

# Endoscopic ultrasound *versus* magnetic resonance cholangiopancreatography in suspected choledocholithiasis: A systematic review

Vinicius Leite De Castro, Eduardo G.H. Moura, Dalton M. Chaves, Wanderley M. Bernardo, Sergio E. Matuguma, Everson L.A. Artifon

Department of Gastroenterology, University of São Paulo, São Paulo, Brazil

## ABSTRACT

**Background and Objectives:** There is a lack of consensus about the optimal noninvasive strategy for patients with suspected choledocholithiasis. Two previous systematic reviews used different methodologies not based on pretest probabilities that demonstrated no statistically significant difference between Endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography (MRCP) for the detection of choledocholithiasis. In this article, we made a comparison of the diagnostic ability of EUS and MRCP to detect choledocholithiasis in suspected patients. **Methods:** We conducted a systematic review in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations with all published randomized prospective trials. We performed the systemic review using MedLine, EMBASE, Cochrane, LILACS, and Scopus reviews through May 2015. We identified eight randomized, prospective, blinded trials comparing EUS and MRCP. All the patients were submitted to a gold standard method. We calculated the study-specific variables and performed analyses using aggregated variables such as sensitivity, specificity, prevalence, positive predictive value (PPV) and negative predictive value (NPV), and accuracy. **Results:** Five hundred and thirty eight patients were included in the analysis. The pretest probability for choledocholithiasis was 38.7. The mean sensitivity of EUS and MRCP for detection of choledocholithiasis was 93.7 and 83.5, respectively; the specificity was 88.5 and 91.5, respectively. Regarding EUS and MRCP, PPV was 89 and 87.8, respectively, and NPV was 96.9 and 87.8, respectively. The accuracy of EUS and MRCP was 93.3 and 89.7, respectively. **Conclusions:** For the same pretest probability of choledocholithiasis, EUS has higher posttest probability when the result is positive and a lower posttest probability when the result is negative compared with MRCP.

**Key words:** Cholangiopancreatography, choledocholithiasis, endosonography, magnetic resonance

## INTRODUCTION

Choledocholithiasis occurs in 15%-20% of patients with gallbladder stones and can cause numerous complications.<sup>[1,2]</sup> There is a lack of consensus about

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### Address for correspondence

Dr. Vinicius Leite De Castro, 255 Dr. Eneas De Carvalho Aguiar Street, Ambulatorios Building - 6<sup>th</sup> Floor, Cerqueira Cesar, Sao Paulo - 05403-000, Brazil. E-mail: viniciuscastro@yahoo.com.br

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the optimal noninvasive strategies for patients with suspected common bile duct (CBD) stones after a negative transabdominal ultrasound (US) and/or computed tomography. Endoscopic retrograde cholangiopancreatography (ERCP) continues to be considered the standard of reference for detection of bile duct stones with the possibility of simultaneous treatment.<sup>[3]</sup> Nevertheless, ERCP remains an invasive method.<sup>[4]</sup> Low-risk tests such as endoscopic ultrasound (EUS) and magnetic resonance cholangiopancreatography (MRCP) have emerged as reliable substitutes for diagnostic ERCP.<sup>[5-10]</sup> A few reports have compared the diagnostic ability of CBD stones between EUS and MRCP.<sup>[11-17]</sup> Two previous systematic reviews demonstrated no statistically significant difference between EUS and MRCP in terms of the detection of choledocholithiasis although both tests were highly effective.<sup>[18,19]</sup> Since the last systematic review, one new prospective study has emerged, accounting for new data with an increased sample population higher than 30%.<sup>[20]</sup>

The aim of this study was to compare the diagnostic ability of EUS and MRCP in cases of suspected choledocholithiasis using data from published comparative studies.

## MATERIALS AND METHODS

### *Protocol and registration*

This systematic review of the literature was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations.<sup>[21]</sup> The review was registered on the PROSPERO international database ([www.crd.york.ac.uk/prospero/](http://www.crd.york.ac.uk/prospero/)) under number CRD42014014670.

### *Eligibility criteria*

- a. *Types of studies:* We focused on prospective comparative trials (clinical trials and/or observational studies).
- b. *Types of participants:* Patients in whom choledocholithiasis was suspected with similar population characteristics (age, sex distribution, and clinical indication for the test).
- c. *Types of intervention:* Studies comparing the outcomes in two diagnostic arms: EUS and MRCP. Both EUS and MRCP were performed for the diagnosis of extrahepatic biliary obstruction followed by one or more of the confirmatory criterion standard tests (ERCP or intraoperative cholangiography with or without cholangioscopy) that were accepted as

criterion standards in all studies. Both procedures were performed temporally close together (24-72 h in most cases) to minimize the chances of a negative study from stone passage. There were no restrictions regarding different technique modalities in each arm except for the blinding of the endosonographer and the radiologist evaluating the patients.

