

Comparison of Radial Echoendoscopy and Predictive Factors in the Evaluation of Patients with Suspected Choledocholithiasis

Patarapong Kamalaporn, M.D.*, Supphamat Chirnakorn, M.D.*, Sasivimol Rattanasiri, Ph.D.***, Taya Kitiyakara, MBBS*

*Department of Medicine, Faculty of Medicine Ramathibodi Hospital, **Department of Clinical Epidemiology and Biostatistics, Faculty of Medicine Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand.

ABSTRACT

Objective: The aim of this study was to compare predictive factors and endoscopic ultrasound (EUS) in the diagnosis of choledocholithiasis.

Materials and Methods: Patients with suspected choledocholithiasis were recruited from April 2011 to January 2018. All patient characteristics, EUS findings and ERCP findings were recorded and analyzed.

Results: Eighty patients were enrolled in this study. Clinical symptoms, blood chemistry and liver function tests were similar in patients with and without choledocholithiasis. Using the findings of ERCP as the gold standard, radial EUS had a sensitivity and specificity for the detection of choledocholithiasis of 90.2% and 97.4%, and for choledocholithiasis and/or common bile duct sludge 92.7% and 100%, respectively. For patients with intermediate likelihood and high likelihood of having choledocholithiasis, as calculated from their predictive factors (33 and 45), radial EUS was positive for choledocholithiasis in 51.5% (17/33) and 46.7% (21/45), and ERCP was positive for choledocholithiasis in 54.5% (18/33) and 48.9% (22/45), respectively.

Conclusion: Predictive factors, for both the intermediate and high likelihood groups, were not accurate to diagnose these patients. EUS is a good diagnostic tool and should be performed in both groups of patients to avoid unnecessary ERCP.

Keywords: Echoendoscopy; choledocholithiasis (Siriraj Med J 2021; 73: 380-385)

INTRODUCTION

Cholelithiasis is a common problem and occurs 6-9% in the population.¹ Most patients are asymptomatic but some can develop biliary colic and other complications. Choledocholithiasis is one of the common complications and can occur in about 20% of these patients.² Once they have choledocholithiasis, cholangitis and acute biliary pancreatitis can occur. The diagnosis of patients

with suspected choledocholithiasis can be made by clinical symptoms, physical examination, changes of liver function test and transabdominal ultrasonography. From previous studies, certain factors were found to improve the diagnostic accuracy of choledocholithiasis by up to 70%. Such factors included clinical ascending cholangitis, the common bile duct being larger than 6 mm with the gall bladder in situ on transabdominal

Corresponding author: Patarapong Kamalaporn

E-mail: Patarakamla@yahoo.com

Received 10 October 2020 Revised 4 January 2021 Accepted 7 January 2021

ORCID ID: <http://orcid.org/0000-0003-0397-1892>

<http://dx.doi.org/10.33192/Smj.2021.50>

ultrasonography, and a bilirubin level higher than 1.8 mg/dL.³ Some imaging methods also have a role in the diagnosis of this condition, such as Endoscopic Ultrasound (EUS), Computerized Tomography (CT), Magnetic Resonance Imaging and Magnetic Resonance Cholangiopancreatography (MRI and MRCP), but the choice of which method to use depends on the local accessibility and the accuracy of each method.

An Endoscopic Ultrasound is an endoscope with an ultrasound probe at the tip which allows the endosonographer to examine the gastrointestinal tract, hepatobiliary tract and pancreas closely by ultrasound. This method is safe and has a low rate of complications, such as bowel perforation and bleeding (0.12%).⁴ The accuracy of hepatobiliary and pancreatic examinations is reported to be as good as MRI and MRCP, at about 91-93% from a previous study.⁵ For CT, MRI and MRCP, patients receive radiation or magnetic resonance as well as intravenous contrast media which may deteriorate renal function. Patients with renal insufficiency may have some limitation for both studies. The gold standard for the detection of choledocholithiasis is Endoscopic Retrograde Cholangiopancreatography (ERCP). ERCP can be both diagnostic and therapeutic at the same time, but as it is more invasive, complications can occur at a higher rate than for EUS, at about 4%, and include acute pancreatitis, perforation, bleeding and infection.⁶

