How should transection of the liver be performed? A prospective randomized study in 100 consecutive patients: comparing four different transection strategies
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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 study compared four different techniques for parenchyma transection in patients with liver resection:

- clamp crushing technique under inflow occlusion (Pringle manoeuvre);
- an ultrasonic dissector (Cavitron Ultrasonic Surgical Aspirator, CUSA; Tyco Healthcare, Mansfield, MA) with ultrasonic energy (23 kHz standard tip, cauter 70 Watt and flush 4 mL/min);
- the Hydrojet (Erbe, Tubingen, Germany) using a pressurised jet of water; and
- a dissecting sealer (TissueLink, Dover, NH) that used radiofrequency energy.

The last three techniques involved no Pringle manoeuvre and inflow occlusion was used only in cases of significant bleeding and when blood loss exceeded 500 mL.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients who underwent liver resection with partial hepatectomy (2 or more segments) for benign and malignant tumours, and an appropriate clotting profile (platelet count >100 x10⁹/L and prothrombin activity >60%) were included in the study. Cirrhotic and cholestatic patients (i.e. serum bilirubin >100 micromol/L) were excluded from the study.

Setting
The interventions were provided by a secondary care provider in an inpatient setting. The economic study was carried out in Zurich, Switzerland.

Dates to which data relate
The effectiveness and resource use data were collected from June 2003 to September 2004. The price year was 2004.

Link between effectiveness and cost data
The costing appears to have been carried out prospectively on the same sample of patients as that used in the economic analysis.
Study sample
Power calculations demonstrated that the study had 80% power to detect a 30% difference in blood loss or resection time during parenchyma transection in at least one group with a level of significance of 0.50. Power calculations were performed using a post hoc 2-sample t-test with a Bonferroni correction. The sample size was also determined in order to detect a 100 IU/L difference in the opening (6 hours after surgery) or peak aspartate aminotransferase levels with a standard deviation of 100 IU/L. The initial sample comprised 110 consecutive patients. Of these, 4 refused to participate and 6 did not receive liver resection because of extrahepatic disease or an unresectable tumour diagnosed at the time of laparoscopy or laparotomy. The 100 eligible patients (53 men and 47 women) were randomised in the four groups, (25 in each group). The mean age was 56 (+/- 1) year.

Study design
The analysis was based on a prospective, randomised controlled trial that was carried out in a single centre. Randomisation was performed for each patient the night before surgery using sealed envelopes. Each patient was followed up for 3 months. It was reported that 4 patients died within 30 days after hepatectomy (1 because of mesenteric arterial infarction and 3 because of sepsis and multi-organ failure). No other patients were reported to have been lost to follow-up.

Analysis of effectiveness
The analysis was conducted on an intention to treat basis. Statistical analyses demonstrated that the patient groups were comparable in terms of their baseline characteristics. The primary health outcomes were blood loss during parenchyma transection, resection time and postoperative hepatocyte injury. The latter was evaluated using daily measurements of postoperative aspartate aminotransferase and alanine aminotransferase levels, bilirubin levels, and prothrombin times until hospital discharge. The procedure for estimating blood loss was reported in detail.

Effectiveness results
The results were reported in detail. However, they are too numerous to list in this abstract, therefore only statistically significant results are reported.

Compared with the other three techniques the clamp crushing technique had a significantly (almost 2-fold) faster transection speed (3.9 +/-0.3 cm2/minute; p=0.001).

The blood loss per resection surface was significantly lower (about 2-fold) for the clamp crushing technique compared with the other three techniques (1.5 +/-0.3 mL/cm2; p=0.003).

The clamp crushing group required fewer blood transfusions (5-fold less) during or within 24 hours after surgery compared with the other three techniques. The difference was statistically significant, (p=0.06).

There were no statistically significant differences between the four techniques in terms of the postoperative prothrombin time and in bilirubin levels.

Clinical conclusions
The authors concluded that “the cramp crushing technique was the most efficient device in terms of resection time, blood loss and blood transfusion frequency compared to the CUSA, the Hydrojet and the dissecting sealer”.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the economic analysis. In effect a cost-consequences analysis was performed.