- d. *Types of outcome measures:* The main outcomes measures were accuracy, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV).

### *Information sources*

Studies were identified by searching several electronic databases and scanning the reference lists of articles. This search was applied for Medline (inclusive of all years) and EMBASE. The Cochrane, LILACS (*via* BVS), Scopus, and CINAHL (*via* EBSCO) databases were also reviewed. A manual search was also conducted for relevant reviews, original articles, and abstract books. The last search was run on May 22, 2015; no language limits were applied.

### *Search*

Comparative trials were identified by conducting a comprehensive search of electronic databases using medical subject headings (MESH) stratified by population — “choledocholithiasis,” intervention — “endosonography,” and comparison — “magnetic resonance cholangiopancreatography.” We further searched the bibliographies of all the included primary studies and existing reviews by hand for additional citations.

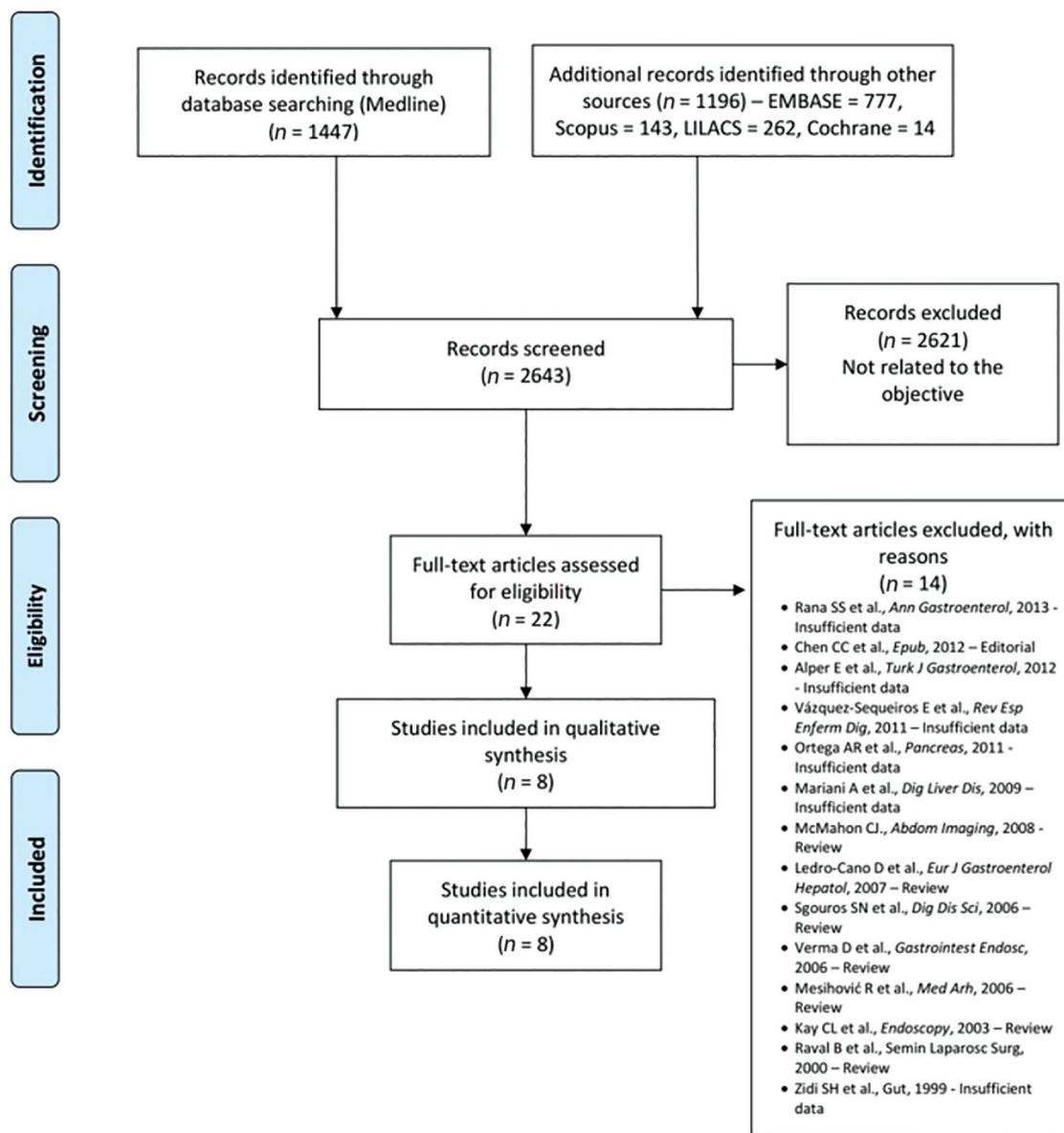
### *Study selection*

We performed the eligibility assessment and the selection of screened records independently in an unblinded, standardized manner with two reviewers. Disagreements between the reviewers were resolved by a consensus.

