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Diagnostic value of endoscopic ultrasonography for common bile duct dilatation without identifiable etiology detected from cross-sectional imaging

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Diagnostic Value of Endoscopic Ultrasonography for Common Bile Duct Dilatation without Identifiable Etiology Detected from Cross-Sectional Imaging

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Background/Aims: Endoscopic ultrasonography (EUS) is warranted when cross-sectional imaging demonstrates common bile duct (CBD) dilatation without identifiable causes. This study aimed to assess the diagnostic performance of EUS in CBD dilatation of unknown etiology.
Methods: Retrospective review of patients with dilated CBD without definite causes undergoing EUS between 2012 and 2017.
Results: A total of 131 patients were recruited. The mean age was 63.2±14.1 years. The most common manifestation was abnormal liver chemistry (85.5%). The mean CBD diameter was 12.2±4.1 mm. The area under the receiver operating characteristic curve (AUROC) of EUS-identified pathologies, including malignancy, choledocholithiasis, and benign biliary stricture (BBS), was 0.98 (95% confidence interval [CI], 0.95-1.00). The AUROC of EUS for detecting malignancy, choledocholithiasis, and BBS was 0.91 (95% CI, 0.85-0.97), 1.00 (95% CI, 1.00-1.00), and 0.93 (95% CI, 0.87-0.99), respectively. Male sex, alanine aminotransferase ≥3× the upper limit of normal (ULN), alkaline phosphatase ≥3× the ULN, and intrahepatic duct dilatation were predictors for pathological obstruction, with odds ratios of 5.46 (95%CI, 1.74-17.1), 5.02 (95% CI, 1.48-17.0), 4.63 (95% CI, 1.1-19.6), and 4.03 (95% CI, 1.37-11.8), respectively.
Conclusions: EUS provides excellent diagnostic value in identifying the etiology of CBD dilatation detected by cross-sectional imaging. **Clin Endosc 2022;55:122-127**

Key Words: Common bile duct; Diagnostic imaging; Endosonography; Three-dimensional imaging

INTRODUCTION

Cross-sectional imaging, including multi-detector computed tomography (MDCT), magnetic resonance imaging (MRI), and magnetic resonance cholangiopancreatography (MRCP), have been widely used to evaluate the pancreaticobiliary system. In detecting pancreatic and biliary disease, MDCT and MRI have a sensitivity of 70%–95% and 85%–96% and a specificity of 75%–85% and 89%–98%, respectively.[1-5] Despite their excellent diagnostic performance, the evaluation of the distal bile duct or ampullary area is often limited. In asymptomatic patients, dilated common bile ducts (CBDs) on imaging may be influenced by age, sex, body mass index, and cholecystectomy history. The common pathological causes of CBDs dilatation are choledocholithiasis, periampullary carcinoma, and benign biliary stricture (BBS); however, these lesions can be missed by MDCT, MRI, and MRCP.[6-12] Endoscopic retrograde cholangiopancreatography (ERCP) has historically been one of the most accurate diagnostic procedures for pancreatic and biliary diseases. However, it should only be done for therapeutic purposes due to its invasive nature and potential lethal complications, such as post-ERCP pancreatitis, bleeding, and

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perforation. Endoscopic ultrasonography (EUS) has evolved as a tool for evaluating hepatobiliary and pancreatic diseases. There is a dearth of literature regarding the utility of EUS in outlining a dilated CBDs.[13] This study aimed to evaluate the diagnostic yield of EUS in dilated CBDs without identifiable causes on MDCT or MRI with or without MRCP findings.

MATERIALS AND METHODS

Study population

The 2012–2017 EUS database at a tertiary care center was retrospectively reviewed. The study protocol was approved by the institutional review board and was adapted to the ethical guidelines of the Declaration of Helsinki. Patients who underwent EUS due to CBDs dilatation without definite etiology detected by MDCT or MRI with or without MRCP were identified. The inclusion criteria were as follows: 1) CBDs dilatation, defined as CBDs diameter ≥7 mm in patients with gall bladder in situ or ≥10 mm in post-cholecystectomy patients and 2) no causes of CBDs dilatation identified by MDCT or MRI with or without MRCP. The exclusion criteria were as follows: 1) patients with definite causes of CBDs dilatation identified by cross-sectional imaging and 2) patients without available MDCT, MRI, or MRCP for review.

Clinical, laboratory, and radiological data

All EUS procedures were performed with either a radial (GF-UE160-AL5; Olympus, Tokyo, Japan) or linear (GF-UC140P-AL5; Olympus, Tokyo, Japan) echoendoscope by an experienced endoscopist who had performed more than 2,000 EUS procedures. Demographic data, clinical presentations, laboratory results, radiological findings, EUS findings, cytopathological results, and follow-up data of all included patients were collected. The definite diagnosis was determined by the results of ERCP, cytology, or histology obtained from EUS-guided tissue acquisition (EUS-TA), surgical pathology, and clinical, laboratory, and radiological follow-up for at least 12 months.

