Preoperative versus postoperative endoscopic retrograde cholangiopancreatography in mild to moderate gallstone pancreatitis: a prospective randomized trial
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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
Routine preoperative endoscopic retrograde cholangiopancreatography (ERCP) with endoscopic sphincterotomy (ES) followed by laparoscopic cholecystectomy, or laparoscopic cholecystectomy with intraoperative cholangiography (IOC) followed by selective postoperative ERCP for proven common bile duct (CBD) stones in patients with mild to moderate gallstone pancreatitis without cholangitis.

Type of intervention
Diagnosis, treatment, and secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study investigated patients with mild to moderate gallstone pancreatitis without cholangitis. Patients considered at high risk for persisting CBD stones who met any of the following three criteria were eligible for study inclusion: CBD dilatation equal to or greater than 8 mm on admission ultrasonography; elevation of the serum total bilirubin equal to or greater than 1.7 mg/dL on hospital day 4; or serum amylase equal to or greater than 150/L on hospital day 4. In addition, patients were randomised only if they demonstrated evidence of resolving pancreatitis, as determined by a decreasing serum amylase level and reduced abdominal pain. Patients with cholangitis or necrotising pancreatitis were excluded. Cholangitis was defined as a temperature greater than 38.6 degrees C, right upper quadrant pain and tenderness, and hyperbilirubinemia. Necrotising pancreatitis was identified by computed tomography of the abdomen using bolus injection of intravenous contrast.

Setting
The study setting was hospital. The economic analysis was carried out in California, USA.

Dates to which data relate
The effectiveness and resource use data corresponded to those patients admitted to the study hospital between July 1994 and September 1996. The price year was not specified.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing was conducted prospectively on the same patient sample as that used in the effectiveness analysis.
Study sample
Power calculations were not used to determine the sample size. A total of 154 patients with a diagnosis of gallstone pancreatitis were admitted to the study hospital; of these 60 patients met the randomisation criteria. One patient refused to participate. The remaining 59 patients were randomly assigned to either routine preoperative ERCP (n=30) with a mean age of 39 +/- 14.7 years or selective postoperative ERCP (n=29) with a mean age of 38.4 +/- 13.8 years.

Study design
The study took the form of a randomised, controlled trial carried out in a single centre. The duration of follow-up appears to have been until discharge or 30 days after operation. The study had no loss to follow-up. Randomisation was performed using sealed envelopes on hospital day 4. Randomisation was delayed until hospital day 4 which allowed time for the pancreatitis to resolve; it also provided the opportunity to apply the authors' previously reported criteria for predicting persisting CBD stones in gallstone pancreatitis to maximise the yield of ERCP.

Analysis of effectiveness
The principle used in the analysis of effectiveness was reported to have been intention to treat. The primary health outcome measure was combined treatment failure rate (failure of IOC and diagnostic ERCP, complications of surgery, and complications of therapeutic ERCP with ES and stone extraction). Other outcomes were length of hospital stay and utilisation rate of ERCP. Outcomes of non-randomised patients were also reported. Comparing the proportion of patients who had CBD stones in patients who met the randomisation criteria and those who did not meet them assessed the utility of randomisation criteria. The study groups were found to be comparable in terms of age, admission laboratory values, and APACHE II and Imrie scores.

Effectiveness results
There were no statistically significant differences between the groups with regard to combined failure rates of cholangiography, CBD stone retrieval, or morbidity rates for ERCP and surgery (10% for the group randomised to preoperative ERCP versus 10.3% for group randomised to postoperative ERCP, odds ratio 1.04, 95% CI: 0.22 - 4.9).

Mean hospital stay was significantly longer in the routine preoperative ERCP group (11.7 days) than in the selective postoperative ERCP group (9.0 days).

The utilisation rate of ERCP was significantly reduced from 100% in the routine preoperative ERCP group to 24% in the selective postoperative ERCP group, (p<0.0001).

In the non-randomised patients (one underwent preoperative ERCP and the rest did not) there were 6% complications overall; two patients required readmission within 30 days for elevated liver chemistries and abdominal pain. A total of 35% (95% CI: 23% - 48%) of patients who met the randomisation criteria had CBD stones versus 9% (95% CI: 3.8% - 18%) in those who did not meet them, (p=0.0001).