To summarize the study selection processes, we used an adapted PRISMA flow diagram [Figure 1].

### *Data collection process*

The method of data extraction from each included study consisted of filling out information sheets after the paper was read. We used a QUADAS-based checklist.<sup>[22]</sup> One review author extracted the data from the included studies and a second author checked the extracted data. Disagreements were resolved *via* a discussion between the two review authors.



**Figure 1.** Search Strategy: EUS *versus* MRCP in the diagnosis of choledocholithiasis

### Data items

The following data items were extracted from each included study:

- Number of patients included in the analysis.
- Clinical and/or laboratory characteristics used as inclusion criteria.
- Number of patients with final diagnoses of choledocholithiasis based on the gold standard.
- These values were calculated from the data provided in the original papers and we excluded patients who did not undergo all three evaluations (EUS, MRCP, and the gold standard). 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. Gold standard criteria were used to confirm choledocholithiasis.

- Interval between EUS and MRCP execution.
- Interval between EUS/MRCP and gold standard execution.
- Tests methods in terms of operators characteristics, test sequence, and gold standard distribution.
- Study design.
- EUS and MRCP accuracy, sensitivity, specificity, PPV, and NPV for choledocholithiasis diagnosis.

### Risk of bias in individual studies

To evaluate the risk of bias and applicability of the primary diagnostic accuracy studies, we used the QUADAS-2 tool.<sup>[22]</sup>

This tool is structured so that the four key domains are each rated in terms of the risk of bias and the concern regarding applicability to the research question.

The first domain is patient selection, the second is index test, the third is the reference standard, and the fourth is flow and timing.

### *Summary measures*

The primary outcome measures that we focused on included sensitivity, specificity, pretest probability, PPV and NPV, and accuracy of EUS and MRCP for the detection of choledocholithiasis.

We performed the analysis using the software Review Manager (RevMan) 5.3 obtained from the website of the Cochrane Informatics and Knowledge Management Department.<sup>[23]</sup> The average data and standard deviation (SD) were obtained using Microsoft Excel software for Windows version 2013.

### *Risk of bias across studies*

QUADAS-2 was applied individually to the selected studies and a global comparative analysis was conducted based on it. Each one of the four key domain tools that included patient selection, index test, reference standard, and flow and timing was filled. We also conducted a comparative analysis of these criteria and checked if the selection of patients, conduct, interpretation of both the index test and reference standard, or patient flow could have introduced bias.

## RESULTS

### *Study selection*

Two thousand and six hundred and forty-three (2,643) studies were screened and the articles assessed for eligibility were selected after the title and abstract were read. Twenty-two studies compared the performance of EUS and MRCP with regard to the detection of choledocholithiasis. Two thousand and six hundred twenty-one (2,621) articles were excluded because they did not include the information outlined above. Fourteen studies were excluded, out of which six did not provide sufficient data, seven were reviews, and one was an editorial. These characteristics are summarized in Figure 1. After the last systematic review, one new study has emerged, accounting for 135 patients.<sup>[20]</sup> Eight published prospective studies that assessed the diagnostic accuracy of EUS and MRCP for the diagnosis of choledocholithiasis in 538 patients were included in our analyses.

### *Study characteristics*

The important characteristics of the selected studies are summarized in Table 1 including the number of patients used in the final analysis. These values were extracted from a careful reading of the included papers. The design, conduct, and outcomes analyses of these studies were similar. The main objective of these studies was to evaluate the performance of EUS and MRCP for the detection of biliary disease, most commonly choledocholithiasis, against criterion standards of ERCP and/or intraoperative cholangiography. The included studies emphasized performing EUS and MRCP temporally close to each other and then evaluating the same patient group with ERCP or intraoperative cholangiography. The procedures were conducted independently, and the individual operators were blinded to the outcome of the results of the other investigation. One of the studies used two subgroups for analysis: Patients with unexplained CBD dilation in standard ultrasonography (US) (Group 1) and patients with a nondilated CBD and a high probability of having choledocholithiasis (Group 2).<sup>[20]</sup> We subdivided this investigation into two studies in terms of data and included all relevant studies irrespective of their favoring one or the other technique.

### *Risk of bias within studies*

Table 2 lists the risks of bias included in the studies based on the QUADAS-2 tool.

All included studies were similar in terms of patient selection and index test risk of bias.

In terms of the reference standard, the results were not interpreted without knowledge of the results of the index test in two studies: Kondo *et al.*<sup>[15]</sup> and Schmidt *et al.*<sup>[17]</sup>

de Lédinghen *et al.*<sup>[11]</sup> did not report if their reference standard results were interpreted without knowledge of the results of the index test.

The studies by de Lédinghen *et al.*,<sup>[11]</sup> Materne *et al.*,<sup>[12]</sup> Kondo *et al.*,<sup>[15]</sup> and Fernández-Esparrach *et al.*<sup>[20]</sup> reported an inappropriate interval between the index test(s) and the reference standard.