EUS and ERCP are both highly accurate for detecting choledocholithiasis. EUS has a sensitivity of 89-94% and a specificity of 94-95% when ERCP findings are used as the gold standard. But EUS has lower complications (Relative risk 0.35, 95% CI 0.2-0.62; $p < 0.001$) and a lower incidence of pancreatitis (Relative risk 0.21, 95% CI 0.06-0.83; $p 0.03$).⁷

The American Society of Gastrointestinal Endoscopy (ASGE) guideline³ categorize patients with suspected choledocholithiasis into low, intermediate and high likelihood using predictive factors. Additional tests (MRCP or EUS) are recommended to confirm choledocholithiasis in the intermediate likelihood group before doing ERCP.

This study was designed to compare the sensitivity and specificity of the patients' predictive factors with the EUS findings in the detection of choledocholithiasis, in patients who underwent ERCP.

MATERIALS AND METHODS

This prospective, descriptive study was approved by Ramathibodi Ethical Committee. The study was performed in Ramathibodi Endoscopic unit from April 2011 to January 2018. We recruited patients 18 to 80 years old who were suspected of having choledocholithiasis

and transabdominal ultrasonography was negative for choledocholithiasis. Patients had at least one of the following: clinical symptoms of cholangitis (fever, abdominal pain and jaundice), alkaline phosphatase > 300 unit/L, direct bilirubin > 1.8 mg/dL, clinical symptoms of gall stone pancreatitis, common bile duct (CBD) dilatation to at least 6 mm in patients with the gall bladder in-situ or common bile duct dilatation to at least 10 mm in patients after cholecystectomy.^{3,8} We excluded patients who were unable to undergo esophagogastroduodenoscopy such as those with esophageal stricture, pyloric stricture and patients who refused to participate in the study. All patients were informed about risks and benefits of both procedures, radial EUS and ERCP. Patients signed the consent forms before starting all procedures.

EUS was performed in these patients as soon as possible by two endosonographers and an Olympus GF-UE160-AL5 Radial Array Ultrasound Gastrovideoscope was used. With the Radial EUS, the CBD was carefully evaluated for choledocholithiasis or common bile duct sludge. We defined choledocholithiasis as a hyperechoic lesion with posterior acoustic shadow or a hypoechoic lesion which was movable in the CBD and common bile duct sludge as hyperechoic foci or content in common bile duct which included microlithiasis and viscous bile fluid. Microlithiasis and viscous bile fluid are known to cause intermittent common bile duct obstruction and pancreatitis.⁹⁻¹¹ ERCP was done either at the same session or within 6 weeks for definite diagnosis and treatment. At ERCP, if the cholangiogram looked suspicious for choledocholithiasis or common bile duct sludge, endoscopic sphincterotomy was done and a balloon or basket extraction was applied to clear common bile duct. The diagnosis was confirmed by two experienced endoscopists.

All predictive factors, findings of radial EUS and findings of ERCP were compared by statistical analysis. All patients were classified by their predictors according to the ASGE guideline 2010 into low, intermediate and high likelihood groups to check the accuracy of this guideline (Fig 1).³ Descriptive data was presented as mean with standard deviation (SD) or median with range. Factors associated with choledocholithiasis were analyzed by Chi-square test or T-test. Statistical significance was defined as p -value < 0.05 . The sensitivity and specificity values for radial EUS for the detection of choledocholithiasis and choledocholithiasis and/ or common bile duct sludge were calculated, using the ERCP findings as the gold standard. All statistical analyses were performed using STATA version 15.

Very strong

Common bile duct stone on transabdominal ultrasonography

Clinical ascending cholangitis

Bilirubin >4 mg/dL

Strong

Dilated common bile duct on transabdominal ultrasonography (>6 mm with gall bladder in situ)

Bilirubin level 1.8-4 mg/dL

Moderate

Abnormal liver biochemical test other than bilirubin

Age older than 55 year

Clinical gall stone pancreatitis

Assigning a likelihood of choledocholithiasis based on clinical predictors

Presence of any very strong predictor	high
Presence of both strong predictor	high
No predictor present	low
All other patients	intermediate