Definition

Choledocholithiasis was determined by visualization of the stones in the CBDs during ERCP. Malignancy was confirmed by cytology or histology obtained by EUS-TA, or surgical pathology. If the tissue diagnosis could not be obtained, clinical, laboratory, and radiological follow-up was required for at least 12 months. BBS was defined as narrowing of the distal CBDs diameter without visualization of stones or masses and negative cytology or histology obtained by EUS-TA or ERCP, combined with no progression of bile duct dilatation and interval symptoms during a 12-month follow-up of clinical condition, laboratory, and radiological studies. If surgical pathology was available, BBS was defined as the absence of malignancy. CBDs dilatation without pathological causes was determined by the absence of progression of bile duct dilatation and interval symptoms during a 12-month follow-up of clinical condition, laboratory, and radiological studies.

Statistical analysis

Descriptive statistics were computed for demographic, clinical, and laboratory data. For normally distributed quantitative variables, results are expressed as means and standard deviations; otherwise, medians and ranges are reported. Qualitative variables were summarized as counts and percentages. The area under the receiver operating characteristic curve (AUROC) was calculated to evaluate the overall accuracy of EUS for identifying the causes of bile duct dilatation. The predictive ability was further analyzed by calculating the sensitivity, specificity, positive likelihood ratio, negative likelihood ratio, positive predictive value (PPV), and negative predictive value (NPV) with their 95% confidence interval (CI)s. Logistic regression models were used to evaluate the relationship between baseline characteristics and the presence or absence of pathology. All statistical tests were performed at the conventional two-tailed α-level of 0.05. SPSS Statistics (version 18.0; SPSS Inc., Chicago, IL, USA) was used for all analyses.

RESULTS

Characteristics of the study cohort

The EUS database showed that 2,954 patients underwent diagnostic EUS during the study period. A total of 175 patients underwent EUS for CBDs dilatation without identifiable causes. Forty-four patients were excluded because of unavailable radiological studies for review. Among the 131 included patients, the mean age was 63.2±14.1 years, 47.3% were male, and the most common clinical manifestations were abnormal liver function tests (85.5%), jaundice (48.9%), and abdominal pain (48.1%). The mean CBDs diameter was 12.2±4.1 mm, and 58% had coexisting intrahepatic duct (IHD) dilatation. Among abnormal liver function tests, elevated total bilirubin (median, 2.3 mg/dL; range, 0.2–37.8), aspartate aminotransferase (median, 66 IU/L), alanine aminotransferase (ALT) (median, 66 IU/L), and alkaline phosphatase (ALP) (median, 249 IU/L) were detected (Table 1).

Definite etiology of CBD dilatation

EUS detected the causes of CBDs dilatation in 88 of 131 patients (67%). Among the 131 patients, 41 patients (31%) had

Table 1. Baseline Characteristics of the Study Population

Baseline Characteristics	Values
Number	131
Male gender	62 (47.3)
Age (years)	63.2±14.1
Body mass index (kg/m^2)	21.8±3.5
History of cholecystectomy	19 (14.5)
Clinical presentation	
Abnormal liver function test	112 (85.5)
Jaundice	64 (48.9)
Abdominal pain	63 (48.1)
Fever	19 (14.5)
Constitutional symptoms	19 (14.5)
Weight loss	29 (22.1)
Palpable gallbladder	5 (3.8)
Laboratory finding	
AST (IU/L)	66 (7–611)
ALT (IU/L)	66 (7–611)
ALP (IU/L)	249 (28–1,630)
Gamma glutamyl transpeptidase (IU/L)	445 (35–1,906)
Total bilirubin (mg/dL)	2.3 (0.2–37.8)
CA 19-9 (IU/L)	62.9 (20–52,843)
Imaging findings	
Common bile duct diameter (mm)	12.2±4.1
Intrahepatic duct dilatation	77 (58.8)
Intraabdominal lymphadenopathy	14 (10.7)
Chronic pancreatitis	6 (4.6)

Data are presented as the number (%) or mean±standard deviation.

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CA, carbohydrate antigen.

malignancy, consisting of distal cholangiocarcinoma (51.2%), ampullary adenocarcinoma (24.3%), pancreatic adenocarcinoma 19.5%), gallbladder carcinoma (2.5%), and duodenal adenocarcinoma (2.5%). A total of 24 (18.3%), 23 (17.6%), and 43 (33%) patients had choledocholithiasis, BBS, and dilated CBDs without a pathological cause of obstruction, respectively.