In terms of receiving the same reference standard, Ainsworth *et al.*<sup>[14]</sup> and Aube *et al.*<sup>[16]</sup> did not introduce bias.

There was a high probability that a patient's flow had introduced bias in the studies of de Lédinghen

**Table 1. Characteristics of the studies**

Study	Patients included in the analysis	Patients with a final diagnosis of choledocholithiasis (gold standard)	Gold standard	EUS x MRCP interval	EUS/MRCP x gold standard interval	Study design	Study inclusion criteria	Tests methods
de Lédighen <i>et al.</i> (1998) <sup>(11)</sup>	32	10	Intraoperative cholangiography/choledochoscopy ERCP	1 day (0-7 days)	4 days, 5 days (1-50 days)	Prospective unblinded study	Clinical or biochemical signs of choledocholithiasis: Epigastric or RUQ pain with fever or jaundice, elevated ALP/GGT/transaminases, acute pancreatitis and unexplained cholestasis	All patients underwent EUS and MRCP by two different operators blinded for the other investigators, results, followed by either ERCP or surgical treatment for the final diagnosis
Materne <i>et al.</i> (2000) <sup>(12)</sup>	50	9	ERCP Intraoperative cholangiography Clinical follow-up	1 day (0-10 days)	ERCP: 1 day (0-14 days) Surgery: 3 days (0-22 days) Follow-up: 6-18 months	Prospective blinded study	Bile duct obstruction suspected by biochemical markers elevated ALP/GGT > twice normal, clinical symptoms: RUQ pain, fever or jaundice and findings of biliary obstruction at transabdominal US	MRCP was performed before EUS in 31 patients and after EUS in 19 patients. The final diagnosis was established with ERCP in 37 patients, from surgery in 9 patients and from follow-up in 4 patients.
Scheiman <i>et al.</i> (2001) <sup>(13)</sup>	28	5	ERCP	<24 h	<24 h	Prospective blinded study	Adult patients (>18 years) referred for ERCP on the basis of clinical signs (abnormal liver enzymes, abnormal transcutaneous US) and symptoms (biliary pain)	EUS and MRCP were performed within 24 h before ERCP; investigators were blinded to the results of the other studies
Ainsworth <i>et al.</i> (2003) <sup>(14)</sup>	163	60	ERCP	<24 h	<24 h	Prospective blinded study	Patients admitted for elective ERCP	Each patient was examined on the first day by EUS and MRCP, in that order, and on the following day by ERCP. No investigator had any knowledge of the findings from the other investigations
Aube <i>et al.</i> (2005) <sup>(16)</sup>	45	16	ERCP Perioperative cholangiography Clinical follow-up	<48 h	ERCP and perioperative cholangiography: No data Clinical follow-up: 3 months	Prospective blinded study	Three groups: 1) Patients with biologic cholestasis or subclinical jaundice, with no suspicion of tumoral disease nor obstruction identified by sonography; 2) acute pancreatitis with no history of chronic alcoholism; 3) abdominal pain associated with degrees of cholestasis defined as elevated transaminases or a transitory increase in serum amylase	MRCP was always performed first by two investigators. EUS was performed no more than 48 h later; investigators were blinded to the results of the other studies
Kondo <i>et al.</i> (2005) <sup>(15)</sup>	28	24	ERCP/IDUS	<2 weeks	<2 weeks	Prospective unblinded study	Patients who were highly suspected of choledocholithiasis based on clinical symptoms (RUQ pain, fever, jaundice) and biochemical abnormalities (elevated ALP/GGT/transaminases/bilirubin) with or without abnormal findings on abdominal US (high echoic spots in the common bile duct or bile duct dilatation)	EUS and MRCP were performed in a random order within two weeks in all patients and the results compared with those of ERCP. Investigators were blinded to the results of the other studies

