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Diagnostic performance of the current risk-stratified approach with computed tomography for suspected choledocholithiasis and its options when negative finding

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ABSTRACT

Background: Several studies evaluated the current guideline of the American Society for Gastrointestinal Endoscopy (ASGE) and reported only suboptimal accuracy. This study evaluated the diagnostic performance of the ASGE guideline based on computed tomography (CT) and role of endoscopic ultrasonography (EUS) and magnetic resonance cholangiopancreatography (MRCP) in patients with suspected choledocholithiasis but negative CT finding.

Methods: Patients with suspected choledocholithiasis undergoing ERCP between January 2016 and January 2017 were retrospectively analyzed. All patients underwent CT to detect choledocholithiasis. EUS or MRCP was performed when the CT scan showed negative findings. Patients were classified into the high and intermediate-risk groups, based on predictors from the ASGE criteria.

Results: Of 583 patients with suspected choledocholithiasis, 340 (58.3%) had stones on ERCP (65.9% in the high-risk group and 40.6% in the intermediate-risk group). The accuracy of ASGE guideline for CT was 63.98% (79.12% sensitivity, 42.80% specificity) and 36.02% (20.88% sensitivity, 57.20% specificity) in the high-risk and intermediate-risk groups, respectively. In 103 patients in the high-risk group underwent both CT and US, the accuracy of CT was higher than that of US for detecting choledocholithiasis (78.64% vs. 53.40%), with a significant difference in area under the curve (AUC) (0.78 vs. 0.59, $P < 0.001$). Of 339 with negative CT finding, the accuracy of EUS was higher than that of MRCP (90.91% vs. 82.76%), but with no significant difference in AUC (0.91 vs. 0.83, $P = 0.347$).

Conclusions: CT-based ASGE guideline showed superior diagnostic performance than US for predicting choledocholithiasis. The diagnostic options, EUS or MRCP, with negative CT finding showed comparable performance. Therefore, the diagnostic modality should be selected based on availability, experience, cost, and contraindications.

Introduction

Approximately 10%–15% of the patients with gallstones present with choledocholithiasis [1,2]. Choledocholithiasis may present as a wide range of conditions, such as biliary colic, or obstructive jaundice and result in serious complications such as cholangitis and gallstone pancreatitis.

Endoscopic retrograde cholangiopancreatography (ERCP) is the standard method for treating confirmed or suspected choledocholithiasis. However, it may cause a substantial number of unnecessary procedures and adverse events in up to 10% of cases, such as post-ERCP pancreatitis, post-sphincterotomy bleeding, cholangitis and perforation [3,4]. To minimize these problems, a method of accurately predicting choledocholithiasis prior to ERCP is very important step in the management of these patients.

To predict the likelihood of choledocholithiasis, the American Society for Gastrointestinal Endoscopy (ASGE) proposed guideline in 2010 that classified patients into high, intermediate or low-risk

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categories, based on the presence of clinical, radiological characteristics based on transabdominal ultrasound (US) and biochemical predictors. In this risk-stratified approach for suspected choledocholithiasis, high-risk patients should proceed directly to removal of stones by surgery or endoscopy without further study. The confirmation of choledocholithiasis in intermediate-risk patients is recommended using additional less invasive testing according to the clinical preference, such as endoscopic ultrasound (EUS) or magnetic resonance cholangiopancreatography (MRCP) [5].

Recently, several studies have attempted to validate the ASGE guideline for the prediction of choledocholithiasis. However, their diagnostic accuracy was somewhat unsatisfactory [6–10]. In addition, most of the patients with choledocholithiasis visited the emergency department and sometimes complained of symptoms similar to those of acute abdomen. In many instances, computed tomography (CT) was performed as a first line diagnostic modality due to its ease of access and differential diagnosis.

The aim of this study was to evaluate the diagnostic performance of CT-based ASGE guideline compared to the original US and diagnostic role of EUS and MRCP as the next options in patients with suspected choledocholithiasis but negative CT finding.

Methods

Study design and population

Consecutive patients, admitted between January 2016 and January 2017 with suspected choledocholithiasis, who underwent an initial CT followed by ERCP, were evaluated retrospectively. Patients were excluded if they had (i) previous ERCP with sphincterotomy, (ii) previous cholecystectomy due to gallstones, (iii) previously diagnosed chronic liver disease or pancreatitis, (iv) combined other biliary tract lesion including malignancy or primary sclerosing cholangitis, and (v) other procedures, such as percutaneous transhepatic cholangiography (PTC) due to comorbidities or surgically altered anatomy.