Diagnostic performance of EUS

The diagnostic performance of EUS in detecting the causes of CBDs dilatation was evaluated, as shown in Table 2. EUS had an excellent diagnostic performance for identifying the etiology of CBDs dilatation with an AUROC, sensitivity, specificity, PPV, and NPV of 0.98 (95% CI, 0.95–1.00), 100% (95% CI, 95.8–100), 95.6% (95% CI, 84.9–99.5), 97.7% (95% CI, 92.0–99.7), and 100% (95% CI, 91.8–100), respectively. Furthermore, we assessed the diagnostic accuracy of EUS for each diagnosis. Among all the diagnoses, EUS performed the best in detecting choledocholithiasis with an AUROC, sensitivity, and specificity of 1.00 (95% CI, 1.00–1.00), 100% (95% CI, 85.8–100), and 100% (95% CI, 96.6–100), respectively. For malignancy, EUS was 82.9% (95% CI, 67.9–92.8) sensitive and 98.9% (95% CI, 94.0–100) specific with an AUROC of 0.91 (95% CI, 0.85–0.97). For BBS, EUS had an AUROC of 0.93 (95% CI, 0.87–0.99) with a high NPV of 98.1% (95% CI, 93.2–99.8).

Predictors for determining the presence of pathological obstruction

Multivariate analysis showed that male sex, ALT ≥3× the upper limit of normal (ULN), ALP ≥3× the ULN, and IHD dilatation were significant predictors for pathological obstruction, with odds ratios of 5.46 (95% CI, 1.74–17.1), 5.02 (95% CI, 1.48–17.0), 4.63 (95% CI, 1.1–19.6) and 4.03 (95% CI, 1.37–11.8), respectively (Table 3).

Table 2. Diagnostic Performance of Endoscopic Ultrasonography for Identifying Causes of Common Bile Duct Dilatation

Definite diagnosis	AUROC (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	LR+ (95% CI)	LR- (95% CI)	PPV (95% CI)	NPV (95% CI)
Pathological obstruction	0.98 (0.95–1.00)	100 (95.8–100)	95.6 (84.9–99.5)	22.5 (5.81–87.2)	0	97.7 (92.0–99.7)	100 (91.8–100)
Choledocholithiasis	1.00 (1.00–1.00)	100 (85.8–100)	100 (96.6–100)	–	0	100 (85.8–100)	100 (96.6–100)
Malignancy	0.91 (0.85–0.97)	82.9 (67.9–92.8)	98.9 (94.0–100)	74.6 (10.6–527)	0.17 (0.09–0.34)	97.1 (85.1–99.9)	92.7 (85.6–97.0)
Benign biliary stricture	0.93 (0.87–0.99)	91.7 (73.0–99.0)	94.4 (88.3–97.9)	16.5 (751–36.2)	0.09 (0.02–0.33)	78.6 (59.0–91.7)	98.1 (93.2–99.8)

AUROC, area under the receiver operating characteristic curve; CI, confidence interval; LR+, positive likelihood ratio; LR-, negative likelihood ratio; NPV, negative predictive value; PPV, positive predictive value.

Table 3. Predictive Factors for Pathological Obstruction and No Pathological Lesion Among Patients with Common Bile Duct Dilatation

Variables	Univariate analysis		Multivariate analysis	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Pathological obstruction				
Male gender	4.10 (1.79–8.97)	0.001	5.46 (1.74–17.1)	0.004
History of cholecystectomy	0.38 (0.14–1.01)	0.052		
Jaundice	20.9 (6.80–64.2)	<0.001		
Abdominal pain	2.24 (1.05–4.76)	0.036		
Fever	10.8 (1.39–83.9)	0.023		
Constitutional symptoms	4.91 (1.18–22.3)	0.040		
Total bilirubin >5 mg/dL	5.41 (2.05–14.3)	0.001		
AST >3 x ULN	2.57 (1.06–6.27)	0.038		
ALT >3 x ULN	4.06 (1.62–10.2)	0.003	5.02 (1.48–17.0)	0.009
ALP >3 x ULN	8.17 (2.33–28.7)	0.001	4.63 (1.10–19.6)	0.037
Intrahepatic biliary dilatation	2.83 (1.33–5.99)	0.007	4.03 (1.37–11.8)	0.011
Intraabdominal lymphadenopathy	7.36 (0.92–58.8)	0.060		

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; OR, odds ratio; ULN, upper limit of normal