**Table 1. (Continued)**

Study	Patients included in the analysis	Patients with a final diagnosis of choledocholithiasis (gold standard)	Gold standard	EUS x MRCP interval	EUS/MRCP x gold standard interval	Study design	Study inclusion criteria	Tests methods
Schmidt <i>et al.</i> (2006) <sup>(17)</sup>	57	18	ERCP Intraoperative cholangiography Clinical follow-up	1 day, 9 days (0-5 days)	ERCP and intraoperative cholangiography: 4 days, 1 day (0-9 days) Clinical follow-up: 123 days (17 days-10 months)	Prospective blinded study	Adult patients with suspected choledocholithiasis; RUQ or epigastric pain, fever and jaundice with associated increase of ALP/ GGT/Bilirubin; acute pancreatitis of suspected biliary origin; biological cholestasis with acute fever or jaundice; acute abdominal pain and clinical history suggestive of biliary stones disease	Prospective evaluation comparing MRCP versus EUS performed by different operators blinded to the results of the other method used within a delay of 5 days; final diagnosis was established by ERCP, cholangiography during cholecystectomy or clinical follow-up
Fernández-Esparrach <i>et al.</i> (2007) <sup>(20)</sup>	63	31	ERCP Surgery EUS Intraoperative cholangiography Clinical follow-up	<24 h	ERCP: 11±13 days (1-73 days) Surgery/ Intraoperative cholangiography: 30±31 days (1-106 days) EUS: <24 h Clinical follow-up: 6 months	Prospective blinded study	Patients with unexplained common bile duct dilation in standard US (Group 1)	EUS and MRCP were performed within a 24-h period after inclusion and the sequence of the examinations was randomly assigned. To ensure blinding, each examination was performed by a different operator unaware of the result of the other procedure; final diagnosis was established by ERCP, intraoperative cholangiography, surgery, EUS-FNA or clinical follow-up
Fernández-Esparrach <i>et al.</i> (2007) <sup>(20)†</sup>	72	30	ERCP Surgery EUS Intraoperative cholangiography Clinical follow-up	<24 h	ERCP: 11±13 days (1-73 days) Surgery/ Intraoperative cholangiography: 30±31 days (1-106 days) EUS: <24 h Clinical follow-up: 6 months	Prospective blinded study	Patients with a nondilated common bile duct and a high probability of having choledocholithiasis: Cholangitis, jaundice, nonsevere pancreatitis and increased ALP/ GGT/transaminases (Group 2)	EUS and MRCP were performed within a 24-h period after inclusion and the sequence of the examinations was randomly assigned. To ensure blinding, each examination was performed by a different operator unaware of the result of the other procedure; final diagnosis was established by ERCP, intraoperative cholangiography, surgery, EUS - FNA or clinical follow-up

†Group 1, †Group 2, ERCP: Endoscopic retrograde cholangiopancreatography, IDUS: Intraductal ultrasound, EUS: Endoscopic ultrasound, MRCP: Magnetic resonance cholangiopancreatography, RUQ : Right-upper quadrant, ALP: Alanine aminotransferase, GGT: Gamma-glutamyltransferase, US: Ultrasonography, FNA: Fine-needle aspiration

**Table 2. Risk of bias within included the studies based on the QUADAS-2 tool**

			de Lédinghen	Materne	Scheiman	Ainsworth	Aube	Kondo	Schmidt	Fernández- Esparrach
Patient selection	Signaling questions	Was a consecutive or random sample of patients enrolled?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
		Was a case-control design avoided?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
		Did the study avoid inappropriate exclusions?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Risk of bias	Could the selection of patients have introduced bias?	Low	Low	Low	Low	Low	Low	Low	Low
		Are there concerns about the included patients not matching the review question?	Low	Low	Low	Low	Low	Low	Low	Low
Index test	Signaling questions	Were the index test results interpreted without knowledge of the results of the reference standard?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
		If a threshold was used, was it ore-specified?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Risk of bias	Could the conduct or interpretation of the index test have introduced bias?	Low	Low	Low	Low	Low	Low	Low	Low
		Concerns regarding applicability	Low	Low	Low	Low	Low	Low	Low	Low
	Reference standard	Signaling questions	Is the reference standard likely to correctly classify the target condition?	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were the reference standard results interpreted without knowledge of the results of the index test?			Unclear	Yes	Yes	Yes	Yes	No	No	Yes
Risk of bias		Could the reference standard, its conduct, or its interpretation have introduced bias?	Low	Low	Low	Low	Low	Low	Low	Low
		Concerns regarding applicability	Low	Low	Low	Low	Low	Low	Low	Low
Flow and timing		Signaling questions	Was there an appropriate interval between the index test(s) and the reference standard?	No	No	Yes	Yes	Yes	No	Yes
	Did all patients receive a reference standard?		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Did all patients receive the same reference standard?		No	No	Yes	Yes	Yes	No	No	No
	Were all patients included in the analysis?		Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
	Risk of bias	Could the patient flow have introduced bias?	High	High	Low	Low	Low	High	Low	High

*et al.*,<sup>[11]</sup> Materne *et al.*,<sup>[12]</sup> Kondo *et al.*,<sup>[15]</sup> and Fernández-Esparrach *et al.*<sup>[20]</sup>

**Results of individual studies**

Table 3 lists the reported accuracies, sensitivities, specificities, prevalence (pretest probability), and PPV and NPV (posttest probability) in the included studies.

All studies reported an EUS accuracy higher than that of MRCP except for Fernández-Esparrach *et al.*<sup>[20]</sup> These authors reported the same accuracy for both methods in Group 1 (95%) and a higher accuracy for MRCP in Group 2 (92% *vs.* 86%).

All studies reported EUS sensitivity higher than that of MRCP.

