SYSTEMATIC REVIEW

EUS vs MRCP for detection of choledocholithiasis

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Background: Numerous published studies have shown the high diagnostic performance of both EUS and MRCP compared with ERCP for the detection of choledocholithiasis.

Design: We undertook a systematic review of all published randomized, prospective trials that compared EUS with MRCP with the primary aim being to compare the overall diagnostic accuracy for the detection of choledocholithiasis in patients with suspected biliary disease.

Methods: A MEDLINE review was performed. We identified 5 randomized, prospective, blinded trials comparing MRCP and EUS for the detection of choledocholithiasis, with subsequent ERCP or intraoperative cholangiography as a criterion standard. The study-specific variables for EUS and MRCP for choledocholithiasis were calculated from the data, and analyses were performed by using aggregated variables (sensitivity, specificity, positive and negative predictive values, and likelihood ratios).

Results: The pooled data set consisted of 301 patients. The aggregated sensitivities of EUS and MRCP for the detection of choledocholithiasis were 0.93 and 0.85, respectively, whereas their specificities were 0.96 and 0.93, respectively. The aggregated positive predictive values for EUS and MRCP were 0.93 and 0.87, respectively, with the corresponding negative predictive values of 0.96 and 0.92, respectively. Positive likelihood ratios were >10 for both tests, and corresponding negative likelihood ratios approached 0.10 for both tests. No statistically significant differences between EUS and MRCP were found in our analysis.

Conclusions: EUS and MRCP have high diagnostic performance overall. Our analysis showed no statistically significant difference between the modalities. We recommend taking into consideration other factors, such as resource availability, experience, and cost considerations in deciding between these 2 tests. (Gastrointest Endosc 2006;64:248-54.)

Choledocholithiasis is a common condition and can cause numerous complications.[1] Until recently, ERCP has been the criterion standard for diagnosis and therapy of choledocholithiasis,[2,3] but the procedure can be associated with complications, including acute pancreatitis, bleeding, and perforation. Low-risk tests, such as EUS and MRCP, are emerging as reliable substitutes for diagnostic ERCP (Fig. 1). Both of these tests have been extensively evaluated independently and in comparison with ERCP with uniformly encouraging results.[4-21]

There is a lack of a consensus on the optimal noninvasive strategy for patients with suspected choledocholithiasis after a negative transabdominal US and/or CT. There are several published prospective studies comparing EUS with MRCP for biliary tract disease, but a systematic review of these studies has not yet been undertaken. The aim of this study was to compare the performance of these 2 noninvasive techniques with regard to the detection of choledocholithiasis when using the data from published prospective comparative trials.

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MATERIALS AND METHODS

Search for published studies

We performed PubMed and Cochrane Controlled Trials Register searches for terms ''EUS and MRCP,'' ''EUS vs MRCP,'' and ''EUS compared with MRCP.'' We also searched the reference list of review articles and relevant studies to complete the search for EUS and MRCP comparison studies. If all relevant data were not listed in the published manuscript, we contacted the authors to obtain additional information.[22]

Inclusion/exclusion criteria

The following a priori criteria were used for selecting published trials for this systematic review: (A) prospective blinded controlled studies published in the English language and indexed in PubMed; (B) both EUS and MRCP were performed in the same patients for the diagnosis of extrahepatic biliary obstruction and followed by 1 or more of the confirmatory criterion-standard tests (ERCP or intraoperative cholangiography with or without choledochoscopy, which were both accepted as criterion standards in all studies); (C) similar patient population characteristics (age, sex distribution, clinical indication for the test) and study design; (D) blinding of the endosonographer and the radiologist evaluating the patients to the findings of the other study; and (E) procedures were performed temporally close together (24-72 hours in most cases) to minimize the chances of a negative study from stone passage.

In studies that included patients with diagnoses other than biliary stones, we limited our analysis to biliary stones and treated these other patients as negative cases for biliary stones, because they did not show any stone(s) with criterion-standard evaluation.

