EUS with EUS-guided fine-needle aspiration as the first endoscopic test for the evaluation of obstructive jaundice

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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 ultrasound (EUS) for the evaluation of patients with obstructive jaundice of unknown or possibly neoplastic origin. An algorithm where EUS or EUS-guided fine needle aspiration (EUS-FNA) was used as the first diagnostic approach was considered.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised adult patients with obstructive jaundice of unknown or possibly neoplastic origin. Patients with probable obstructive jaundice were defined as individuals with a total bilirubin of 3mg% or greater (51 micromol/L) and a clinical history, physical examination and laboratory evaluation suggesting extrahepatic obstruction.

Setting
The setting was secondary care. The economic study was conducted in the USA.

Dates to which data relate
The effectiveness and resource use data were gathered between June 1995 and March 2000 and were also derived from studies published between 1991 and 2000. The price year was not reported.

Source of effectiveness data
The effectiveness evidence was derived from a single study, completed studies and authors' assumptions.

Link between effectiveness and cost data
The costing was conducted on the same sample of patients as that used in the effectiveness study. It was carried out both prospectively and retrospectively, depending on the patient group.

Study sample
The use of power calculations was not reported. From a sample of 216 consecutive patients referred for evaluation of probable obstructive jaundice, 69 had ERCP first and were then excluded from the study sample. Reasons to perform ERCP first were possible choledocholithiasis (35 patients), possible bacterial cholangitis (1), known inoperable malignancy (20), known benign condition (3), Billroth II anatomy (2), suspected sclerosing cholangitis (1),
unavailability of EUS (1) and physician preference (6). Therefore, the final group of patients comprised 147 consecutive patients. In 6 of these 147 patients, ERCP was attempted first without success. The mean age was 69.4 years (age range: 26 - 91) and 62% of the patients were men. Ninety-six patients (65%) had malignancy as the cause of jaundice (mainly pancreatic cancers).

Study design
This was a diagnostic study that was based on a case series of patients who received EUS evaluation as the first diagnostic approach. Information on the centres where the study was conducted was not reported. The patients were prospectively followed until a definitive diagnosis was made. One endosonographer performed the diagnostic EUS and any subsequent EUS-guided FNA. The same endoscopist performed ERCP if it was indicated after EUS. Survival data were also assessed for a tumour registry. Once the final outcome and therapy of each patient was known, the course of each patient's evaluation was re-assessed assuming that, instead of EUS, ERCP was the first endoscopic procedure performed. No patient was lost to the follow-up assessment.

Analysis of effectiveness
The analysis of effectiveness was conducted on all patients in whom EUS was the first endoscopic approach taken. The outcomes used were:

- the success of EUS,
- the number of procedures performed,
- the outcomes of EUS patients,
- the diagnostic results of ERCP performed after an initial EUS evaluation, and
- survival.

Effectiveness results
Initial EUS was successful in all 147 patients and 54% of those patients who had EUS-FNA as part of their evaluation. Seventy-four patients had a positive diagnosis of malignancy, which was confirmed when the procedure was performed. One patient (0.7%) was misdiagnosed by the EUS-first approach. Eighty-three patients had an ERCP within 90 days of the EUS. Five ERCPs were confirmatory and none of them demonstrated additional findings. Of the remaining 78 patients, ERCP provided additional useful information in 14 of them (17%), although the information obtained was clearly superior in only 2 of these 14 patients. The EUS findings were clearly superior to those of ERCP in 20 patients. Similar results were observed in 51 patients. Of the 64 patients with pancreatic cancer, 37 had operations (25 resections and 12 bypasses) where operability could be assessed surgically. Four patients had metastatic liver disease confirmed by EUS-FNA. Four patients had resectable tumours by EUS, but were then deemed inoperable because of major co-morbidity or extreme age. Nineteen patients who were considered by EUS criteria to have unresectable tumours had a median
survival of 158 days (range: 11 - 283).

If ERCP were performed as first strategy (and using some of the literature-based assumptions reported below), there would have been 80 ERCPs more than when using EUS as the first diagnostic procedure but 20 EUS and 31 EUS-FNA would not have been performed. However, because of the initial diagnostic results, a significant number of post-ERCP procedures (including EUS or occasionally exploratory laparotomy) would have been required.

Clinical conclusions
The effectiveness analysis showed that EUS-FNA correctly identified the cause of obstructive jaundice in all but one patient (also missed by ERCP and operation). In addition, the total number of patients needing ERCP was reduced by 47%.

Outcomes assessed in the review
The outcomes assessed from the literature were assumptions about patient management.

Study designs and other criteria for inclusion in the review
Not stated.

Sources searched to identify primary studies
Not stated.

Criteria used to ensure the validity of primary studies
Not stated.

Methods used to judge relevance and validity, and for extracting data
Not stated.

Number of primary studies included
Eleven primary studies were used to support some of the assumptions made in the analysis.

Methods of combining primary studies
Not stated.

Investigation of differences between primary studies
Not stated.

Results of the review
If a patient was found to have a biliary stricture at ERCP, then a plastic stent would be placed to minimise the risk of ERCP-induced cholangitis.

If a malignant-appearing stricture of the bile duct or pancreatic duct was seen by ERCP, an attempt at cytologic or tissue diagnosis by brush cytology, transpapillary FNA and/or biopsy would be made.