The MRCP specificity was higher than EUS in four studies. Scheiman *et al.*,<sup>[13]</sup> Aube *et al.*<sup>[16]</sup> and Schmidt *et al.*<sup>[17]</sup> reported the same specificity in both methods (96.0%, 96.5%, and 94.4%, respectively.) The EUS

specificity was higher than that of MRCP in de Lédighen *et al.*<sup>[11]</sup> and Ainsworth *et al.*<sup>[14]</sup>

In terms of pretest probability, the values varied from 18 to 86.

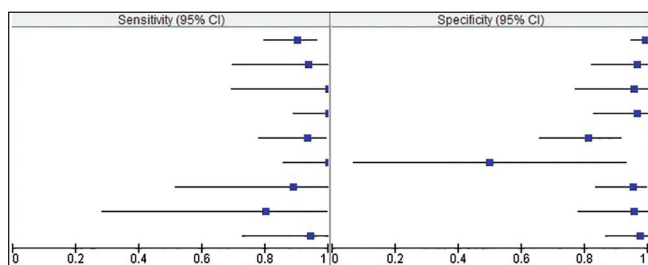
The EUS PPVs were higher than those of MRCP in four studies. Schmidt *et al.*<sup>[17]</sup> reported the same PPVs in both methods (97%).

In terms of the NPVs, those of EUS were higher than those of MRCP in all studies except for de Lédighen *et al.*<sup>[11]</sup>

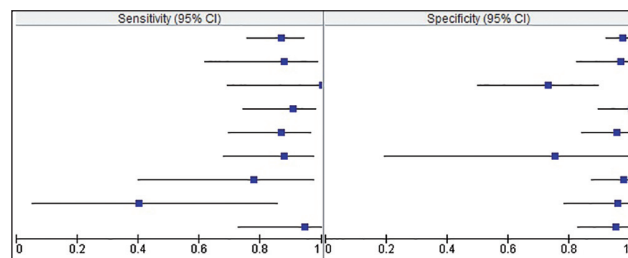
**Synthesis of results**

Figure 2 graphically shows the EUS sensitivities and specificities variance for the diagnosis of choledocholithiasis in the included studies.

Figure 3 graphically shows the variance of MRCP sensitivities and specificities for the diagnosis of choledocholithiasis in the included studies.



**Figure 2.** EUS sensitivities and specificities for choledocholithiasis diagnoses



**Figure 3.** MRCP sensitivities and specificities for choledocholithiasis diagnosis

**Table 3. Performance of EUS and MRCP for evaluation of choledocholithiasis**

Study	de Lédighen	Materne	Scheiman	Ainsworth	Aube	Kondo	Schmidt	Fernández-Esparrach <sup>†</sup>	Fernández-Esparrach <sup>†</sup>
Accuracy									
EUS	97	92	93	93	95	93	96	95	86
MRCP	81	88	86	91	93	86	95	95	92
Sensitivity									
EUS	100	89	80	90	94	100	97	100	93
MRCP	100	78	40	87	87	88	95	90	87
Specificity									
EUS	95	95	96	99	96	50	94	91	81
MRCP	73	98	96	97	96	75	94	100	95
Pretest probability									
	31	18	18	37	35	86	32	49	42
Positive predictive value									
EUS	91	80	80	98	94	92	97	91	78
MRCP	63	88	66	95	93	95	97	100	93
Negative predictive value									
EUS	100	98	96	94	96	100	94	100	94
MRCP	100	95	88	93	93	50	89	91	91

EUS: Endoscopic ultrasound, MRCP: Magnetic resonance cholangiopancreatography, <sup>†</sup>Group 1, <sup>†</sup>Group 2



A comparison between EUS and MRCP is shown in Table 4. For the detection of choledocholithiasis, the sensitivity of EUS was superior to that of MRCP; the former showed an average of 93.7 and SD of 7.1; the latter was characterized by an average of 83.5 and SD of 18.6. The specificity of EUS was slightly inferior to that of MRCP with an average value of 88.5 and SD of 16.1 *versus* 91.5 and SD of 10.7. In terms of pretest probability, the mean value was 38.7 with a SD of 21.8. The mean PPV of EUS was 89 with SD of 6.9. For MRCP, the mean value was 87.8 with SD of 14.4. The mean NPV of EUS was 96.9 with SD of 2.6 and the corresponding values for MRCP were a mean value of 87.8 and SD of 15.5. Finally, the aggregated accuracies of EUS were slightly superior to those of MRCP: An average of 93.3 and SD of 1.7 *versus* 89.7 and SD of 5.0.

The receiver operating characteristic (ROC) curve graphically shows the highest accuracy of EUS for diagnosis of choledocholithiasis as well as the sensitivity values according to the specificity of EUS and MRCP [Figure 4].

