Randomized study comparing banding and propranolol to prevent initial variceal haemorrhage in cirrhotics with high-risk esophageal varices

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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.

Health technology
The use of endoscopic, multi-shot banding (Speedband Microvasive Inc., Natick; Saeed Six-Shooter, Wilson-Cook Inc., Winston-Salem) for prophylactic oesophageal variceal ligation in patients with cirrhosis with large or high-risk oesophageal varices.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients referred for orthotopic liver transplantation (OLT). Enrolled patients were those who had given written consent, were between 18 and 75 years of age, had clinically evident or biopsy proven cirrhosis of the liver, and large or high-risk non bleeding oesophageal varices documented endoscopically. These patients also had no prior upper gastrointestinal bleed, no prior endoscopic or surgical treatment of varices or ascitis, no current beta-blocker therapy, and a life expectancy of at least 24 months (as judged by the hepatologist). Patients with co-morbid illness, contraindication to beta-blockers, severe coagulopathy, severe thrombocytopenia, increased alpha fetoprotein, or documented hepatoma, portal or hepatic vein thrombosis were excluded. Other exclusion criteria were large volume ascitis, contraindication to therapeutic endoscopy, the presence of moderate or large gastric or duodenal varices, oesophagitis or oesophageal stricture, and severe recurrent upper gastrointestinal bleeding. Women with positive beta human chorionic gonadotropin were also excluded.

Setting
The setting was tertiary care. The economic study was carried out in three medical centres in California, USA, where OLT was available.

Dates to which data relate
The effectiveness data and the cost data were collected between July 1996 and June 2001.

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

Link between effectiveness and cost data
The cost data were prospectively based on the same patient sample that provided the effectiveness results.
Study sample
Power calculations were used to determine the sample size. A total of 259 patients with cirrhosis, without prior haemorrhage, were referred for possible randomisation after assessment according to the inclusion and exclusion criteria. Of these, 197 were excluded from randomisation and 62 were randomised. Randomisation assigned 31 to prophylactic oesophageal variceal ligation and 31 to prophylactic propranolol.

Study design
The study was an RCT that was carried out in three centres (Los Angeles Medical Centre, San Diego Medical Centre and Veterans Administration Los Angeles HealthCare System). A separate randomisation schedule was provided for each centre in permuted blocks of 4. The follow-up period was up to 2 years. Treatment was assigned by the opening of sealed opaque envelopes. Compliance was good and no patient was lost to follow-up. Two patients on propranolol developed symptomatic hypotension and first-degree heart block, and propranolol was discontinued.

Analysis of effectiveness
The analysis of effectiveness was conducted on an intention to treat basis. The primary outcome for the clinical study was treatment failure (i.e. endoscopically documented variceal haemorrhage, or severe medical complication requiring discontinuation of therapy).

Effectiveness results
The treatment failure rate was significantly higher in the propranolol patients (6 of 31) than in the banding patients (0 of 31). The difference was 19.4% (95% confidence interval, CI: 6.4 - 37.2), (p=0.0098).

Significantly more propranolol patients (4 of 31) than banding patients (0 of 31) had oesophageal variceal haemorrhage. The difference was 12.9% (95% CI: 0.8 - 29), (p=0.44).

Overall mortality was higher in the propranolol group (4 of 31 versus 0 of 31). The difference was 12.9% (95% CI: 0.8 - 29).

No other difference in secondary outcomes was significant. The rates of liver transplantation were similar in both groups.

Clinical conclusions
For patients with cirrhosis with high-risk oesophageal varices and no history of variceal haemorrhage, propranolol-treated patients had significantly higher rates of treatment failure, first oesophageal haemorrhage and cumulative mortality than banding patients.

Measure of benefits used in the economic analysis
The authors did not use a summary benefit measure in the economic analysis. In effect, the study was a cost-consequences analysis.

Direct costs
The quantities and costs were estimated using data from the study, but the resource quantities and the unit costs were not reported separately. The quantity of resources was measured during the study period. Discounting was not carried out, but it would not have been relevant as the costs were mainly incurred in less than 2 years. All the direct costs up to and including bleed-related hospitalisation were included in the final cost analysis. The direct fixed and variable costs of medical care were estimated for all resources consumed. Physician or technical fees were estimated using Medicare reimbursement rates. The price year was not specified.
Statistical analysis of costs
The mean values and p-values were provided. The authors employed several statistical tests according to the characteristics of the data. An unspecified test was used for the costs.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
Due to the cost-consequences approach undertaken, see the 'Effectiveness Results' section.

Cost results
The mean overall direct cost was $3,300 (standard deviation, SD=1,289) for the prophylactic propranolol therapy group and $2,228 (SD=495) for band ligation.

Synthesis of costs and benefits
The costs and benefits were not combined because of the cost-consequences approach.

Authors' conclusions
Prophylactic banding seems to be a more promising therapy than propranolol for the prevention of initial variceal bleeding in compliant patients who are at high risk of initial variceal haemorrhage and who are candidates for liver transplantation. The propranolol group had significantly higher treatment failures and, arithmetically, more frequent adverse events requiring the discontinuation of therapy. The direct costs of the propranolol group were not significantly less than those for banding.

CRD COMMENTARY - Selection of comparators
The comparator was explicitly stated and, although no detailed justification was given for its selection, it would appear to represent current practice in the authors' setting. You should decide if the comparator represents current practice in your own setting.

Validity of estimate of measure of effectiveness
The study sample was representative of the study population and the patient groups were shown to be comparable at analysis. The estimates of effectiveness are likely to have been valid because of the absence of selection bias; group allocation was decided by drawing of lots. There were no missing data. Appropriate statistical analysis were performed and clearly reported. The sample size was determined by a power calculation.

Validity of estimate of measure of benefit
The estimate of benefits used was obtained directly from the effectiveness analysis in the form of a cost-consequences approach. The comments in the 'Validity of estimate of measure of effectiveness' field (above) therefore apply.
Validity of estimate of costs
The costs and the quantities were not reported separately but a statistical analysis of the mean costs was performed. Although the costs for a 3-year follow-up were calculated, most of the costs were incurred in less than 2 years. Discounting was therefore unnecessary and, appropriately, was not carried out. The date to which the prices related was not reported, but these were obtained from a paper published 2 years before the study.

Other issues
The authors made appropriate comparisons of their findings with those from other studies. The issue of generalisability to other situations was not addressed. The authors provided a wide and comprehensive discussion of the reliability of their results and highlighted relevant caveats.

Implications of the study
The authors suggested that prophylactic banding reduces the rate of initial haemorrhage in comparison with propranolol, but does not reduce bleed-related mortality or overall mortality. There were no specific recommendations for further research.

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