Survival and cost-effectiveness analysis of competing strategies in the management of small hepatocellular carcinoma

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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

CRD summary
This study examined the cost-effectiveness of immediate transarterial chemoembolisation or radiofrequency ablation compared with expectant monitoring for small (less than 2cm) hepatocellular carcinoma in patients with compensated cirrhosis. The authors concluded that immediate treatment with either transarterial chemoembolisation or radiofrequency ablation was cost-effective compared with expectant monitoring. A conventional analytic approach was used and the authors’ conclusions appear to be robust, despite limited reporting of the clinical sources of evidence.

Type of economic evaluation
Cost-effectiveness analysis

Study objective
This study examined the cost-effectiveness of immediate transarterial chemoembolisation or radiofrequency ablation, compared with monitoring without treatment, for small (less than 2cm) hepatocellular carcinoma, in patients with compensated cirrhosis that cannot be resected.

Interventions
The two strategies were treatment versus monitoring. Treatment was immediate transarterial chemoembolisation or radiofrequency ablation, with monitoring every three months and re-treatment if there was progression or referral for orthotopic liver transplantation if the hepatocellular carcinoma met the Milan criteria for prioritising liver transplants. The Milan criteria were a tumour greater than 2cm, but less than 5cm in diameter or no more than three tumours of less than 3cm in diameter. Monitoring was every three months, without initial treatment, but with subsequent transarterial chemoembolisation or radiofrequency ablation or referral for orthotopic liver transplantation if the hepatocellular carcinoma met the Milan criteria.

Location/setting
USA/hospital.

Methods
Analytical approach:
The analysis was based on a Markov model, with a 10-year horizon. The authors did not explicitly state the perspective adopted.

Effectiveness data:
The clinical data were from a selection of relevant studies. Most of the data on transplant lists were from transplant centres. The clinical inputs for disease progression with or without treatment were the key inputs to the model and they were all from published studies. Some assumptions were required.

Monetary benefit and utility valuations:
Not considered.

Measure of benefit:
Life-years were the summary benefit measure and they were discounted at an annual rate of 3%.
Cost data:
The economic analysis included the costs of monitoring, transarterial chemoembolisation, radiofrequency ablation, liver transplant, and post-transplant care (clinic visits, laboratory work, and tacrolimus). The costs were based on pairings from the Surveillance, Epidemiology, and End Results database and the Medicare database and they included facility and physician fees as well as drugs and materials for diagnosis and treatment. The patterns of resource consumption reflected evidence-based best practice, rather than actual routines that can be wasteful. The costs were in US dollars ($) and a 3% annual discount rate was applied.

Analysis of uncertainty:
All the costs and probabilities were varied over broad ranges to determine whether or not the model outcomes were robust.

Results
With transarterial chemoembolisation, the expected costs were $142,869 with immediate treatment and $183,105 with monitoring. The life-years were 4.269 with treatment and 4.324 with monitoring. The incremental cost per life-year gained with monitoring over transarterial chemoembolisation was $739,602.

With radiofrequency ablation, the expected costs were $92,094 with treatment and $144,427 with monitoring. The life-years were 5.273 with treatment and 5.236 with monitoring. Radiofrequency ablation was the dominant strategy as it was more effective and less expensive than monitoring.

Orthotopic liver transplantation was reduced by 10% with transarterial chemoembolisation and 12% with radiofrequency ablation.

The base-case findings were robust to variations in the clinical and economic inputs, even though the magnitude of cost savings or life-years gained changed. The most influential input was the rate of listing for orthotopic liver transplantation, but immediate treatment remained cost-effective or dominant in all cases.

Authors' conclusions
The authors concluded that immediate treatment of small hepatocellular carcinoma with either transarterial chemoembolisation or radiofrequency ablation was cost-effective compared with monitoring and liver transplant at a later tumour stage.

CRD commentary
Interventions:
The selection of the comparators was appropriate as they were the two available strategies for patients with small hepatocellular carcinoma. The authors stated the weaknesses and advantages of each approach.

Effectiveness/benefits:
The clinical data were not satisfactorily presented. The method used to identify the relevant sources of data was not reported; a systematic search of the evidence would have been appropriate. No information on the characteristics of these sources was given, which makes it impossible to judge the validity of the clinical estimates; the authors stated that the best available sources were used. They did not investigate potential heterogeneity between the published studies and the criterion used to select the best estimate, where multiple sources were available, was not described. Life-years were an appropriate benefit measure, given the impact of the disease on life expectancy. They also permit comparisons to be made with the benefits of other health care interventions.

Costs:
The authors did not explicitly state the perspective adopted, but the types of costs and their sources suggest the perspective of a reimbursement authority, such as a third-party payer. The unit costs and resource quantities were not presented separately; most of the costs were reported as category totals. The sources for the costs correctly represented the authors’ context and were typical of those used in the USA. The cost estimates were appropriately varied in the sensitivity analyses. The price year was not reported, making reflation exercises for other time periods impossible.
Analysis and results:
The results were extensively presented and the costs and benefits were appropriately synthesised, using an incremental approach. The uncertainty was partly investigated, using a deterministic approach, which considered variations in individual inputs one at a time. The decision model used to simulate the natural history of disease and its management appears to have been appropriate and was extensively described. The resource use and costs represented the US context and cannot easily be transferred to other settings.

Concluding remarks:
A conventional analytic approach was used and the authors’ conclusions appear to be robust, despite limited reporting of the clinical sources of evidence.

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