#### Risk of bias across studies

In terms of patient selection, index test, and reference standard, all studies reported a low risk of bias. However, in terms of flow and timing there was a high risk of bias in the studies of de Lédinghen *et al.*,<sup>[11]</sup> Materne *et al.*,<sup>[12]</sup> Kondo *et al.*,<sup>[15]</sup> and Fernández-Esparrach *et al.*<sup>[20]</sup>

## DISCUSSION

There has been much recent interest in performing an initial evaluation of patients with suspected choledocholithiasis with less invasive or noninvasive modalities such as EUS and MRCP.

There have been two previous systematic reviews that conducted different methodologies not based in PRISMA recommendations. These reviews demonstrated no statistically significant difference between EUS and MRCP in terms of the detection of choledocholithiasis. Despite a high aggregated diagnostic accuracy being shown for both modalities, there is no superiority between the tests with respect to sensitivity, specificity, PPV, and NPV.

ERCP is at present a well-established method for the treatment of pancreatobiliary disease. Since it is

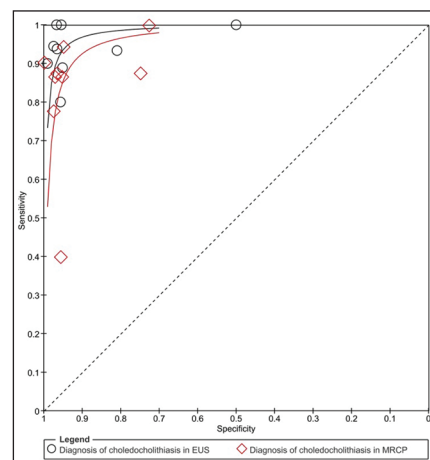


Figure 4. ROC curve

Table 4. Average and variance of diagnostic variables

	EUS	MRCP
SN	93.7 SD 7.1 (86.6; 100)	83.5 SD 18.6 (64.9; 100)
SP	88,5 SD 16.1 (72.4; 100)	91.5 SD 10.7 (80.8; 100)
PP	38.7 SD 21.8 (16.9; 60.5)	
PPV	89 SD 6.9 (82.1; 95.9)	87,8 SD 14.4 (73.4; 100)
NPV	96.9 SD 2.6 (94.3; 99.5)	87,8 SD 15.5 (72.3; 100)
Accuracy	93.3 SD 1.7 (91,6; 95)	89.7 SD 5.0 (84,7; 94.7)

SN: Sensitivity, SD: Standard deviation, SP: Specificity, PP: Pretest probability, PPV: Positive predictive value, NPV: Negative predictive value

associated with a small risk of significant morbidity and mortality, including severe complications such as acute pancreatitis, bleeding, perforation, sepsis, and even but rarely death, its use must be dedicated to treatment instead of diagnosis.<sup>[4]</sup>

We have compared the diagnostic ability of EUS and MRCP to detect choledocholithiasis in suspected patients. This study demonstrated a high diagnostic accuracy of both methods, with the highest sensitivity for EUS and the highest specificity for MRCP.

The major advantage of MRCP is its completely noninvasive nature compared with EUS, perhaps making it a better test for high-risk patients such as the elderly or the severely ill. This study reported a mean MRCP specificity of 91.5 for the detection of choledocholithiasis, demonstrating a very low failure rate. Nevertheless, a high level of technical expertise is crucial to ensure an accurate review of MRCP images and this method requires a high level of patient cooperation.<sup>[24]</sup> The presence of air bubbles inside the bile duct it is one contributing factor to EUS false negative results.

EUS yields very high-resolution images because of the proximity of the endoscope probe to the internal structures. This high resolution, which exceeds that of MRCP, makes EUS extremely sensitive to small stones. This systematic review demonstrated a mean EUS sensitivity of 93.7 to detect choledocholithiasis. If stones are demonstrated by EUS, therapeutic ERCP can potentially be performed immediately after the completion of EUS while the patient is still sedated. However, EUS brings with risks of sedation, bleeding, and perforation.

Both EUS and MRCP demonstrated a high posttest probability, with the advantage going to EUS (PPV 89 and NPV 96.9). Given that both tests are highly accurate, additional large-scale trials may be required to elucidate a difference.

### Limitations

The gold standard used in a variety of studies has been ERCP although its accuracy is not 100%. Another limitation could be the long interval between EUS and MRCP executions and between EUS/MRCP and the reference standard reported in some tests, which can favor the passage of stones and disagreement between tests.

An evaluation concerning microlithiasis could not be made because the studies did not contain enough data about the number and sizes of the stones.

## CONCLUSION

We have demonstrated that for the same pretest probability of choledocholithiasis, EUS exhibits a higher posttest probability when the result is positive and a lower posttest probability when the result is negative compared to MRCP.

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### Conflicts of interest

There are no conflicts of interest.