Five published prospective studies that assessed the diagnostic accuracy of EUS and MRCP for diagnosis of choledocholithiasis involving 301 patients were identified.[22-26] Some studies that dealt with similar comparisons were excluded from the analysis because of failure to perform all 3 tests in all patients[27] or because the focus was on biliary strictures and not stones.[28] The important characteristics of these studies are summarized in Table 1, including the number of patients included and excluded in the final analysis. The design, the conduct, and the outcomes analysis of these studies were similar. The main objective of these studies was evaluating the performance of EUS and MRCP for the detection of biliary disease, most commonly choledocholithiasis, against the criterion standards of ERCP and/or intraoperative cholangiography. These studies emphasized performing EUS and MRCP temporally close to each other and then evaluating the same patient group with ERCP or intraoperative cholangiography. These procedures were done independently, and the individual operators were blinded to the outcome of the results of the other investigation. With an emphasis on trial selection and uniformity of the data gathering,[29] this analysis was limited only to 5 studies. We included all relevant studies irrespective of positive or negative results.

Statistical analysis

A total of 301 patients comprised the pooled data set. The study population was first classified according to the presence or the absence of the stones defined by the criterion-standard test. Because this study is focused on the ability to detect common bile duct (CBD) stones, we only included patients with a final diagnosis of choledocholithiasis as a positive result for the analysis. Other patients, including those with no CBD pathology or with a diagnosis other than biliary stone, were classified as a negative result for stones (Table 2). By using these values, we calculated sensitivity, specificity, positive and negative predictive values, and likelihood ratios of EUS and MRCP for the detection of choledocholithiasis for each study (Table 3). These values were calculated from the data provided in the original papers. This analysis excluded 11 patients from the study of de Ledinghen et al,[26] 2 patients each from the studies by Scheiman et al[23] and Kondo et al,[25] and 4 patients from the study by Ainsworth et al[22] because they did not undergo all 3 evaluations (EUS, MRCP, and ERCP). No patients were excluded from the study by Materne et al.[24]

To compare the performance of these 2 modalities (EUS and MRCP), a test for homogeneity of the proportions across the 5 studies was performed. The test of homogeneity across all 5 studies with respect to sensitivity was not significant ($P = .43$). However, the minimum expected frequency requirements of the χ^2 test were not met because of the small sample size of some of the studies. Therefore, the choice of methodology for estimating aggregate outcome measures (in this case sensitivities, specificities, and positive and negative predictive values), all expressed as proportions (p), was the random effects model. This methodology assumes that outcome measures (p) for individual studies vary around an overall proportion μp and variance.[29,30] When using the data from the 5 studies, the mean is estimated by the weighted average of the proportions from the individual studies $\left(=\sum_{i=1}^{5} p_i w / \sum_{i=1}^{5} w_i\right)$ and σ_p^2, is estimated as the difference between the sample variance of the p's and the average sampling variance. For the data under consideration, the estimation of σ_p^2 was either negative or close to zero, thereby considerably simplifying the analysis.

By using this methodology, we calculated individual and aggregated sensitivity, specificity, positive and negative

Capsule Summary

What is already known on this topic

- EUS and MRCP are emerging as reliable, low-risk substitutes for diagnostic ERCP, a procedure associated with complications.

What this study adds to our knowledge

- A systematic review of the 5 randomized, prospective trials, comparing EUS and MRCP showed no significant differences between these modalities in terms of sensitivity, specificity, positive and negative predictive values, or likelihood ratios.
- When deciding between EUS and MRCP, clinicians should consider other factors, such as resource availability, experience, and costs.