DISCUSSION

CBDs dilatation without a discernible cause is not an unexpected finding on cross-sectional imaging. EUS is generally performed in cases of unexplained CBDs dilatation to evaluate the distal bile duct and ampullary area. Nonetheless, evidence-based guidelines have not been established for this clinical setting because of a lack of data. Retrospective studies have evaluated the diagnostic yield of EUS for causes of dilated CBDs, particularly in asymptomatic patients with unexplained CBDs dilatation with both normal and elevated serum liver enzymes.[6,8,12,14,15] EUS was able to detect bile duct pathologies, including dilated CBDs with no obvious etiology, in cross-sectional imaging studies of 6%–21% of asymptomatic patients with normal liver chemistry.[8,14,15] For those with combined CBDs dilatation and abnormal liver chemistry, 50%–100% had pathologies detected by EUS.[12,15] These results emphasized the importance of EUS in this setting; nonetheless, the diagnostic accuracy is yet to be explored.

In the current study, approximately 50% of the patients were symptomatic, and the majority had abnormal liver chemistry. EUS detected bile duct pathologies in 67% of the patients with inconclusive MDCT or MRI with or without MRCP, and the diagnostic performance of EUS in detecting pathologic lesions was excellent, with an AUROC of 0.98. In contrast to other studies, the most common pathologic etiology in our study was malignant obstruction, accounting for one-third of the cohort, with distal cholangiocarcinoma being found in 51%. Choledocholithiasis was the second most common etiology, accounting for 18.3%, while most studies showed that choledocholithiasis was the most common cause, with rates up to nearly 40%, followed by malignancy. We hypothesized that the discrepancy between our results and those of other studies could be attributed to the differences in patient characteristics, including presenting symptoms and the degree of liver chemistry abnormalities. Studies in asymptomatic patients with normal liver chemistry have demonstrated a lower percentage of abnormalities and malignancies detected by EUS. In contrast, 49% of our patients presented with jaundice and a mean total bilirubin level of 5 mg/dL, suggesting underlying pathological bile duct obstruction. Furthermore, the most common malignancy was distal cholangiocarcinoma, which could be difficult to identify using a MDCT scan or MRI. EUS has increasingly become the imaging tool of choice of malignant etiology in dilated CBDs due to its high sensitivity and accuracy, especially in patients with distal biliary obstruction.[16,17] Prior studies have reported a sensitivity of EUS in detecting biliary malignancy, including hilar cholangiocarcinoma, ranging from 40%–90%.[18-20] In addition, there has been a report of EUS detection of distal CBD tumor, whereas CT scan and MRCP suggested stone formation.[21] The current study underscores the excellent diagnostic performance of EUS in diagnosing malignancy as a

cause of bile duct dilatation with an AUROC of 0.91 and specificity of 98.9%.

The exceptional diagnostic accuracy of EUS in detecting choledocholithiasis has been widely accepted. Although EUS and MRCP were comparable in terms of sensitivity, specificity, and accuracy for detecting choledocholithiasis,[22] EUS has detected very small choledocholithiasis missed by MDCT and MRCP with 100% diagnostic accuracy, avoiding unnecessary ERCP and surgery.[21,23] Scheiman et al.[24] suggested that implementing the initial EUS strategy to evaluate patients with suspected biliary disease had the greatest cost-utility, resulting in less unnecessary ERCPs and ERCP-related complications.[24] Similarly, our results showed that EUS performed the best in detecting choledocholithiasis with the AUROC of 1.0. It is important to point out that EUS detection of choledocholithiasis has been reported in CBDs dilatation of unknown etiology in patients with both normal and abnormal liver chemistry, highlighting the necessity of EUS in managing this clinical scenario. Factors that may help predict pathological obstruction are male sex, serum ALT level ≥3× the ULN, serum ALP ≥3× the ULN, and IHD dilatation. Thus, when the dilated bile duct was noted on cross-sectional imaging along with the above parameters, further investigation with EUS is warranted. In contrast, clinical follow-up without further invasive investigations might be sufficient in patients without these parameters. Oppong et al.[14] reported that a history of cholecystectomy, which was identified in 36% of the cases, is a causative factor for non-obstructive CBDs dilatation. In contrast, only 14% of our patients had prior cholecystectomy.

This study was limited by its retrospective nature and the need to use clinical follow-up as part of the definite diagnosis instead of undergoing ERCP or surgery in all cases. However, the strength of the study was high-quality radiologic imaging in all recruited patients and a long-term follow-up of at least 12 months.

In conclusion, EUS is a useful modality for evaluating CBDs dilatation in inconclusive MDCT, MRI, or MRCP. It should be routinely performed for clinically or biochemically indicated pancreatobiliary diseases. The excellent diagnostic performance of EUS could help avoid unnecessary ERCP or surgery in clinical practice.

Conflicts of Interest

The authors have no potential conflicts of interest.

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Author Contributions

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