Funnel plot

We did not obtain a funnel plot because of the inclusion of only one trial in this review.

Discussion

Surgery immediately after diagnosis of an uncomplicated benign condition is rarely feasible particularly in a health system funded by the government because of the limited availability of resources. The resources available should be appropriately allocated to deal quickly with diseases with a potential to cause severe harm to the patient.

This review has shown that placing the patients on waiting list for biliary colic exposes the patient to serious harm and can even lead to fatal sequences. Furthermore, 35% of the patients required hospital admission at least once and the rate of emergency admission per person per month was 0.11 in the only trial included in this review. Around 80% of the cases of elective cholecystectomy in UK are performed for biliary colic ([Somasekar 2002](#)). In a retrospective study from Canada, the rate of emergency hospital admission in patients placed on waiting list for biliary colic was 3.6 per 100 patients per month ([Sobolev 2003](#)). The rate of emergency admission increased from 3.2 per 100 patients per month in the first four weeks to 22.8 per 100 patients per month after 40 weeks. In UK, the mean waiting for elective laparoscopic cholecystectomy in UK is 12 months ([Somasekar 2002](#)). In this study 23.7% of the 156 patients (80% of whom were placed on the waiting list for biliary colic) required emergency hospital admission. The rate of emergency hospital admission in this study was 2.5 admissions per 100 patients per month. Another retrospective study in the USA reviewed the events during the waiting time for elective laparoscopic cholecystectomy ([Rutledge 2000](#)). In this study, 22.6% of the patients developed complications of gallstone disease such as acute cholecystitis, pancreatitis or jaundice. Those who developed complications had a 30% increase in operating time, 10-fold increase in hospital stay, and a 4-fold increase in conversion to open cholecystectomy. The rate of emergency hospital admission for biliary colic in this study was 12.9 per 100 patients per month.

There are however resource implications. By following a policy of early laparoscopic cholecystectomy for biliary colic, all patients with suspected biliary colic have to undergo emergency ultrasound. The positive predictive value of biliary colic in the diagnosis of gallstones in the referred population is 50% ([Berger 2000](#)) i.e. half the patients suspected (by doctors) to have gallstones because of symptoms of biliary colic have gallstones. Once these patients have been diagnosed to have gallstones, they must be operated as a "planned" emergency. Further more, in the UK, an additional financial resource implication is that the costs of the emergency laparoscopic cholecystectomy are borne by the acute trust and the costs of elective laparoscopic cholecystectomy are borne by the primary care trust.

In the only trial included in this review, 20% of patients diagnosed to have biliary colic based on temperature, white cell count, and ultrasound had acute cholecystitis. The sensitivity of ultrasound in diagnosing acute cholecystitis varies from 60% ([Bingener 2004](#)) to 88% ([Shea 1994](#)). The sensitivity of clinical and laboratory values in the diagnosis of acute cholecystitis varies between 63% and 81% ([Trowbridge 2003](#)). Thus it is possible that some patients with acute cholecystitis may be misdiagnosed as biliary colic. However, in a Cochrane review, the first two authors of this review found that early laparoscopic cholecystectomy for acute cholecystitis is safe, provided it was carried out within a week of onset of symptoms ([Gurusamy 2006](#)). So, it is advisable to perform early laparoscopic cholecystectomy within a week of onset of symptoms.

While the results of the only trial included in this review are overwhelmingly in favour of early laparoscopic cholecystectomy and the reports of retrospective studies support the findings, further high quality randomised clinical trials are necessary to confirm the findings of the trial.

Reviewers' conclusions

Implications for practice

Based on evidence from one trial, it appears that early laparoscopic cholecystectomy decreases the morbidity during the waiting period for elective laparoscopic cholecystectomy, decreases the conversion to open cholecystectomy, decreases operating time, and decreases hospital stay.

Implications for research

- (1) Further randomised clinical trials are necessary urgently.
- (2) Future trials need to be conducted and reported according to the CONSORT Statement (www.consort-statement.org) ([Moher 2001](#)).

Acknowledgements

- (1) To Dr Martyn Parker, author of more than 15 Cochrane reviews, who inspired me to write Cochrane reviews.
- (2) To The Cochrane Hepato-Biliary Group for the support that they have provided.

Potential conflict of interest

None.

