Surgical and oncologic outcomes following laparoscopic versus open liver resection for hepatocellular carcinoma: a meta-analysis

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CRD summary
The review concluded that laparoscopic tumour removal was safe and feasible for selected patients with liver cancer (hepatocellular carcinoma) without affecting oncological outcomes or increasing tumour recurrence. There were benefits for blood loss, complications, risk of transfusion and hospital stay compared with open resection. Given the limited evidence base and potential bias, the authors’ conclusions should be treated with caution.

Authors’ objectives
To compare the surgical and oncological outcomes of patients with hepatocellular carcinoma undergoing laparoscopic versus open hepatectomy.

Searching
MEDLINE and The Cochrane Library were searched for relevant studies published from 1993 to May 2011; search terms were reported. Reference lists of retrieved studies were searched.

Study selection
Studies that compared laparoscopic with open hepatectomy in patients with hepatocellular carcinoma were eligible for inclusion in the review. Studies had to report on at least one surgical outcomes (duration of operation, operative blood loss, need for transfusion, conversion to open surgery, duration of hospital stay, overall complications), or tumour resection details with laparoscopy (type of hepatectomy, tumour location and size), or one oncologic outcome (surgery margin, margin positive rate, tumour recurrence or follow-up). Where duplicates were identified, the publication with the highest quality or the most recent was included in the review.

The mean age of participants ranged from 58 to 72 years. The ratio of men to women was 1.7:1.0 (the proportion of men ranged from 20% to 88%).

The authors did not state how many reviewers selected studies for the review.

Assessment of study quality
Studies were assessed for quality using the modified Newcastle-Ottawa Scale. Overall scores were calculated ranging from 0 to 9 stars.

Two reviewers independently assessed studies for quality.

Data extraction
Data were extracted to calculate odds ratios (ORs) for dichotomous data (transfusion need, complications and hospital stay) and mean differences (MDs) for continuous data (surgery margins, operating time, blood loss and tumour recurrence), with corresponding 95% confidence intervals (CIs).

Two reviewers independently extracted data, with discrepancies resolved by discussion.

Methods of synthesis
Studies were pooled in meta-analyses and summary odds ratios and weighted mean differences (WMDs), with 95% confidence intervals, were estimated using a random-effects model.

Heterogeneity was assessed with $X^2$ and quantified with the $I^2$ value ($I^2$ of 50% or more represented substantial heterogeneity).

Publication bias was assessed by inspection of funnel plots.
Results of the review
Ten studies (627 patients, range 21 to 179) were included in the review. Six studies had a case control design and four were retrospective analyses. Six studies had overall quality scores of 6 stars and four studies had 3 stars (out of a maximum of 9 stars).

Surgical outcomes: Compared with open hepatectomy, laparoscopic hepatectomy was associated with significantly lower blood loss (WMD -223.2mL, 95% CI -331.8 to -114.5; substantial heterogeneity with $I^2=65%$; six trials) and significantly lower risk of transfusion (OR 0.4, 95% CI 0.2 to 0.8; $I^2=0%$; five trials). There was no evidence of a difference in the duration of operation ($I^2=91%$; seven studies). Compared with open hepatectomy, laparoscopic hepatectomy was associated with significantly shorter hospital stay (WMD -5.1 days, 95% CI -7.8 to -2.3; substantial heterogeneity of $I^2=87%$; seven trials) and significantly fewer complications (OR 0.5, 95% CI 0.3 to 0.8; $I^2=0%$; nine trials). In the laparoscopic group, 6.6% of patients converted to the open procedure (where reported).

Tumour resection details: The mean/median tumour size ranged from 2.5 to 4.3cm in the laparoscopic group and from 2.5 to 6.0cm in the open group. In the laparoscopic group, tumours were located in the II-VIII sectors (where reported). In the laparoscopic group, types of hepatectomy included left lateral segmentectomy, segmentectomy, subsegmentectomy, right hepatectomy, left hepatectomy and bisegmentectomy (where reported).

Oncologic outcomes: There was no evidence of a significant difference between groups for the surgery margin, the margin positive rate or tumour recurrence.

There was no evidence of publication bias.

Authors’ conclusions
Laparoscopic resection was a safe and feasible option for selected patients with hepatocellular carcinoma. Although it did not affect oncologic outcomes and increased tumour recurrence, it was associated with less blood loss, fewer complications, lower risk of transfusion, and shorter hospital stay.

CRD commentary
The review addressed a clear research question, supported by appropriate inclusion criteria. A limited number of sources were searched for relevant studies. No specific attempts were made to find unpublished studies, so publication bias (missed studies) could not be ruled out. Although formal assessment of publication bias was undertaken by inspection of a funnel plot, this may not have been adequate given the limited number of studies. Appropriate methods were used to extract data and assess studies for quality, but the authors did not report how many reviewers selected studies for the review, so reviewer error and bias could not be excluded. Studies were assessed for quality by a valid risk of bias tool, but they generally had small sample sizes, were not randomised and had variable quality, which made it difficult to determine the reliability of the results. Synthesis of studies and assessment of heterogeneity were appropriate. Some of the outcomes had substantial heterogeneity; the authors did not try to explain the variation. The authors qualified their conclusion by stating that laparoscopic resection was appropriate only for selected patients and suggested that some of the criteria required for laparoscopy were superficial or peripheral tumours. However, the inclusion criteria for the review did not specify any restrictions on size or location of tumour. Follow-up was not reported, so it was unclear how outcomes that relied on follow-up (such as tumour recurrence) could be interpreted.

Due to the limited evidence base and the potential for bias in the review, the authors’ conclusions should be treated with caution.

Implications of the review for practice and research
Practice: The authors stated that laparoscopic resection for selected patients with hepatocellular carcinoma was safe.

Research: The authors stated that further RCTs were required to confirm the conclusions because of the limited evidence base.

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