Endoscopic ultrasonography versus cholangiography for the diagnosis of choledocholithiasis

Canto M I, Chak A, Stellato T, Sivak M V

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
Using EUS (endoscopic ultrasonography) with cholangiography in the diagnosis of pre and post-cholecystectomy patients with suspected choledocholithiasis.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Pre and post-cholecystectomy patients with a history of gallstones, who were referred for suspected choledocholithiasis.

Setting
Hospital. The economic study was carried out in Ohio, USA.

Dates to which data relate
Effectiveness and resource use data related to patients diagnosed and treated between January and December 1994 with a follow-up to January 1996. The fiscal year was not explicitly specified.

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

Link between effectiveness and cost data
Costing was prospectively performed on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample initially consisted of 70 patients, 6 of whom refused to participate in the study. The remaining 64 patients had a mean age of 53 (range: 22 - 92) years. The distribution of patients across different risk groups was as follows:

20 patients with a mean age of 56 (range: 30 - 92) in the high-risk group
14 patients with a mean age of 62 (range: 31 - 91) in the moderate-risk group
22 patients with a mean age of 48 (range: 22 - 83) in the indeterminate-risk group
8 patients with a mean age of 45 (range: 24 - 73) in the low-risk group.

**Study design**
The study was a prospective, sequential, self-controlled, blinded study, carried out in a single centre. EUS and ERCP were sequentially performed on all patients. EUS was independently performed by one of two experienced endosonographers blinded to the clinical history of patients, laboratory data, or radiologic imaging results. Immediately after EUS, ERCP was performed by one of three experienced biliary endoscopists blinded to the results of the EUS, but aware of the clinical history and results of transabdominal ultrasonography (US), computed tomography (CT), or prior attempted ERCP. The duration of the follow-up was at least 12 months until January 1996. No loss to follow-up was reported.

**Analysis of effectiveness**
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified.

Patients were categorised by risk group (high, moderate, indeterminate, and low) based on predefined clinical, biochemical, and radiographic criteria.

The clinical outcome measures were success rate, image quality (rated on a three-point ordinal scale of excellent, good, poor), diagnostic certainty (rated on a three-point ordinal scale of very certain, moderately certain, and uncertain or indeterminate)), accuracy, sensitivity, specificity, positive and negative predictive value (PPV and NPV), diagnostic yield, and procedure-related complications.

The actual prevalence of choledocholithiasis was determined by stone extraction at ERCP or cholecystectomy.

The percentage of patients with choledocholithiasis diagnosed by US and/or CT in different risk groups was also reported.

The concordance between EUS and ERCP results was determined by calculating the Kappa score.

**Effectiveness results**
The overall prevalence of choledocholithiasis determined by stone extraction at ERCP or cholecystectomy was 31%; with a distribution of 71% in the high-risk group, 28% in the moderate-risk group, 0% in the low-risk group, and 4% in the indeterminate-risk group (p=0.001, for the differences among the groups).

The percentage of patients with choledocholithiasis diagnosed by US and/or CT was 36% in the high-risk group and 0% in other risk groups.

The success rate of EUS was 98% versus 94% for ERCP, (p=0.71).

The percentage of images with good or excellent quality was 92% for EUS and 91.7% for ERCP, (p=0.68).

The diagnostic certainty of EUS was 92% versus 95% for ERCP, (p=0.49).

US/CT sensitivity rates were 20%, specificity rates were 95% and accuracy rates were 71%. For EUS the sensitivity rate was 84%, specificity was 98% and accuracy was 94%. This compared to 95% sensitivity rates, 98% specificity rates and 97% accuracy rates for ERCP.

The observed agreement between EUS and ERCP was 91.5% with a Kappa value of 0.79 (excellent).

EUS had an overall PPV of 94% and NPV of 93%.

There were three cases of false negative results for EUS versus two for ERCP.
The accuracy, sensitivity, specificity, PPV, and NPV of EUS for choledocholithiasis by risk group were as follows:

- for high-risk group, 90% accuracy, 85% sensitivity, 100% specificity, 100% PPV, and 75% NPV;
- for moderate-risk group, 93% accuracy, 75% sensitivity, 100% specificity, 100% PPV, and 91% NPV;
- for low-risk group, 100% accuracy, NA (not applicable) sensitivity, 100% specificity, NA PPV, and 100% NPV;
- and for indeterminate-risk group, 95% accuracy, 100% sensitivity, 95% specificity, 75% PPV, and 100% NPV.

The prevalence of choledocholithiasis in terms of pre-cholecystectomy (n=36) was 19% and post-cholecystectomy (n=28) 43%, (p=0.04).

The accuracy of US/CT for pre-cholecystectomy patients was 80% and for post-cholecystectomy patients was 64%, (p>0.05). The accuracy of EUS for pre-cholecystectomy patients was 94% and for post-cholecystectomy patients was 93%, (p>0.05). The corresponding values for ERCP were 97% for pre-cholecystectomy patients and 96% for post-cholecystectomy patients, (p>0.05). The differences between US/CT accuracy and EUS accuracy for both pre- and post-cholecystectomy patients were significant (p<0.05). The corresponding differences between EUS and ERCP were not significant.

