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 only due to its invasive nature and potential lethal complications, such as post-ERCP pancreatitis, bleeding, and...
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.\textsuperscript{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 \( \geq 7 \) mm in patients with gall bladder in situ or \( \geq 10 \) 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**

Cholecodocholithiasis 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). 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 \( \alpha \)-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...
Pausawasdi N et al. The Diagnostic Value of EUS for CBD Dilatation

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, 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, 93.2–98.8).

### 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).
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. 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. For those with combined CBDs dilatation and abnormal liver chemistry, 50%–100% had pathologies detected by EUS. 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. Prior studies have reported a sensitivity of EUS in detecting biliary malignancy, including hilar cholangiocarcinoma, ranging from 40%–90%. In addition, there has been a report of EUS detection of distal CBD tumor, whereas CT scan and MRCP suggested

<table>
<thead>
<tr>
<th>Variables</th>
<th>Univariate analysis</th>
<th>Multivariate analysis</th>
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<tbody>
<tr>
<td>OR (95% CI)</td>
<td>p-value</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Pathological obstruction</td>
<td></td>
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<tr>
<td>Male gender</td>
<td>4.10 (1.79-8.97)</td>
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<tr>
<td>History of cholecystectomy</td>
<td>0.38 (0.14-1.01)</td>
<td>0.052</td>
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<tr>
<td>Jaundice</td>
<td>20.9 (6.80-64.2)</td>
<td>&lt;0.001</td>
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<tr>
<td>Abdominal pain</td>
<td>2.24 (1.05-4.76)</td>
<td>0.036</td>
</tr>
<tr>
<td>Fever</td>
<td>10.8 (1.39-83.9)</td>
<td>0.023</td>
</tr>
<tr>
<td>Constitutional symptoms</td>
<td>4.91 (1.18-22.3)</td>
<td>0.040</td>
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<tr>
<td>Total bilirubin &gt;5 mg/dL</td>
<td>5.41 (2.05-14.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>AST &gt;3 x ULN</td>
<td>2.57 (1.06-6.27)</td>
<td>0.038</td>
</tr>
<tr>
<td>ALT &gt;3 x ULN</td>
<td>4.06 (1.62-10.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>ALP &gt;3 x ULN</td>
<td>8.17 (2.33-28.7)</td>
<td>0.001</td>
</tr>
<tr>
<td>Intrahepatic biliary dilatation</td>
<td>2.83 (1.33-5.99)</td>
<td>0.007</td>
</tr>
<tr>
<td>Intraabdominal lymphadenopathy</td>
<td>7.36 (0.92-58.8)</td>
<td>0.060</td>
</tr>
</tbody>
</table>

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CI, confidence interval; OR, odds ratio; ULN, upper limit of normal
Funding in clinical practice. The performance of EUS could help avoid unnecessary ERCP or surgery in patients with suspected biliary disease in our patients had prior cholecystectomy.

Similarly, our results showed that EUS performed the best in detecting choledocholithiasis with an AUROC of 1.0. It is important to point out that EUS detection of choledocholithiasis has been 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, clinical follow-up without further invasive investigations might be sufficient in patients without these parameters. Oppong et al. 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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None.

REFERENCES