Fig 1. Predictors of choledocholithiasis³**RESULTS**

Eighty patients were recruited into this study from a total of 722 patients who underwent ERCP for choledocholithiasis in the same time period. For the 80 patients with suspected choledocholithiasis and negative choledocholithiasis on transabdominal ultrasonography, the mean (\pm SD) of age was 65.2 (\pm 14.9) years old and 46 patients were female. Patients presented with abdominal pain 87.5% (70/80), fever 58.8% (47/80) and jaundice 71.3% (57/80). The median (range) for alkaline phosphatase was 183 u/L (62-1309), serum glutamic-oxaloacetic transaminase level 112 (16-4289) U/L, serum glutamic-pyruvic transaminase level 142 (13-1782) U/L, total bilirubin 2.5 (0.2-16) mg/dL and direct bilirubin 1.7 (0.1-12) mg/dL. In 69 patients, radial EUS and ERCP were done on the same day/ same setting. For nine patients these two procedures were done with an interval of one day, and in two patients, the interval was 35 days. No complication was noted in all recruited patients.

Radial EUS showed choledocholithiasis in 37 patients and ERCP confirmed choledocholithiasis in 41 patients. The sensitivity and specificity of radial EUS for detecting choledocholithiasis were 90.2% (37/41) and 97.4% (38/39), respectively (Table 1). Baseline characteristics for patients with and without choledocholithiasis, including symptoms,

blood chemistry and liver function tests, were similar (Table 2). Only the mean age of patients was higher in patients with choledocholithiasis, mean \pm SD: 68.66 (14.58) vs 61.54 (14.49), $p=0.032$.

When we included patients with choledocholithiasis and/ or common bile duct sludge, radial EUS was positive in 63 patients and ERCP was positive in 68 patients. The sensitivity and specificity of radial EUS for detecting choledocholithiasis and / or sludge in common bile duct were 92.7% (63/68) and 100% (12/12), respectively (Table 1). When we analyzed the performance of radial EUS in detecting only common bile duct sludge, the sensitivity was 72.5% (29/40) and the specificity was 95% (38/40), (Table 1).

When the predictors for choledocholithiasis were used to classify the patients according to the ASGE guideline 2010, 2 of our patients were in the low likelihood group, 33 in the intermediate likelihood group and 45 in the high likelihood group. The guideline recommended further investigations for the intermediate group. In this group, radial EUS was positive for choledocholithiasis in 17 patients (51.5%, 17/33) and ERCP was positive for choledocholithiasis in 18 patients (54.5%, 18/33). When we included patients with choledocholithiasis and/ or common bile duct sludge, Radial EUS was positive

TABLE 1. Performance of EUS (ERCP findings as gold standard)

Performance of EUS	Sensitivity	Specificity	ROC area, (95% CI)
	EUS/ERCP, n (%)	EUS/ERCP, n (%)	
For choledocholithiasis	37/41 (90.2%)	38/39 (97.4%)	0.94 (0.89-0.99)
For CBD sludge	29/40 (72.5%)	38/40 (95%)	0.86 (0.79-0.93)
For choledocholithiasis and/or CBD sludge	63/68 (92.7%)	12/12 (100%)	0.96 (0.93-0.99)
Categorized by ASGE guideline:			
Intermediate likelihood group			
For choledocholithiasis	17/18 (94.4%)	15/15 (100%)	0.97 (0.92-1)
For choledocholithiasis and/or CBD sludge	25/28 (89.3%)	5/5 (100%)	0.95 (0.89-1)
High likelihood group			
For choledocholithiasis	21/22 (95.4%)	23/23 (100%)	0.97 (0.93-1)
For choledocholithiasis and/or CBD sludge	36/38 (94.7%)	7/7 (100%)	0.97 (0.94-1)

Abbreviations: CBD: common bile duct, ROC: Receiver operating characteristic

in 25 patients (75.8%, 25/33) and ERCP was positive in 28 patients (84.8%, 28/33). For the high likelihood group, radial EUS was positive for choledocholithiasis in 21 patients (46.7%, 21/45) and ERCP was positive for choledocholithiasis in 22 patients (48.9%, 22/45). When we included patients who were positive for choledocholithiasis and/ or sludge in the analysis, radial EUS was positive in 36 patients (80%, 36/45) and ERCP was positive in 38 patients (84.4%, 38/45). The accuracy of EUS in the diagnosis of choledocholithiasis, and choledocholithiasis and/ or common bile duct sludge was high in both groups of patients and is shown in [Table 1](#).