Characteristics of included studies

Study	Methods	Participants	Interventions	Outcomes	Notes	Allocation concealment
Salman 2005	Randomised clinical trial Generation of the allocation sequence: adequate (random number table).	Country: Turkey. Number randomised: 75. Mean age: 43 years (63 patients). Females: 41/63 (65.1%).	Participants were randomly assigned to two groups. Group 1: early laparoscopic cholecystectomy (n = 35). Group 2: Delayed	The main outcome measures were mortality, morbidity during the waiting period, surgical morbidity, conversion to open cholecystectomy,	Of the 75 patients, 7 patients in group 1 and 5 patients in group 2 were excluded after randomisation. In group 1, the patients were excluded	B

Allocation concealment: unclear.	Inclusion criteria: (1) Biliary colic. (2) Normal white cell count. (3) Normal liver function tests.	laparoscopic cholecystectomy (n = 40). Timing: Early laparoscopic cholecystectomy: < 24 hours. Delayed laparoscopic cholecystectomy : put on waiting list for elective surgery. The mean waiting time from the time of diagnosis of biliary colic was 4.2 months.	operating time, hospital stay, number of visits to emergency department, and number of hospital admissions during waiting period.	because of intra-operative acute cholecystitis. In group 2, the patients were excluded because of acute severe pancreatitis and death (1); empyema of gallbladder (1); gallbladder perforation (1); and acute cholecystitis (2). Wherever possible, these patients have been included as we performed the analysis by an "intention-to-treat" analysis.
Blinding: not done.				
Follow-up: adequate.				
Intention-to-treat analysis: no.	Exclusion criteria (1) Acute cholecystitis. (2) Obstructive jaundice. (3) Cholangitis. (4) Pancreatitis.			
Sample size calculation: no.				

References to studies

References to included studies

Salman 2005 {published data only}

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* indicates the primary reference for the study

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Comparisons and data

01 Early or delayed laparoscopic cholecystectomy for biliary colic

01.01 Mortality

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	1	40

01.02 Morbidity during waiting period

01.02.01 Pancreatitis

Study ID	Early n	Early N	Delayed n	Delayed N

Salman 2005	0	35	1	40
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01.02.02 Empyema of gallbladder

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	1	40

01.02.03 Gallbladder perforation

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	1	40

01.02.04 Acute cholecystitis

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	2	40

01.02.05 Cholangitis

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	2	40

01.02.06 Obstructive jaundice

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	2	40

01.02.07 Recurrent biliary colic requiring hospital visits

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	5	40

01.03 Surgery related morbidity

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	28	0	35

01.04 Conversion to open cholecystectomy

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	28	8	40

01.05 Number requiring endoscopic retrograde pancreato cholangiogram

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	28	1	40

01.06 Operating time (minutes)

Study ID	Early N	Early Mean	Early SD	Delayed N	Delayed Mean	Delayed SD
Salman 2005	28	35.10	6.74	35	49.90	6.12

01.07 Hospital stay (days)

Study ID	Early N	Early Mean	Early SD	Delayed N	Delayed Mean	Delayed SD
Salman 2005	28	1.06	0.40	35	2.31	2.36

01.08 Number of patients with at least one emergency admission during waiting period

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	28	14	40

02 Early or delayed laparoscopic cholecystectomy for biliary colic (Risk difference)**02.01 Mortality**

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	1	40

02.02 Morbidity during waiting period

02.02.01 Pancreatitis

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	1	40

02.02.02 Empyema of gallbladder

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	1	40

02.02.03 Gallbladder perforation

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	1	40

02.02.04 Acute cholecystitis

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	2	40

02.02.05 Cholangitis

Study ID	Early n	Early N	Delayed n	Delayed N

Salman 2005	0	35	2	40
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02.02.06 Obstructive jaundice

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	2	40

02.02.07 Recurrent biliary colic requiring hospital visits

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	35	5	40

02.03 Surgery related morbidity

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	28	0	35

02.04 Conversion to open cholecystectomy

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	28	8	40

02.05 Number requiring endoscopic retrograde pancreato cholangiogram

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	28	1	40

02.06 Number of patients with at least one emergency admission during waiting period

Study ID	Early n	Early N	Delayed n	Delayed N
Salman 2005	0	28	14	40

Additional tables

01 Search Strategy

Database	Period of Search	Search Strategy
The Cochrane Hepato-Biliary Group Controlled Trials Register	Date will be given at review status.	(biliary OR gallbladder OR gall-bladder OR gall bladder) AND (colic* OR pain OR pains OR cramp* OR ache OR aches) AND (cholecystecto* OR colecystecto*)

