The survival and value of liver transplantation for liver carcinoma: a single-center experience


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.

Health technology
The study investigated the use of orthotopic liver transplantation for the treatment of hepatocellular carcinoma (HCC) in different stages. Liver transplantation was performed without venovenous bypass, while all patients received three to six courses of chemotherapy after the operation (20 mg epirubicin for 2 days, 750 mg 5-fluorouracil for 5 days, and 6 mg mitomycin for 2 days).

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with liver carcinoma with HBV cirrhosis. No further inclusion or exclusion criteria were reported.

Setting
The setting was tertiary care (i.e. Institute of Organ Transplantation). The economic analysis was carried out in China.

Dates to which data relate
The effectiveness data were obtained between January 1999 and February 2002. The dates to which the cost data referred were not reported. The price year was also not reported.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was carried out retrospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The sample size was not determined in the planning phase of the study. In addition, power calculations were not performed retrospectively, based on the existing sample. During the study period, 138 patients had a liver transplant but only 50 (36.3%) cases were selected according to their disease (i.e. only those patients suffering from HCC). Forty-two of these patients were men and 8 were women. These 50 patients were divided into three categories according to their stage of disease. Stage I (early stage) comprised 4 patients with a tumour size less than 5 cm and apparent cirrhosis.
Stage II (middle stage) comprised 32 patients either with a tumour size greater than 5 cm or where the number of tumour nodules was more than two masses but was limited to the liver. Stage III (late stage) comprised 14 patients with cancer embolism in the portal vein, or with local invasion and metastasis.

**Study design**
The analysis was based on a single-centred, retrospective cohort study. The patients were followed up until their death. The longest follow-up period was 3 years after transplantation (up to the date of publication of the study). No blinded assessment was reported.

**Analysis of effectiveness**
The primary health outcome used in the analysis was the survival rate after liver transplantation. A secondary health outcome was the recurrence rate of HCC. All of the patients were included in the analysis. The authors do not seem to have investigated whether the characteristics of the patients were comparable at baseline and no adjustment for confounding factors was reported.

Survival rates between the groups were compared using the log-rank test, where a p-value of less than 0.05 was considered statistically significant.

**Effectiveness results**
All patients in stage 1 survived until the date of publication of the study. Their survival ranged from 1 to 3 years.

The survival rates of patients in stage II was 71.9% at 4 months after transplantation, 65.64% at 8 months and 39.38% at 1 year. Only 7 patients survived more than 1 year after the operation.

The survival rate of patients in stage III was 57.14% at 4 months after transplantation and 14.28% at 8 months. Only one patient survived 12 months.

The results of the statistical analysis demonstrated that the survival rates differed significantly according to the stage of HCC, (p<0.01).

The rate of HCC recurrence after transplantation was 56.0% in stage II and 64.3% in stage III.

**Clinical conclusions**
The authors concluded that patients in stage I face better survival rates and have a chance of radical cure after liver transplantation. On the other hand, liver transplantation followed by chemotherapy may increase survival rates for Stage II patients, while the operation had very poor outcomes in Stage III patients.

**Measure of benefits used in the economic analysis**
The authors did not derive a summary measure of benefits. In effect, a cost-consequences analysis was performed.

**Direct costs**
The costs of liver transplantation (medical/hospital), hospitalisation, and medical treatment for 0.5 years after transplantation were included. The costs and the quantities were not analysed separately and the unit costs were not reported. Resources use was most probably derived from the effectiveness analysis, while the source of the cost data and the price year were not reported. Discounting was not relevant since the costs were incurred during less than 2 years. In the cost analysis for patients in stage III, the costs of 12 patients who survived less than 0.5 years after transplantation were not included. The average costs per patient were reported.
Statistical analysis of costs
Comparisons of costs between the patients in the three stage groups were carried out using variance analysis and Q test. A p-value of less than 0.05 was considered statistically significant.

Indirect Costs
No indirect costs were included in the economic analysis.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The authors reported that the average cost for liver transplantation was $27,100 (+/- 108) for Stage I patients, $31,500 (+/- 260) for Stage II patients and $35,500 (+/- 134) for Stage III patients.

The statistical analysis demonstrated that the cost for Stage I patients was significantly lower than that for Stage II and Stage III patients (this result was not shown).

Synthesis of costs and benefits
The costs and benefits were not combined.

Authors’ conclusions
Liver transplantation is an effective treatment option that "achieves good economic results" for patients in early-stage liver carcinoma. However, it is connected with high medical costs and poor outcomes in patients with advanced liver cancer.

CRD COMMENTARY - Selection of comparators
The selection of the health technology used was justified on the grounds that it is a commonly used treatment option in the authors' setting. However, the authors did not discuss the existence of alternative therapies. If there are any, which is likely, it makes this study only a partial analysis.

Validity of estimate of measure of effectiveness
The analysis was based on a retrospective cohort study. The study referred to patients with liver carcinoma with HBV cirrhosis. It is likely that the study sample was representative of the study population as there was no sample selection. However, no further details of the patients were provided and the baseline characteristics of the patients were not compared. Hence, the generalisability of the findings may be limited. An appropriate statistical analysis was undertaken to compare the survival rates of the patients, but no statistical analyses were reported in which potential biases and confounding factors were considered. In addition, no power calculations were reported, making it difficult to ascertain whether the sample size was sufficient to detect statistically significant differences in the outcomes.
Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefits. In effect, a cost-consequences analysis was performed.

Validity of estimate of costs
The perspective adopted was not reported, and the use of summary costs makes it impossible to ascertain what aspects of costs were included. As the analysis did not include the cost of the 12 patients who survived less than 0.5 years in the Stage III group, the expenses of these patients might have been underestimated. The costs and the quantities were not reported separately, thus it would be difficult to rework the analysis for other settings. The source of the resource quantities, although not explicitly stated, was the effectiveness study, but no statistical analysis of the quantities was performed. The source of the prices (unit costs) was not reported, and no statistical analysis of the prices was conducted. These facts limit the generalisability of the results. Discounting was not relevant since the costs were incurred during less than 2 years and, appropriately, was not carried out. The authors did not report any currency conversions or the price year, which may impede any future reflation exercises.

Other issues
The authors did not compare their findings with those from other studies, so it is not known whether their results are consistent with those from other published studies. The issue of the generalisability of the results to other settings was not addressed. The authors do not appear to have presented their results selectively. The study enrolled patients with liver carcinoma in different stages and with HBV cirrhosis, and this was reflected in the authors' conclusions. The authors did not report any limitations to their study.

Implications of the study
The authors recommended "the patient's stage of liver carcinoma should be first estimated and a survival-value analysis should be performed before liver transplantation, so as to choose the patients who are fit for liver transplantation making full use of the precious donor liver and the expensive medical fees". The authors did not make any explicit recommendations for further research. They also suggested that preventing tumour recurrence is still a key question in patients in stage II. Options suggested included "treatment of HCC before transplantation, preventing tumour dissemination and metastasis during the operation, as well as application of special and sensitive chemotherapy after transplantation".

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