Mortality and complications associated with laparoscopic cholecystectomy: a meta-analysis

Authors' objectives
To perform a meta-analysis of large laparoscopic cholecystectomy case series and compare results concerning complications, particularly bile-duct injury, to those reported in a meta-analysis of open cholecystectomy.

Searching
MEDLINE was searched through 1995 for articles published in the English language, using the keyword 'cholecystectomy'. The bibliographies of retrieved articles were examined for additional titles.

Study selection
Study designs of evaluations included in the review
Case series and randomised controlled trials (RCTs) with more than 100 patients, which appeared to be representative of the general population of patients undergoing cholecystectomy in the United States, were included. Excluded were the following: animal studies, non-original data; non-Western populations; atypical patients; data limited to special topics; journals without a national audience; studies with no data on length of stay, time to return to work or normal activities, or frequency of readmissions, reoperations, relief of symptoms, complications or mortality; non-standard or unusual applications of procedure; biased patient sample; and redundant patients.

Specific interventions included in the review
Laparoscopic cholecystectomy and open cholecystectomy were studied.

Participants included in the review
The participants included both in- and out-patients who were undergoing cholecystectomy. Aggregating the data across the included studies reporting such data gave the average proportion of women as 76% (standard deviation, SD=5%), and the mean age weighted by sample size as 49.0 years (SD=3.2 years). The leading indication for surgery was chronic cholecystitis or symptomatic cholelithiasis.

Outcomes assessed in the review
The main outcomes assessed were: mortality, common bile-duct injury, and conversion rates from laparoscopic cholecystectomy to open cholecystectomy. Secondary outcomes included length of stay, length of time for return to work or normal activities, frequency of readmissions, reoperations, relief of symptoms and complications.

How were decisions on the relevance of primary studies made?
Two non-physician research staff members independently read the abstracts and selected articles for full review based on pre-specified inclusion and exclusion criteria. Three trained research staff members subsequently extracted data, and on this basis decisions were made about excluding the article from consideration.

Assessment of study quality
The following nine variables were selected to describe reporting thoroughness: age and gender of patients, additional information about patients, date of patients' enrolment, time frame of study, study design, patient follow-up, patient exclusions, methods of establishing diagnosis, and clinical or pathological diagnosis of the patient sample. Data on the nine variables selected to describe reporting thoroughness were recorded during abstraction. These variables were subjected to a principal component analysis, and were observed following projection onto three components. The three components were treated as covariates in the regression models, whilst subscale scores were treated as ordinal variables.

Data extraction
Each article was reviewed by three trained research staff members who separately extracted data on the following:
patient population, surgical details, study characteristics and outcomes. Any differences were resolved by consensus of
the three readers. The articles were divided into three groups for analysis:

1) laparoscopic cholecystectomy series from a single hospital institution, system, health care provider or community;
2) laparoscopic cholecystectomy series reporting the experiences of multiple institutions; and
3) open cholecystectomy series from a single institution.

**Methods of synthesis**

*How were the studies combined?*

Aggregated data about the rates of mortality, common bile-duct injury and conversion from laparoscopic to open
cholecystectomy were calculated. Group level logistic regression, with the study as the unit of analysis, was used to
assess which clinical and patient characteristics were associated with mortality, common bile-duct injury and conversion
from laparoscopic to open cholecystectomy. Each study was weighted by the number of patients in the study.

*How were differences between studies investigated?*

The possible causes of heterogeneity were discussed. Group level logistic regression was performed in an attempt to
identify the sources of systematic variation from single institution laparoscopic cholecystectomy studies.

**Results of the review**

Fifteen studies were used to assess laparoscopic cholecystectomy from multiple institutions (N=48,795).

Twenty-eight studies were used to assess open cholecystectomy from a single institution (N=12,973).

Seventy-five studies were used to assess reasons for conversion from laparoscopic to open cholecystectomy (N=25,763,
of whom 1,400 had a conversion).

Eighty-three studies were used to assess laparoscopic cholecystectomy from a single institution (N=30,052).

There was variation in the amount and type of data reported.

Laparoscopic cholecystectomy from a single institution: mortality ranged from 0.0014 to 0.0016; common bile-duct
injury ranged from 0.0036 to 0.0047; conversion rates ranged from 0.049 to 0.052.

Laparoscopic cholecystectomy from multiple institutions: mortality ranged from 0.00086 to 0.00091; common bile-duct
injury ranged from 0.0046 to 0.0047; conversion rates were 0.055.

Open cholecystectomy from a single institution: mortality ranged from 0.0066 to 0.0074; common bile-duct injury
ranged from 0.0019 to 0.0029.

Group level logistic regression to identify the sources of systematic variation from single institution laparoscopic
cholecystectomy studies: available variates were not helpful in identifying factors associated with mortality rates;
variables significantly associated with common bile-duct injury, after adjustment using covariates based on reporting
thoroughness, were presence of patients operated on as out-patients and the year the study started; variables associated
with higher conversion rates after adjustment were multisurgeon studies, patients operated on as in-patients, the
inclusion of patients with acute cholecystitis, and studies initiated in 1990.

Conversion to open cholecystectomy was most commonly due to technical reasons (55% of conversions).

**Authors’ conclusions**

There is wide variability in the amount and type of data reported within any single study, and patient populations may
not be comparable across studies. Except for a higher common bile-duct injury rate, laparoscopic cholecystectomy
appears to be at least as safe as open cholecystectomy. There are still some considerable uncertainties that need to be addressed by better-designed studies and more complete reporting, even though an extremely large body of data concerning laparoscopic cholecystectomy has been reported and some reasonably secure conclusions can be drawn.

CRD commentary
This is a well-written, clearly-presented review with a sound methodology for the selection of primary studies and an excellent discussion on the potential sources of bias. Limiting the literature search to English language articles registered on MEDLINE may have omitted some relevant studies. Unambiguous exclusion criteria coupled with a structured selection procedure should have excluded selection bias from the retrieved studies.

Potential sources of heterogeneity between studies were investigated by logistic regression. Fuller details of the methodological quality of the primary studies, including completeness of follow-up and blinded assessments of outcome, would have been useful.

As the authors state, there are a number of potential sources of bias in such a study comparing mortality and morbidity rates from different surgical procedures; these include the lack of consideration of differing patient selection criteria, lower clinical thresholds for laparoscopic cholecystectomy, differing study settings, the variability in reporting of complication rates, publication bias with surgeons reporting more favourable data, the under-reporting of certain complications of laparoscopic cholecystectomy given the early discharge of these patients, and the lower mortality rates for laparoscopic cholecystectomy reflecting the restriction of this procedure to the healthiest patients. The review is limited, as the authors state, by the extensive variability in the range and type of information reported in any single article.

Implications of the review for practice and research
For laparoscopic cholecystectomy, as for any new procedure, complete reporting of data from studies is necessary to assess the cost-effectiveness of the procedure.

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