Cochrane Central Register of Controlled Trials (CENTRAL) in The Cochrane Library	Latest issue.	<p>#1 MeSH descriptor Biliary Tract Diseases explode all trees #2 MeSH descriptor Biliary Tract explode all trees #3 MeSH descriptor Gallbladder explode all trees #4 MeSH descriptor Gallbladder Diseases explode all trees #5 biliary OR gallbladder OR gallbladder OR "gall bladder" #6 (#1 OR #2 OR #3 OR #4 OR #5) #7 MeSH descriptor Colic explode all trees #8 MeSH descriptor Pain explode all trees #9 colic* OR pain OR pains OR cramp* OR ache OR aches #10 (#7 OR #8 OR #9) #11 MeSH descriptor Cholecystectomy explode all trees #12 cholecystecto* OR colecystecto* #13 (#11 OR #12) #14 (#6 AND #10 AND #13)</p>
MEDLINE	1987 to the date of search.	<p>(biliary OR "Biliary Tract Diseases"[MeSH] OR "Biliary Tract"[MeSH] OR gallbladder OR gallbladder OR "gall bladder" OR "Gallbladder"[MeSH] OR "Gallbladder Diseases"[MeSH]) AND (colic* OR pain OR pains OR cramp* OR ache OR aches OR "Colic"[MeSH] OR "Pain"[MeSH]) AND (cholecystecto* OR colecystecto* OR "cholecystectomy"[MeSH]) AND (((randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized controlled trials [mh] OR random allocation [mh] OR double-blind method [mh] OR single-blind method [mh] OR clinical trial [pt] OR clinical trials [mh] OR ("clinical trial" [tw]) OR ((singl* [tw] OR doubl* [tw] OR trebl* [tw] OR tripl* [tw]) AND (mask* [tw] OR blind* [tw]))) OR (placebos [mh] OR placebo* [tw] OR random* [tw] OR research design [mh:noexp]) NOT (animals [mh] NOT human [mh])))</p>
		<p>1 BILIARY-COLIC#.DE. 2 (biliary OR gallbladder OR gall-</p>

EMBASE	1987 to the date of search.	bladder OR gall ADJ bladder) AND (colic\$ OR pain OR pains OR cramp\$ OR ache OR aches) 3 1 OR 2 4 CHOLECYSTECTOMY#.W..DE. OR cholecystecto\$ OR colecystecto\$ 5 3 AND 4 6 RANDOMIZED-CONTROLLED- TRIAL#.DE. OR RANDOMIZATION#.W..DE. OR CONTROLLED-STUDY#.DE. OR MULTICENTER-STUDY#.DE. OR PHASE-3-CLINICAL-TRIAL#.DE. OR PHASE-4-CLINICAL-TRIAL#.DE. OR DOUBLE-BLIND-PROCEDURE#.DE. OR SINGLE-BLIND- PROCEDURE#.DE. 7 RANDOM\$ OR CROSSOVER\$ OR CROSS-OVER OR CROSS ADJ OVER OR FACTORIAL\$ OR PLACEBO\$ OR VOLUNTEERS\$ 8 (SINGLE OR DOUBLE OR TREBLE OR TRIPLE) NEAR (BLIND OR MASK) 9 6 OR 7 OR 8 10 9 AND HUMAN=YES 11 5 AND 10
Science Citation Index Expanded (http://portal.isiknowledge.com/portal.cgi?DestApp=WOS&Func=Frame)	1987 to the date of search.	#1 TS=(biliary OR gallbladder OR gall- bladder OR gall bladder) #2 TS=(colic* OR pain OR pains OR cramp* OR ache OR aches) #3 TS=(cholecystecto* OR colecystecto*) #4 TS=(random* OR blind* OR placebo* OR meta-analysis) #5 #4 AND #3 AND #2 AND #1

Notes

Unpublished CRG notes

Exported from Review Manager 4.2.10

Published notes

Amended sections

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