Laparoscopic vs open hepatic resection for benign and malignant tumors: an updated meta-analysis

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CRD summary
The authors concluded that laparoscopic hepatic resection for malignant tumours was associated with long-term survival that was at least comparable if not superior to open hepatic resection. There was no difference in disease recurrence. The reliability of the conclusions is uncertain given some methodological weaknesses (potential for missing studies, risk of error and bias, inclusion of weaker study designs).

Authors' objectives
To compare laparoscopic hepatic resection (LHR) with open hepatic resection (OHR) for benign and malignant tumours.

Searching
MEDLINE, Cochrane Central Register of Controlled Trials (CENTRAL) and EMBASE were searched between January 1998 and May 2009. Search terms were reported. Reference lists of selected articles were handsearched. There were no language restrictions.

Study selection
Studies that compared LHR with OHR in patients who underwent liver resection for benign and malignant neoplasm were eligible for inclusion if they had clear documentation of operative techniques. Studies had to report at least one of the outcome measures: operative measures (such as operative blood loss, operative time, risk of receiving a blood transfusion, risk of portal triad clamping, duration of clamp time), oncologic clearance (such as number of positive surgical margins and margins less than 1cm), postoperative parameters (such as time to first oral intake, duration of hospital stay, duration of intravenous narcotic requirements), morbidity (such as liver resection-related and general complications) and long-term outcomes (such as all-cause mortality, recurrence of malignant tumours). Further details about definitions and assessments of outcomes were reported.

Study settings varied. All were conducted in high-income countries (two were in UK). Most studies assessed both benign and malignant tumours. Characteristics of included patients were incompletely reported.

The authors did not state how many reviewers assessed studies for inclusion.

Assessment of study quality
Study quality was assessed using the modified Newcastle-Ottawa Scale. The maximum number of points for each quality category were: 3 (selection), 4 (comparability) and 2 (outcomes). The authors did not state how many reviewers assessed study quality.

Data extraction
Two reviewers independently extracted data to enable calculation of mean differences (MDs) (continuous outcomes), relative risks (RRs) (dichotomous outcomes) and hazard ratios (HRs) (survival outcomes), all with 95% confidence intervals (CIs). Hazard ratios were calculated from Kaplan-Meier curves where required survival data were not reported in the primary studies. Disagreements were resolved through discussion and consensus.

Methods of synthesis
Pooled weighted mean differences (WMDs), relative risks and hazard ratios and their corresponding 95% CIs were calculated using random-effects meta-analysis. Heterogeneity was assessed using \( I^2 \). Publication bias was assessed using funnel plots and the Egger test. Sensitivity analyses examined estimates of effects for studies published in 2006 or later, studies with at least 20 patients in each group and studies of high quality with at least 6 points.
Results of the review
Twenty-six studies (n=1,890 participants, range 10 to 373) were included. All were observational design. Ten studies used prospective designs, six were retrospective, and 10 used mixed designs. In terms of study quality, half of the studies scored the maximum for selection, nine scored the maximum for comparability and 22 scored the maximum for outcomes.

Blood loss (mL) was significantly lower in the LHR group compared to the OHR group (WMD -161, 95% CI -209 to -114; 21 studies). No significant differences were reported for operative time (minutes), risk of receiving a blood transfusion, risk of portal triad clamping and duration of clamp time (minutes) between LHR and OHR groups. Significant heterogeneity was detected with regard to operative time ($I^2=92.9\%$), operative blood loss ($I^2=84\%$), risk of portal triad clamping ($I^2=88.1\%$) and duration of clamp time ($I^2=93.3\%$). There was no significant difference in the risk of a positive resection margin, but the risk of surgical margin smaller than 1cm was about two times higher in the LHR group (RR 1.99, 95% CI 1.31 to 3.02; five studies). No significant heterogeneity was found.

Duration of hospital stay (days) was significantly lower in the LHR group compared to the OHR group (WMD 3.52, 95% CI -4.27 to -2.77; 23 studies). Duration until oral intake (days) and duration of intravenous narcotic requirements (days) were significantly shorter in the LHR group: oral intake (WMD -1.14, 95% CI -1.84 to -0.43; seven studies) and narcotic requirements (WMD -2.15, 95% CI -3.11 to -1.20; three studies). There was significant heterogeneity for duration of hospital stay ($I^2=85.5\%$) and time until oral intake ($I^2=97.1\%$).

The risk of having any postoperative complication was significantly lower in the LHR group (RR 0.40, 95% CI 0.31 to 0.52; 23 studies). No significant heterogeneity was found. The hazard ratio of all-cause mortality for malignant tumours until two to five years of follow-up was significantly lower in the LHR group (HR 0.64, 95% CI 0.42 to 0.99; six studies). No significant heterogeneity was found ($I^2=0\%$). The hazard ratio of recurrence for malignant tumours until two to five years of follow-up was not significantly different between the two groups. No significant heterogeneity between studies was found ($I^2=0\%$).

No evidence of publication bias was found. Overall measures of effects did not change in most cases in sensitivity analyses; further details were reported.

Authors’ conclusions
LHR for malignant tumours was associated with a long-term survival that was at least comparable if not superior to OHR. There was no difference in disease recurrence. Use of LHR for benign and malignant tumours was a safe alternative to OHR and had potential operative and postoperative benefits.

CRD commentary
The review question was clearly stated with regard to eligible interventions, patients and outcomes. Eligible designs were not explicitly prespecified. Three major databases were searched without language restrictions, which minimised potential language bias. There were no reported efforts to search for unpublished papers and so some relevant papers may have been missed. Data extraction was conducted in duplicate, which minimised risks of error and bias; it was unclear whether similar processes were used in study selection and quality assessment. Study quality was assessed using an acceptable scale and results were reported. Heterogeneity was explored and study results were combined using appropriate methods.

The reliability of the authors’ conclusion is uncertain due to some methodological weaknesses (potential for missing studies, risk of error and bias in the review process and inclusion of weaker study designs) in the review.

Implications of the review for practice and research
Practice: The authors did not state any implication for clinical practice.

Research: The authors stated that there was an on-going randomised controlled trial in South Korea registered with ClinicalTrials.gov.
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