DISCUSSION

Endoscopic Ultrasound is a low risk endoscopic procedure which can evaluate the common bile duct in patients with suspected choledocholithiasis. Previous studies have suggested that a strategy of EUS-directed ERCP for choledocholithiasis allowed 50-70% of the patients to avoid a diagnostic ERCP and reduced complications by 4-7%. At 1-year follow-up, there was no difference in outcomes between patients in both groups.¹²⁻¹⁴

In this study, we recruited patients with suspected choledocholithiasis from clinical symptoms and blood chemistry, without visible choledocholithiasis on transabdominal ultrasonography. The reason that our study recruited this group of patients was that patients who were positive for choledocholithiasis on transabdominal ultrasonography would go straight for ERCP. They would not need to have another non-invasive imaging technique such as EUS to confirm choledocholithiasis. Most of the patients in this study (69/80) underwent radial EUS and ERCP back-to-back, and 9/80 patients had both procedures with an interval of only one day. As a result, the results of both procedures, and the difference between them would unlikely be confounded by the passage of stones in between the procedures. A long waiting time between the two procedures would allow the passing of choledocholithiasis and give a false negative ERCP result. Conversely, cholelithiasis could also be passed into the common bile duct during the waiting time. This would produce a positive ERCP result, and decrease the sensitivity of EUS.

TABLE 2. Comparison baseline characteristic between positive and negative choledocholithiasis (CBD stone) from ERCP.

Characteristic	ERCP_CBD=negative (n=39)	ERCP_CBD=positive (n=41)	P-value
Age, mean (SD)	61.54 (14.49)	68.66 (14.58)	0.032
Sex, n (%)			
male	14 (35.9)	20 (48.78)	0.244
female	25 (64.1)	21 (51.22)	
Abdominal pain, n (%)			
no	5 (12.82)	5 (12.2)	1.000
present	34 (87.18)	36 (87.8)	
Fever, n (%)			
no	18 (46.15)	15 (36.59)	0.385
present	21 (53.85)	26 (63.41)	
Jaundice, n (%)			
no	8 (20.51)	15 (36.59)	0.112
present	31 (79.49)	26 (63.41)	
ALP, median (range)	174 (64, 1309)	196 (62, 503)	0.434
SGOT median (range)	118 (24, 4289)	99 (16, 1065)	0.713
SGPT median (range)	143 (23, 1782)	137 (13, 782)	0.906
GGT median (range)	353 (9, 2344)	462 (31, 1396)	0.201
TB median (range)	2.40 (0.210, 10.80)	2.70 (0.20, 16)	0.721
DB median (range)	1.70 (0.10, 8.60)	1.50 (0.10, 12)	0.743
Categorized by ASGE guideline			
Low likelihood, n (%)	1 (2.56)	1 (2.43)	
Intermediate likelihood, n (%)	15 (38.46)	18 (43.9)	
High likelihood, n (%)	23 (58.97)	22 (53.65)	

Abbreviations: ALP: alkaline phosphatase, SGOT: serum glutamic-oxaloacetic transaminase, SGPT: serum glutamic-pyruvic transaminase, GGT: gamma glutamyl transferase, TB: total bilirubin, DB: direct bilirubin

Common bile duct sludge is known to cause similar complications to choledocholithiasis such as cholangitis, common bile duct obstruction and gall stone pancreatitis. So we also analyzed choledocholithiasis and/ or common bile duct sludge in the study. Radial EUS was found to have high sensitivity and specificity for the detection of choledocholithiasis, at 90.2% and 97.4% respectively, and also for choledocholithiasis and/or common bile duct

sludge, at 92.7% and 100%, respectively. Radial EUS had a lower sensitivity, 72.5%, but still a high specificity, 95%, for detecting only common bile duct sludge. The amount of sludge in the common bile duct varied for each patient and may have affected the performance of the radial EUS.