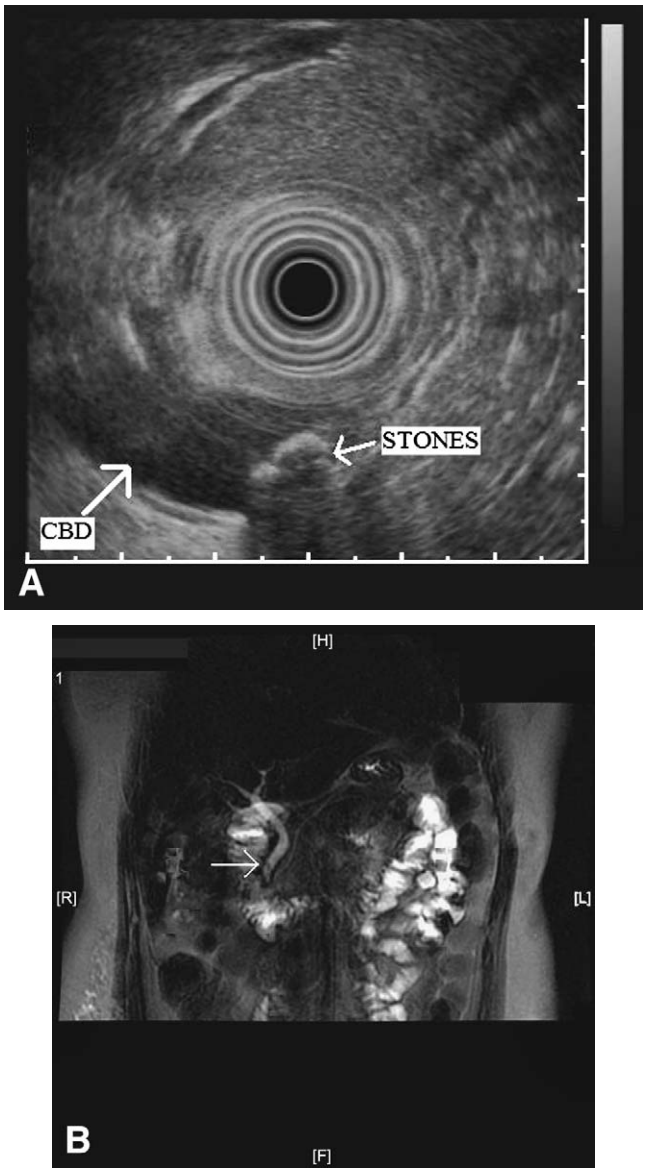

Figure 1. A, Representative EUS image demonstrating choledocholithiasis. Note multiple stones in distal common bile duct. Stones have a hyperechoic interface with the EUS transducer and postacoustic shadowing. Image courtesy of Douglas K. Pleskow, MD. **B**, Representative MRCP image, demonstrating choledocholithiasis with a single stone in the distal common bile duct (*arrow*).

predictive values, and likelihood ratios for EUS and MRCP.

RESULTS

For the detection of choledocholithiasis, the aggregated sensitivities of EUS and MRCP were 0.93, 95% confidence interval (CI) 0.87-0.98, and 0.85, 95% CI, 0.77-0.93, whereas their corresponding specificities were 0.96, 95% CI, 0.91-1.0, and 0.93, 95% CI, 0.88-0.98, respectively. The aggregated positive predictive values for EUS and MRCP were 0.93, 95% CI, 0.87-0.99, and 0.87, 95% CI, 0.79-0.94, with the corresponding negative predictive values of 0.96, 95% CI, 0.94-0.98, and 0.92, 95% CI, 0.87-0.96. The aggregated positive and negative likelihood ratios for EUS were 23.04, 95% CI, 11.6-46.50, and 0.07, 95% CI, 0.04-0.15, and that for MRCP were 12.14, 95% CI, 7.22-20.43, and 0.16, 95% CI, 0.10-0.25 (Table 4).

The analysis demonstrated that, with respect to sensitivity, specificity, and positive and negative predictive values, there was no statistically significant difference between EUS and MRCP for the detection of choledocholithiasis. Both studies provided high likelihood ratios for positive and negative results, which markedly altered the probability of the disease status after the performance of the study. Hence, they can suitably be used as a screening modality for choledocholithiasis.

DISCUSSION

ERCP is well established for the evaluation and the treatment of pancreatobiliary disease. Continued refinement of ERCP equipment and improved experience has led to improved outcomes and decreased complications.[31-35] Nonetheless, ERCP remains a technically challenging procedure, with failure rates ranging from 3% to 10%, and it is highly dependent on operator skill and experience.[36,37] ERCP is associated with a small risk of significant morbidity and mortality, including severe complications, such as acute pancreatitis; bleeding; perforation; sepsis; and even, rarely, death.[38,39] There has been much recent interest in performing the initial evaluation of patients with suspected choledocholithiasis with less invasive or noninvasive modalities, such as EUS and MRCP.

This systematic review evaluated the performance of EUS and MRCP, and compared their ability to accurately diagnose the choledocholithiasis. This analysis showed high aggregated diagnostic accuracy for both modalities but failed to show any statistically significant differences in their overall performance. In addition, with regard to choledocholithiasis, both EUS and MRCP had likelihood ratios in excess of 10, indicating a high post-test probability of the disease state being present in individuals with a positive test.[40-42] Thus, at this time, 1 test cannot be endorsed over the other with regard to diagnostic accuracy. Given that both tests are highly accurate, it may take more large-scale trials to allow a difference to become apparent.