Clinical conclusions
The timing of ERCP (routine preoperative versus selective postoperative) did not affect clinical outcomes (combined treatment failure rate). The combined treatment failure rate was acceptable (10%) (95% CI: 4% - 21%), supporting the use of selective postoperative ERCP. In the present study, all CBD stones were successfully retrieved or passed spontaneously without the need for further operation.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only individual clinical outcomes were reported. The economic analysis appears to have been conducted on the basis of cost-minimisation based on the equal efficacy of the two alternative treatment approaches in terms of the primary clinical measure (combined failure rate).
Direct costs
Costs were not discounted but this was appropriate for the short time frame of the cost analysis. Some quantities were reported separately from the costs and cost items were reported separately. The cost analysis covered the costs of hospital stay (intensive care unit (ICU) and ward), diagnostic ERCP, and therapeutic ERCP with ES and stone extraction. The perspective adopted in the cost analysis was not explicitly specified. Hospital charges and Medicare reimbursement were used to calculate the total costs; the authors reported that they had been unable to obtain actual costs for all aspects of patient care. The price year was not explicitly specified. The cost analysis did not cover anaesthesia costs.

Statistical analysis of costs
The Wilcoxon rank-sum test was reported to have been used to compare the groups in terms of continuous variables (which included costs).

Indirect Costs
Indirect costs were not considered.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was conducted.

Estimated benefits used in the economic analysis
See effectiveness results reported above.

Cost results
The mean (SD) total cost was $10,210 (3,839) in the group randomised to preoperative ERCP versus $8,586 (3520) in the group randomised to postoperative ERCP, (p=0.049).

Synthesis of costs and benefits
Costs and benefits were not combined, which was appropriate as the economic analysis was performed on a cost-consequences/cost-minimisation basis.

Authors' conclusions
In patients with mild to moderate gallstone pancreatitis without cholangitis, selective postoperative ERCP and CBD stone extraction is associated with a shorter hospital stay, less cost, no increase in combined treatment failure rate, and a significant reduction in ERCP use compared with routine preoperative ERCP.

CRD COMMENTARY - Selection of comparators
No specific strategy was regarded as the comparator as the authors believed that the role and timing of ERCP in mild to moderate gallstone pancreatitis remains controversial. You, as a database user, should consider which strategy is widely used in your own setting.

Validity of estimate of measure of effectiveness
The internal validity of the effectiveness results is likely to be high due to the randomised nature of the study design,
the comparability of the study groups, and the fact that the effectiveness analysis was based on intention to treat. However, the limited sample size precluded a more precise comparison of the combined failure rates between the two treatment approaches; this was reflected in the relatively wide 95% CI for the odds ratio comparing these rates (0.22 - 4.9). The study group appears to have been representative of the study sample (patients at high risk for CBD stones).

**Validity of estimate of measure of benefit**
The analysis of benefits appears to have been based upon therapeutic equivalence of treatment alternatives. The economic analysis therefore included only costs.

**Validity of estimate of costs**
The following features of the analysis may have enhanced the validity of the cost analysis: some details of methods of cost estimation were given; and statistical analyses were performed on resource use and cost data. However, the resource use profile was not fully reported separately from the costs; the price year and perspective adopted in the cost analysis were not specified; the cost data were based on charges/Medicare reimbursement data rather than on true costs; the effects of alternative treatment strategies on indirect costs were not addressed. These features mean that the cost results may not be generalisable outside the study setting.

**Other issues**
The authors’ conclusions appear to be justified given the uncertainties in the data. The authors did not specifically address the issue of generalisability to other settings or countries, although appropriate comparisons were made with other studies. The degree to which the study sample was representative of the study population was addressed in the authors comments.

**Implications of the study**
In terms of clinical practice selective postoperative ERCP and CBD stone extraction offers both clinical and economic benefits. Additionally, the utility of the study inclusion criteria has recently been prospectively confirmed, although on multivariate analysis the single best predictor of CBD stones proved to be a serum total bilirubin greater than 1.35 mg/dL, on hospital day 2. The authors plan to use this revised criterion henceforth.

Had those 77 patients who did not meet randomisation criteria been randomised (using a wider inclusion criterion), the costs of diagnostic ERCP would have increased substantially, with only a very small increase in the number of CBD stones retrieved.

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