Direct costs
Costs related to liver resection were included in the analysis. These covered the devices (i.e. clamp crushing technique, CUSA, Hydrojet, and dissecting sealer), including the cost of capital, maintenance and disposal material, as well as operating room time, additional methods to control bleeding, and transfused red blood cell units. The costs were reported per case and capital equipment incurred 5-year depreciation. The resources used and cost data were derived from the accounting department in the authors' setting. Physicians' fees and costs of postoperative complications, intensive care unit and hospital stay were demonstrated not to differ significantly amongst the groups and were therefore not accounted for in the economic analysis.

**Statistical analysis of costs**
Comparisons between groups were performed using an analysis of variance. The post hoc Bonferroni test was also used when necessary.

**Indirect Costs**
Inline with the perspective adopted, productivity losses were not included in the analysis.

**Currency**
Euros (EUR).

**Sensitivity analysis**
Since the costs of capital equipment and maintenance depend on the number of cases performed per year, the authors investigated the impact of the volume of liver resections performed on the economic results using a one-way sensitivity analysis. Three different scenarios were estimated, accounting for 10, 50 or 100 liver resections performed per year.

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

**Cost results**
The total costs were reported as the mean cost per case (liver resection).

For clamp crushing, the cost was EUR 497 (+/- 38) for all three scenarios (10, 50, or 100 liver resections performed per year).

For dissecting sealer, the cost was EUR 1,618 (+/- 45) for the three scenarios.

For CUSA, the cost ranged from EUR 2,912 (+/- 73) for a centre volume of 10 cases per year to EUR 1,587 (+/- 73) for a volume of 100 cases per year.

For the Hydrojet, the cost ranged from EUR 2,235 (+/- 97) for a centre volume of 10 cases per year to EUR 1,125 (+/- 97) for a volume of 100 cases per year.

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

**Authors' conclusions**
"The clamp crushing technique proved to be the most cost-efficient device with the highest cost-saving potential among all four tested devices."
CRD COMMENTARY - Selection of comparators
A justification was provided for the technologies compared. They are commonly used in the authors' setting but their relative merits were unknown. You should decide if these represent valid health technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a prospective, single-centred, randomised controlled trial. Power calculations were performed to ensure that the size of the study sample was adequate. The authors described the study sample in some detail, thus enabling readers to draw comparisons between their own patients and those in the study. The fact that the patients were enrolled sequentially (rather than selectively) may provide a strong indication that the sample was typical of the study population. The methods of randomisation, length of stay and loss to follow-up were all reported, suggesting that the internal validity of the study is likely to be reasonably high. The study protocol was thoroughly reported and designed so as to minimise potential bias. In addition, adequate statistical analysis was undertaken and the analysis was handled credibly.

Validity of estimate of measure of benefit
The authors did not derive a summary measure of benefit in the economic analysis. In effect, a cost-consequences analysis was performed. The reader should refer to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
Although the perspective adopted in the economic analysis was not explicitly reported, the costs included suggest that the perspective was that of a health service provider. Resource use appears to have been determined using a micro-costing methodology, therefore detailing all the cost components might not have been possible. Price information and resource use data were obtained from the accounting department in the authors' setting. However, it is not possible to comment on the generalisability of the costing. Some relevant costs were omitted from the analysis on the assumption that they were similar in all groups and, as such, their omission is unlikely to have affected the authors' conclusions. The costs were incurred during a short time therefore discounting was not relevant. Statistical analysis of the costs was undertaken, but a sensitivity analysis was not performed to investigate uncertainty in the cost estimates used; it was only performed to investigate the impact of volume of surgeries performed.

Other issues
The authors compared their findings with those from other studies which, in general, were in agreement. The results of the study do not appear to have been presented selectively, and the conclusions appear to be an adequate reflection of the scope of the analysis. The authors reported a number of limitations to their study. First, the study had insufficient power to detect differences in postoperative mortality, morbidity and bile leak. To deal with this shortcoming, the authors included routine ultrasound at the fifth day after surgery and a computed tomography scan at 3 months. Second, as patients were followed up for 3 months the long-term outcomes were not investigated. In addition, since postoperative liver biopsy was not included in the study, complicated postoperative issues such as hepatocyte apoptosis, area of necrosis, and activation of pathways of injury were not investigated. The authors appear to have presented a balanced discussion, enlightening various aspects of the analysis.

Implications of the study
As this was the first randomised controlled trial to be conducted that compared the four techniques, the authors recommend further research to explore the clinical effect of CUSA, Hydrojet and dissecting sealer in patients with a diseased liver.

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