The major advantage of MRCP is its completely noninvasive nature in comparison with both EUS and ERCP, perhaps making it a better test in high-risk populations, such as elderly or severely ill patients. There is no requirement for contrast media, and the test has a very low failure rate. In addition, MRCP is much more widely available than EUS and is clearly a more established technique, although a high level of technical expertise is crucial to an accurate review of MRCP images.[21,32,43-45] The continuous

TABLE 1. Prospective trials characteristics

Study (y)	Ainsworth et al[22] (2003)	de Ledinghen et al[26] (1998)	Materne et al[24] (2000)	Scheiman et al[23] (2001)	Kondo et al[25] (2005)
Study sample size	167	43	50	30	30
Patients included for analysis	163	32	50	28	28
Sex ratio (M:F)	59:104	18:25	23:27	14:14	16:12
Age, (mean, median), y	64 (24-89)	60.9 (25-81)	59 (16-90)	46.5 (23-68)	64 (38-93)
Study inclusion criteria	Patients admitted for elective ERCP.	Clinical/biochemical signs of choledocholithiasis: RUQ/epigastric pain with fever or jaundice, elevated ALP/GGT/ transaminases/ unexplained cholestasis.	Patients with suspicion of bile-duct obstruction: clinical symptoms-RUQ pain, fever, or jaundice; biochemical markers-elevated ALP, GGT > twice the normal; signs of biliary obstruction on transabdominal sonography.	Adult patients (>18 y) referred for ERCP on the basis of clinical signs/symptoms.	Consecutive patients with high suspicion of choledocholithiasis were enrolled prospectively in the study.
Study design	Prospective blinded study	Prospective blinded study	Prospective blinded study	Prospective blinded study	Prospective blinded study
Tests methods	Each patient underwent EUS followed by MRCP, and then ERCP within 24 h of initial procedure by different investigators unaware of findings from other investigations.	All patients underwent EUS and MRCP by 2 different operators blinded for the other investigators, results, followed by either ERCP or surgical treatment for final diagnosis.	MRCP performed before or after EUS in 31 and 19 patients, respectively, with median time delay of 1 d (range, 1-10 d) between the 2 procedures; final diagnosis established by ERCP or intraoperative cholangiography in 21 and 16 patients, respectively; 4 patients were followed clinically.	MRCP and EUS performed within 24 h before the ERCP; investigators were blinded for results of the other studies.	MRCP, EUS, and helical CT performed in a random order before obtaining the ERCP evaluation performed within 24 h before the ERCP; investigators were blinded for results of the other studies.

RUQ, Right upper quadrant; *ALP*, alkaline phosphate; *GGT*, gamma-glutamyl transferase.

improvement of MRCP scanners and software packages will likely continue to provide better performance as time passes.[20,46] On the downside, MRCP is time consuming, requires a high level of patient cooperation, and is not well tolerated by 1% to 5% of patients because of claustrophobia.[47] Variations among MRCP techniques and/or patient-related situations could simulate or mask pathologic conditions, leading to false-positive or false-negative examinations, respectively. Factors that can lead to false or misleading images include, but are not limited to, image reconstruction artifacts that obscure small filling defects; limited spatial resolution, which caused overestimation of ductal narrowing; motion artifacts; as well as intraductal artifacts, such as blood or air (pneumobilia) mimicking a stone; or CBD sludge, which simulated a stenosis.[13,43,48-50] The accuracy of MRCP for the detection of choledocholithiasis varies with the size of the duct, but whether narrow or dilated ducts are more favorable for the detection of stones remains unclear.[51,52]

EUS yields very high resolution images because of the proximity of the endoscope probe to the internal structures. Both types of commonly used echoendoscopes (radial and linear) are reliable for evaluation and detection of choledocholithiasis.[11,53] The higher resolution offered by EUS (0.1 mm) when compared with MRCP (1.5 mm), makes it extremely sensitive for small stones. EUS also offers the distinct advantage of dynamic imaging in comparison to MRCP. Images can be manipulated via magnification and alterations in endoscope position and US frequency in real time to better visualize structures under scrutiny. If stones are demonstrated by EUS, therapeutic ERCP can potentially be performed (often by the same endoscopist) immediately after the completion of EUS while the patient is still sedated. This offers a convenient approach for low-to-moderate–risk patients, who would otherwise undergo diagnostic ERCP. This is a distinct advantage of EUS over MRCP, because MRCP is, by definition, performed by radiologists in a separate location and often