## REFERENCES

- Gallstones and Laparoscopic Cholecystectomy. NIH Consensus Statement 1992;10:1-20.
- Hermann RE. The spectrum of biliary stone disease. *Am J Surg* 1889;158:171-3.
- Pickuth D, Spielmann RP. Detection of choledocholithiasis: Comparison of unenhanced spiral CT, US, and ERCP. *Hepatogastroenterology* 2000;47:1514-7.
- Loperfido S, Angelini G, Benedetti G, *et al.* Major early complications from diagnostic and therapeutic ERCP: A prospective multicenter study. *Gastrointest Endosc* 1998;48:1-10.
- Kohut M, Nowakowska-Dulawa E, Marek T, *et al.* Accuracy of linear endoscopic ultrasonography in the evaluation of patients with suspected common bile duct stones. *Endoscopy* 2002;34:299-303.
- Palazzo L, Girollet PP, Salmeron M, *et al.* Value of endoscopic ultrasonography in the diagnosis of common bile duct stones: Comparison with surgical exploration and ERCP. *Gastrointest Endosc* 1995;42:225-31.
- Chan YL, Chan AC, Lam WW, *et al.* Choledocholithiasis: Comparison of MR cholangiography and endoscopic retrograde cholangiography. *Radiology* 1996;200:85-9.
- Soto JA, Barish MA, Yucel EK, *et al.* Magnetic resonance cholangiography: Comparison with endoscopic retrograde cholangiopancreatography. *Gastroenterology* 1996;110:589-97.
- Becker CD, Grossholz M, Becker M, *et al.* Choledocholithiasis and bile duct stenosis: Diagnostic accuracy of MR cholangiopancreatography. *Radiology* 1997;205:523-30.
- Varghese JC, Liddell RP, Farrell MA, *et al.* Diagnostic accuracy of magnetic resonance cholangiopancreatography and ultrasound compared with direct cholangiography in the detection of choledocholithiasis. *Clin Radiol* 2000;55:25-35.
- de Lédinghen V, Lecesne R, Raymond JM, *et al.* Diagnosis of choledocholithiasis: EUS or magnetic resonance cholangiography? A prospective controlled study. *Gastrointest Endosc* 1999;49:26-31.
- Materne R, Van Beers BE, Gigot JF, *et al.* Extrahepatic biliary obstruction: Magnetic resonance imaging compared with endoscopic ultrasonography. *Endoscopy* 2000;32:3-9.
- Scheiman JM, Carlos RC, Barnett JL, *et al.* Can endoscopic ultrasound or magnetic resonance cholangiography replace ERCP in patients with suspected biliary disease? A prospective trial and cost analysis. *Am J Gastroenterol* 2001;96:2900-4.
- Ainsworth AP, Rafaelsen SR, Wamberg PA, *et al.* Is there a difference in diagnostic accuracy and clinical impact between endoscopic ultrasonography and magnetic resonance cholangiopancreatography? *Endoscopy* 2003;35:1029-32.
- Kondo S, Isayama H, Akahane M, *et al.* Detection of common bile duct stones: Comparison between endoscopic ultrasonography, magnetic resonance cholangiography, and helical-computed-tomographic cholangiography. *Eur J Radiol* 2005;54:271-5.
- Aube C, Delorme B, Yzet T, *et al.* MR cholangiopancreatography versus endoscopic sonography in suspected common bile duct lithiasis: A prospective, comparative study. *AJR Am J Roentgenol* 2005;184:55-62.
- Schmidt S, Chevallier P, Novellas S, *et al.* Choledocholithiasis: Repetitive thick-lab single-shot projection magnetic resonance cholangiopancreatography versus endoscopic ultrasonography. *Eur Radiol* 2007;17:241-50.
- Verma D, Kapadia A, Eisen GM, *et al.* EUS versus MRCP for detection of choledocholithiasis. *Gastrointest Endosc* 2006;64:248-54.
- Ledro-Cano D. Suspected choledocholithiasis: Endoscopic ultrasound or magnetic resonance cholangio-pancreatography? A systematic review. *Eur J Gastroenterol Hepatol* 2007;19:1007-11.
- Fernández-Esparrach G, Ginès A, Sánchez M, *et al.* Comparison of endoscopic ultrasonography and magnetic resonance cholangiopancreatography in the diagnosis of pancreatobiliary diseases: A prospective study. *Am J Gastroenterol* 2007;102:1632-9.
- Moher D, Liberati A, Tetzlaff J, *et al.*; PRISMA Group. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Ann Intern Med* 2009;151:264-9, W64.
- Whiting P, Rutjes AW, Dinnes J, *et al.* Development and validation of methods for assessing the quality of diagnostic accuracy studies. *Health Technol Assess* 2004;8:iii, 1-234.

23. Cochrane Informatics and Knowledge Management Department. Review Manager (RevMan). Available from: <http://tech.cochrane.org/revman>. [Last accessed on 2014 Nov 20].
24. Lee MG, Lee HJ, Kim MH, *et al.* Extrahepatic biliary diseases: 3D MR cholangiopancreatography compared with endoscopic retrograde cholangiopancreatography. *Radiology* 1997;202:663-9.