There was no significant difference in the baseline characteristics between patients with choledocholithiasis

and without choledocholithiasis, particularly in terms of clinical symptoms (abdominal pain, fever and jaundice) and blood chemistry including the liver function test. It seems that the predictors were not so useful in this study.

For patients with intermediate likelihood and high likelihood of choledocholithiasis according to the ASGE guideline 2010³ classification, ERCP was positive for choledocholithiasis 54.5% (18/33) and 48.9% (22/45), respectively. The accuracy of the predictors from this guideline was also low for our patients in both groups. EUS findings were more accurate than the predictors.

Although this study was prospective in design, it only had a small number of patients, making it difficult to suggest the applicability of the findings with any strength. A further large study may confirm the findings of this study.

CONCLUSION

Endoscopic Ultrasound with a radial echoendoscope was highly accurate and a safe endoscopic procedure for the detection of choledocholithiasis when performed by experienced endosonographers. For patients in both the intermediate likelihood and the high likelihood groups, EUS showed benefit and allowed patients to avoid unnecessary Endoscopic Retrograde cholangiopancreatography and its related complications.

REFERENCES

1. Everhart JE, Khare M, Hill M, Maurer KR. Prevalence and ethnic differences in gallbladder disease in the United States. *Gastroenterology* 1999;117(3):632.
2. Freitas ML, Bell RL, Duffy AJ. Choledocholithiasis: evolving standards for diagnosis and management. *World J Gastroenterol* 2006;12:3162-7.
3. ASGE Standards of Practice Committee, Maple JT, Ben-Menachem T, Anderson MA, Appalaneni V, Banerjee S, et al. The role of endoscopy in the evaluation of suspected choledocholithiasis. *Gastrointest Endosc* 2010;71:1-9.
4. Buscarini E, De Angelis C, Arcidiacono PG, Rocca R, Lupinacci G, Manta R, et al. Multicentre retrospective study on endoscopic ultrasound complications. *Digestive and Liver Disease* 2006;38:762-7.
5. Ledro-Cano D. Suspected choledocholithiasis: endoscopic ultrasound or magnetic resonance cholangio-pancreatography? A systematic review. *Eur J Gastroenterol Hepatol* 2007;19:1007-11.
6. Cotton PB, Garrow DA, Gallagher J, Romagnuolo J. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. *Gastrointest Endosc* 2009;70:80-8.
7. Petrov MS, Savides TJ. Systematic review of endoscopic ultrasonography versus endoscopic retrograde cholangio-pancreatography for suspected choledocholithiasis. *Br J Surg* 2009;96:967-74.
8. Kim JE, Lee JK, Lee KT, Park DI, Hyun JG, Paik SW, et al. The clinical significance of common bile-duct dilatation in patients without biliary symptoms or causative lesions on ultrasonography. *Endoscopy* 2001;33:495-500.
9. Venu RP, Geenen JE, Hogan W, Stone J, Johnson GK, Soergel K. Idiopathic recurrent pancreatitis. An approach to diagnosis and treatment. *Dig Dis Sci* 1989;34(1):56.
10. Lee SP, Maher K, Nicholls JF. Origin and fate of biliary sludge. *Gastroenterology* 1988;94(1):170.
11. Neoptolemos JP, Davidson BR, Winder AF, Vallance D. Role of duodenal bile crystal analysis in the investigation of 'idiopathic' pancreatitis. *Br J Surg* 1988;75(5):450.
12. Lee YT, Chan FKL, Leung WK, Chan HLY, Wu JCY, Yung MY, et al. Comparison of EUS and ERCP in the investigation with suspected biliary obstruction caused by choledocholithiasis: a randomized study. *Gastrointest Endosc* 2008;67:660-8.
13. Liu CL, Fan ST, Lo CM, Tso WK, Wong Y, Poon RTP, et al. Comparison of early endoscopic ultrasonography and endoscopic retrograde cholangiopancreatography in the management of acute biliary pancreatitis: a prospective randomized study. *Clin Gastroenterol Hepatol* 2005;3:1238-44.
14. Polkowski M, Regula J, Tilszer A. Endoscopic ultrasound versus endoscopic retrograde cholangiography for patients with intermediate probability of bile duct stones: a randomized trial comparing two management strategies. *Endoscopy* 2007;39:296-303.