EUS had a diagnostic yield of 93% over US/CT for bile duct stones. In 21% of patients EUS was associated with correctly identifying significant additional or alternative diagnoses compared to US and/or CT. ERCP, similarly to EUS, diagnosed all pathologic abnormalities, except for the malignant lymph nodes. The overall complication rate was 1.6% for EUS versus 12.5% for ERCP, (p=0.001), and 9.4% for diagnostic ERCP, (p<0.05).

Clinical conclusions
The extremely low failure rate of EUS is one distinct advantage over ERCP, which has a failure rate of 5% to 10% even in experienced hands. Hence EUS is an excellent alternative imaging modality to perioperative ERCP. Furthermore, the lack of exposure to ionising radiation and contrast make EUS the best diagnostic test for pregnant patients and those with contrast allergy. Most importantly, EUS was significantly much safer than diagnostic ERCP.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported. The economic analysis may therefore be regarded as a cost-consequences analysis.

Direct costs
Costs were not discounted and it is not clear whether this was justified due to the varying periods to which the cost analysis related. Few quantities were reported separately from the costs. Cost items were reported separately in terms of risk group rather than detailed resource use. The cost analysis covered the costs of hospital facility and professional fees for EUS, diagnostic ERCP, endoscopic sphincterotomy, stone extraction; diagnosis, treatment, and hospitalisation for procedure-related complications; and extra procedures performed because of failure or diagnostic uncertainty, or false positives. The perspective adopted in the cost analysis was that of the third-party payer. The costing was based on actual resource use and the existing approach to the management of bile duct stones at the study institution. The unit costs were Medicare reimbursement figures (rather than charges), which were collected from the university hospital and faculty practice billing offices. The date of the price data was not explicitly specified. The cost analysis did not cover the costs of radiology related to ERCP (use of fluoroscopy and radiology technicians) since “all ERCPs were performed in the Digestive Disease Centre's fluoroscopy room without a technician”.

Statistical analysis of costs
The comparison of costs between the two EUS and ERCP-based strategies was conducted using nonparametric methods, including the Wilcoxon rank-sum test.
Indirect Costs
Not considered.

Currency
US dollars ($).

Sensitivity analysis
Not conducted.

Estimated benefits used in the economic analysis
Not applicable. The reader is referred to the effectiveness results reported above.

Cost results
The EUS based strategy had an overall mean total cost of $754 versus $1,109 for the ERCP-based strategy. The corresponding values for the high-risk group (n=20) were $1,772 for EUS and $1,718 for ERCP, (p=0.45). For the moderate or indeterminate risk group (n=36), the cost was $1,125 for EUS and $1,610 for ERCP, (p=0.003), and for the low-risk group (n=8) cost was $770 for EUS and $1,190 for ERCP, (p=0.008).

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

Authors’ conclusions
EUS is comparably accurate, but safer and less costly than ERCP in evaluating patients with suspected choledocholithiasis. It is useful in patients with an increased risk of having common bile duct stones based on clinical criteria and those with contraindications for or prior unsuccessful ERCP. EUS may enable selective performance of ERCP and improve the cost-effectiveness of diagnosing choledocholithiasis.

CRD COMMENTARY - Selection of comparators
It is not clear why the comparator used was chosen, nor do the authors provide a justification for its choice. The authors point out a number of alternative comparators that were not assessed in their analysis (see implications below). You, as a database user, should decide whether the health technologies studied are widely used in your own setting.

Validity of estimate of benefit:
The analysis was based on a prospective, sequential, self-controlled, blinded design, which was appropriate for the study question and which is likely to have high validity. The study sample would appear to have been representative of the study population.

Validity of estimate of costs
For the chosen perspective, some relevant costs were omitted from the analysis. The costs of radiology related to ERCP (use of fluoroscopy and radiology technicians) were excluded because all ERCPs were performed in the Digestive Disease Centre's fluoroscopy room without a technician. However, these omissions are unlikely to significantly affect the cost-effectiveness results. The reliability of the cost results is weakened by the fact that quantities were not fully reported separately, and no statistical analysis of quantities was performed. Medicare reimbursement data were used to proxy costs and no price year was given, both of which may also limit the generalisability of the findings.
Other issues
The authors reported a number of limitations to their study, namely not considering all potential alternatives for managing bile duct stones, and certain inherent limitations of EUS (for example, the impossibility, in some cases, of passing the ultrasonic endoscope into the duodenum; or the operator-dependency of the EUS sensitivity which leads to differing accuracy rates in the community and in academic centres with less experience in EUS). The authors did make appropriate comparisons of their findings with those of other studies.

The issue of generalisability to other settings or countries was partially addressed by pointing out the possible setting-dependency of the accuracy rate of EUS. The authors do not appear to have presented their results selectively. The study covered patients with suspected choledocholithiasis in all risk categories which meant that it suffered from low sample size in each risk category, but the authors’ conclusion did not take fully into account this limitation.

Implications of the study
Future studies should compare the clinical utility and cost-effectiveness of EUS with other diagnostic modalities for choledocholithiasis, such as intraoperative cholangiography, magnetic resonance cholangiography, and laparoscopic ultrasonography.

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