TABLE 2. Study population characteristics

Study (y)	Ainsworth et al[22] (2003)	de Ledinghen et al[26] (1998)	Materne et al[24] (2000)	Scheiman et al[23] (2001)	Kondo et al[25] (2005)
Study patients	167	43	50	30	30
Patients included in the analysis	163	32	50	28	28
Patients with final diagnosis of stones	60	10	9	5	24
Final diagnosis other than stones (A)	39	0	24	3	0
No pathology (B)	64	22	17	20	4
Total stone negative = A + B	103	22	41	23	4

TABLE 3. Performance of EUS and MRCP for evaluation of choledocholithiasis in prior published studies (including only patients with a final diagnosis of stones)

	EUS						MRCP					
Study	SN	SP	PPV	NPV	LR+	LR−	SN	SP	PPV	NPV	LR+	LR−
Scheiman et al[23]	0.80	0.96	0.80	0.96	20	0.2	0.40	0.96	0.66	0.88	10	0.62
Kondo et al[25]	1	0.50	0.93	1	2	0	0.88	0.75	0.96	0.50	3.5	0.16
de Ledinghen[26]	1	0.96	0.91	1	25	0	1	0.73	0.63	1	3.7	0
Materne et al[24]	0.89	0.95	0.80	0.98	17.8	0.2	0.78	0.98	0.88	0.95	39	0.22
Ainsworth et al[22]	0.90	0.99	0.98	0.94	90	0.1	0.87	0.97	0.95	0.93	19.4	0.13

SN, Sensitivity; *SP*, specificity; *PPV*, positive predictive value; *NPV*, negative predictive value; *LR*, likelihood ratio.

TABLE 4. Mean and variance of diagnostic variables as proportions

Aggregated variables	EUS (95% CI)	MRCP (95% CI)
SN	0.93 (0.87-0.98)	0.85(0.77-0.93)
SP	0.96 (0.91-1.0)	0.93 (0.88-0.98)
PPV	0.93 (0.87-0.99)	0.87 (0.79-0.94)
NPV	0.96 (0.94-0.98)	0.92 (0.87-0.96)
LR +	23.04 (11.6-46.50)	12.14 (7.22-20.43)
LR –	0.07 (0.04-0.15)	0.16 (0.10-0.25)

SN, Sensitivity; *SP*, specificity; *PPV*, positive predictive value; *NPV*, negative predictive value; *LR*, likeliood ratio.

on a separate day. However, the higher level of invasiveness of EUS, coupled with the requirement of sedation, demands careful consideration of the need to perform EUS in low-risk patients. Even a purely diagnostic EUS carries with it the risks of sedation, bleeding, and perforation. A distinct drawback of EUS is the limited availability of EUS hardware and adequately trained endosonographers in comparison with more widely available trained radiologists.[54] In addition, technical limitations often make it difficult for EUS to provide adequate intrahepatic ductal visualization, and intrahepatic stones may thus be more difficult to identify at EUS.[55,56] In cases where the US transducer cannot be positioned into the duodenum (pyloric stenosis, Billroth II anatomy, severe ulcer disease), EUS cannot be effectively used for the detection of choledocholithiasis.[7,57]

Low-risk patients would be more likely to have a negative ERCP and, as such, may not warrant the risks associated with ERCP, as well as the cost of the procedure.[7,58-60] Previous studies found greater cost reduction when EUS before ERCP was compared with either MRCP before ERCP or ERCP alone in low-to-moderate–risk patients.[59] EUS use for low-to-moderate–risk patients significantly impacted the ERCP utilization, resulting in fewer ERCP procedures performed, whereas MRCP failed to reduce the number of ERCPs performed.[60] Furthermore, decision analysis models on the value of MRCP have not universally demonstrated a reduction in the number of ERCPs performed in patients with suspected choledocholithiasis or other pancreatobiliary diseases.[59,61]

Overall, this study demonstrated no statistically significant difference between EUS and MRCP for the detection of choledocholithiasis, although both tests were highly effective. The investigators suggest such factors as patient suitability and local expertise be considered when selecting between EUS and MRCP in patients with suspected choledocholithiasis.

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DISCLOSURE

The authors have no financial disclosures or conflicts of interest regarding this manuscript.

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