Meta-analysis of the therapeutic effect of hepatectomy versus radiofrequency ablation for the treatment of hepatocellular carcinoma  
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CRD summary
The authors concluded that radiofrequency ablation may be comparable to surgical resection of the liver in hepatocellular carcinoma if tumour recurrence after radiofrequency ablation could be detected in timely fashion and effectively treated. The authors’ conclusions appeared to reflect the evidence, but apparent differences between studies make it difficult to assess their reliability.

Authors' objectives
To compare the therapeutic effect of hepatic resection versus radiofrequency ablation for the treatment of hepatocellular carcinoma.

Searching
MEDLINE, EMBASE and the Cochrane Library were searched between 1995 and December 2007 for studies in any language. Search terms were reported. Reference lists were also screened.

Study selection
Studies that compared hepatectomy with radiofrequency ablation in patients with hepatocellular carcinoma and liver cirrhosis were eligible for inclusion. Patients were required to: have received no previous treatment for hepatocellular carcinoma; have either a single hepatocellular carcinoma up to 5cm in diameter or up to three hepatocellular carcinomas each up to 3cm in diameter; have no metastatic carcinoma.

The review outcomes were: death rate; one, two, three and five-year survival rates; one, three and five-year recurrence-free survival rates; recurrence; and complications.

Most patients in the included studies were male. The mean age per treatment group ranged from 49 to 68 years. Most patients were classified as Child-Pugh score A. Most patients had a single hepatocellular carcinoma tumour. The most common causes of cirrhosis were hepatitis B/C virus.

Two reviewers independently selected studies and resolved disagreements on inclusions by consensus.

Assessment of study quality
It appeared that two reviewers independently assessed quality using the Jadad criteria (reporting of randomisation, blinding and withdrawals) justification of sample size. Disagreements were resolved by consensus.

Data extraction
Odds ratios (ORs) with 95% confidence intervals (CIs) were used for dichotomous data and mean differences used for continuous data. Study authors were contacted for additional information where required.

Two reviewers independently extracted data and resolved disagreements by consensus.

Methods of synthesis
Pooled odds ratios and weighted mean differences (WMDs), with 95% confidence intervals were calculated using a fixed-effect method in the absence of significant heterogeneity; otherwise a random-effects model was used. According to forest plots, heterogeneity was assessed using the $\chi^2$ and $I^2$ statistics.

Sensitivity analysis was undertaken by repeating the analysis after excluding each study in turn.

The potential for publication bias was reported for survival at five years.
Results of the review

Eight studies were included in the review (n=1,188 patients). The number of patients per treatment group ranged from 18 to 155.

All studies were reported as scoring 3 points of the Jadad scale. The quality table reported that all were described as randomised and all used appropriate methods of sequence generation. None were double-blinded and none specifically described allocation concealment.

There was no statistically significant difference between hepatectomy and radiofrequency ablation in the complication rate (three studies) or death rate (three studies provided data).

Survival rates were significantly lower in the radiofrequency ablation group at three years (OR 1.66, 95% CI 1.21 to 2.27; six studies), but there was no significant difference in survival rates between radiofrequency ablation and hepatectomy at one year (seven studies), two years (two studies) and five years (six studies).

Recurrence-free survival rates were significantly lower in radiofrequency ablation groups at one year (OR 1.54, 95% CI 1.07 to 2.12; five studies), three years (OR 2.02, 95% CI 1.48 to 2.75; five studies) and five years (OR 1.52, 95% CI 1.12 to 2.06; six studies).

Radiofrequency ablation was associated with a significantly higher rate of recurrence at the previous site (OR 0.28, 95% CI 0.12 to 0.65; four studies) and a significantly lower rate of recurrence in new areas (OR 1.97, 95% CI 1.29 to 2.99; four studies). There was no statistically significant difference between hepatectomy and radiofrequency ablation for recurrence in extra-hepatic areas (two studies).

The authors stated that there was no significant heterogeneity was found for any of these analyses. Forest plots showed that I² values of 50% or more for analyses of three-year survival plus one- and three- and five-year recurrence-free survival. Studies of five-year recurrence-free surgical showed different directions of treatment effect.

The authors stated that the funnel plot of survival at five years showed symmetry ‘indicating no serious publication bias’. The funnel plot appeared asymmetrical on inspection.

Authors’ conclusions

Radiofrequency ablation may have comparable effects with surgical resection in patients with hepatocellular carcinoma if recurrence of the hepatocellular carcinoma after radiofrequency ablation could be detected in a timely fashion and effectively treated.

CRD commentary

The review question was clearly stated. Inclusion criteria were appropriately defined for participants and interventions and were broadly specified for study design. Several relevant sources were searched and attempts were made to minimise language bias. No attempts were made to minimise publication bias; the funnel plot was of limited value due to the small number of studies, it was not clear why one particular outcome was selected to assess publication bias; the funnel plot was described in the text as symmetrical, but appeared to be asymmetrical. Suitable methods were used to minimise reviewer error and bias during the review process.

Study quality was assessed and results were reported. However, the design of included studies was not at all clear and this cast doubt on the reliability of review findings. Appropriate methods were used for the meta-analyses and heterogeneity was assessed. It was not clear what level of I² value was taken as indicative of heterogeneity; several analyses that would have been classified as heterogeneous (using I² of 50% or more) were reported as statistically homogeneous.

The authors’ conclusions appeared to reflect the evidence, but apparent differences between studies, inconsistencies in the descriptions of study design and other aspects of the review, make it difficult to assess their reliability.
Implications of the review for practice and research

Practice: The authors did not state any implications for practice.

Research: The authors stated that that a RCT is required to compare radiofrequency ablation with hepatectomy for patients with hepatocellular carcinoma.

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