If a stent was placed for malignancy, a plastic stent would be placed initially and changed by ERCP at a later date to a metallic stent if subsequent evaluation showed that the patient was not an operative candidate and had a potential
survival of more than 6 months.

**Methods used to derive estimates of effectiveness**  
The authors made assumptions to derive some effectiveness estimates.

**Estimates of effectiveness and key assumptions**  
The failure rate for ERCP was assumed to be 0. It was assumed that EUS or EUS-FNA would not be performed on the same day after an ERCP, because it would be unreasonable to use another biopsy technique until the results of the samples taken at ERCP were available.

**Measure of benefits used in the economic analysis**  
The health outcomes were left disaggregated and no summary benefit measure was used in the analysis. In effect, a cost-consequences analysis was conducted.

**Direct costs**  
Discounting was not relevant since the costs were incurred during a timeframe shorter than 2 years. The unit costs of most diagnostic procedures were reported but other costs were reported in macro-categories. The health services included in the economic evaluation were all diagnostic tests and procedures, treatment of complications, and hospitalisation. The costs were estimated from Medicare regional charges as well as from fee-for-service charges, thus reflecting the two different perspectives evaluated in the two separate cost analyses. Both sources of data were considered reasonable, owing to the difficult estimation of the "true cost" of EUS and ERCP. Some costs were also estimated from published studies. The resource use data came mainly from assumptions and estimates derived from the single study. The price year was not reported.

**Statistical analysis of costs**  
The costs were treated deterministically in the base-case.

**Indirect Costs**  
The indirect costs were not considered.

**Currency**  
US dollars ($).

**Sensitivity analysis**  
Sensitivity analyses were conducted to assess the impact of variations in several assumptions on the estimated costs of the two diagnostic strategies. Further, a scenario unfavourable to EUS was considered. One-way and multivariate sensitivity analyses were conducted.

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

**Cost results**  
Under base-case assumptions, the use of EUS as the first diagnostic approach in place of ERCP led to cost-savings of $1,007 per patient using Medicare costs and $1,313 per patient using fee-for-service provider costs.
From the sensitivity analysis, the factors that affected the cost-savings associated with EUS were:

- the inpatient versus outpatient status,
- the yield of a positive cytologic or tissue diagnosis by ERCP and EUS-FNA,
- the hospitalisation rate after an outpatient ERCP, and
- the true cost of EUS relative to ERCP.

However, within reasonable ranges of variation, EUS was cost-saving relative to ERCP.

Only in the very unfavourable scenario, in which all assumptions were against EUS, were the cost-savings effectively negated. In particular, the relative cost of EUS/EUS-FNA to ERCP had to be more than doubled in order to eliminate cost-savings associated with the EUS-first approach.

**Synthesis of costs and benefits**

A synthesis of the costs and benefits was not relevant since a cost-consequences analysis was conducted.

**Authors’ conclusions**

The use of endoscopic ultrasound (EUS) or EUS-guided fine needle aspiration (EUS-FNA) as the first diagnostic approach for patients with suspected obstructive jaundice reduced the need for almost half of the endoscopic retrograde cholangiopancreatographies (ERCPs) that would otherwise be needed and was cost-saving under general reimbursing conditions. However, the authors admitted that several factors affected the cost-advantage of EUS over ERCP.

**CRD COMMENTARY - Selection of comparators**

The rationale for the choice of the comparator was clear. The use of ERCP as the first diagnostic approach for patients with obstructive jaundice was quite common and ERCP was likely to represent a standard diagnostic procedure. However, other diagnostic approaches (i.e., other imaging techniques) were available, although they were not yet commonly performed. You should decide whether ERCP is a valid comparator in your own setting.

**Validity of estimate of measure of effectiveness**

The effectiveness evidence came mainly from a diagnostic study in which only one approach was actually assessed, while the outcomes associated with the comparator were estimated from assumptions and final diagnosis information. Clearly, an actual, concurrent and prospective comparison of the two strategies would have been more appropriate. The assumptions were made on the basis of published evidence or authors’ opinion. Some of these estimates were then varied in the sensitivity analysis. The study sample comprised consecutive patients who were probably identified at a single centre. Little information on the patient demographics was reported. Thus, it was unclear whether the study sample was representative of the patient population. The outcome assessment was not blind, which could have affected the results of the analysis, in particular for the hypothetical comparison group of patients being evaluated using ERCP. These issues tend to limit the internal validity of the analysis.

**Validity of estimate of measure of benefit**

No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted.

**Validity of estimate of costs**

The cost analysis was conducted from two distinct perspectives since two different sources of costs were considered, neither of which represented the true costs of the interventions. However, charges were used, although the application of a cost-to-charge ratio would have been useful. Some unit costs were provided, while other items were presented as macro-categories and were estimated from published literature. This will limit the possibility of replicating the study in...
other settings. A breakdown of the costs was provided and the price year was reported, which will facilitate reflation exercises in other settings.

Other issues
The authors did not make extensive comparisons of their findings with those from other studies. In addition, the issue of the generalisability of the study results to other settings was not explicitly addressed. However, several sensitivity analyses were conducted and the results were clearly reported. This had a positive impact on the external validity of the analysis. The study involved patients with suspected obstructive jaundice and this was reflected in the authors’ conclusions.

Implications of the study
The study results suggested that EUS or EUS-FNA should be an integral and early part of the diagnostic approach for patients with suspected obstructive jaundice.

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Other publications of related interest


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