Individual patients' medical records, including laboratory finding and radiological records (CT, US, MRCP, and EUS) were reviewed. Each patient was categorized as high, intermediate, or low risk for choledocholithiasis according to the ASGE guideline, using CT variables instead of the original US. We excluded low-risk patients classified by the ASGE criteria because they have a low probability of choledocholithiasis (<10%) and recommended no further evaluation. ERCP and EUS procedures were performed by six endoscopists who had more than five years of experience. Our institute had more than 10,000 cases of ERCP and EUS annually, and each endoscopist performed more than 1500 cases of both modalities per year.

This study was approved by the institutional review board of Soonchunhyang University Bucheon Hospital and written informed consent was obtained from all patients.

Definitions

A diagnosis of choledocholithiasis on CT or MRCP was made only when there was direct visualization of stones or a particle described by experienced radiologists. Common bile duct (CBD) dilatation was defined as a maximal CBD diameter > 6 mm on the CT scan. Positive US or EUS finding was defined as the presence of a hyperechoic lesion with or without posterior acoustic shadowing in the bile ducts, excluding sludge such as non-shadowing echo layering. The positive finding of stones on the ERCP was defined as a definite filling defect observed on a cholangiogram and confirmed based on a visual assessment of endoscopy within the duodenum. If there is only sludge or sand-like bile with no definite stones detected during ERCP, we did not consider it to be choledocholithiasis.

Clinical cholangitis was defined as a combination of typical abdominal pain, signs of systemic infection [fever and/or leukocytosis or C-reactive protein (CRP) elevation] and jaundice based on Charcot's triad. Clinical pancreatitis was defined as typical abdominal pain of acute onset that lasted for >24 h with pancreatic enzyme levels at least three times higher than the upper normal limit.

Study end points

The primary end point of the study was to assess the diagnostic performance of ASGE guideline for suspected choledocholithiasis, based on CT in comparison with US. The secondary end point was to evaluate the role of EUS and MRCP as a preoperative option when choledocholithiasis was suspected but CT finding was negative.

Statistical analysis

Continuous variables are presented as means ± standard deviation (SD), which were compared using a Student's *t*-test. Categorical variables were described as frequencies and percentages, which were compared using the Chi-square test or Fisher's exact test. Sensitivity, specificity, positive predictive value (PPV), and negative predictive values (NPV), and accuracy of each criteria for suspected choledocholithiasis were calculated with a 95% confidence interval (95% CI). The area under the curve-receiver operating characteristic (AUC-ROC) was used to calculate the performance of each imaging modalities for choledocholithiasis and compared using DeLong's test for discriminative power. A P value < 0.05 indicates statistical significance. The statistical analysis was performed using SPSS version 21.0 (Armonk, New York, USA) and R version 3.2.0 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Patient population

Between January 2016 and January 2017, 754 patients with suspected choledocholithiasis were assessed for eligibility. After 161 patients were excluded, 593 patients were applied with the ASGE criteria for stratifying the risk of choledocholithiasis. A total of 408 (68.8%) patients met the criteria for high-risk of choledocholithiasis, while 175 (29.5%) patients met the criteria for intermediate-risk for choledocholithiasis. Ten (1.7%) patients who met criteria for low risk for choledocholithiasis were excluded, and data was analyzed for the remaining 583 patients (Fig. 1). The mean age of study subjects was 57.6 years and 52.7% were male. Baseline characteristics and biochemical variables among subjects with and without choledocholithiasis on ERCP are shown in Table 1. A significant difference was found in the age between the two groups ($P < 0.001$).

ASGE predictors for choledocholithiasis on ERCP

Among the ASGE very strong predictors for choledocholithiasis, only choledocholithiasis observed by CT showed a significant difference between subjects with and without choledocholithiasis (57.4% vs. 20.2%, $P < 0.001$). Among strong predictors, a CBD diameter of > 6 mm with gallbladder in situ showed a statistical difference between the two groups (73.8% vs. 48.1%, $P < 0.001$). In moderate predictors, age >55 years showed a statistically higher frequency in patients with choledocholithiasis on

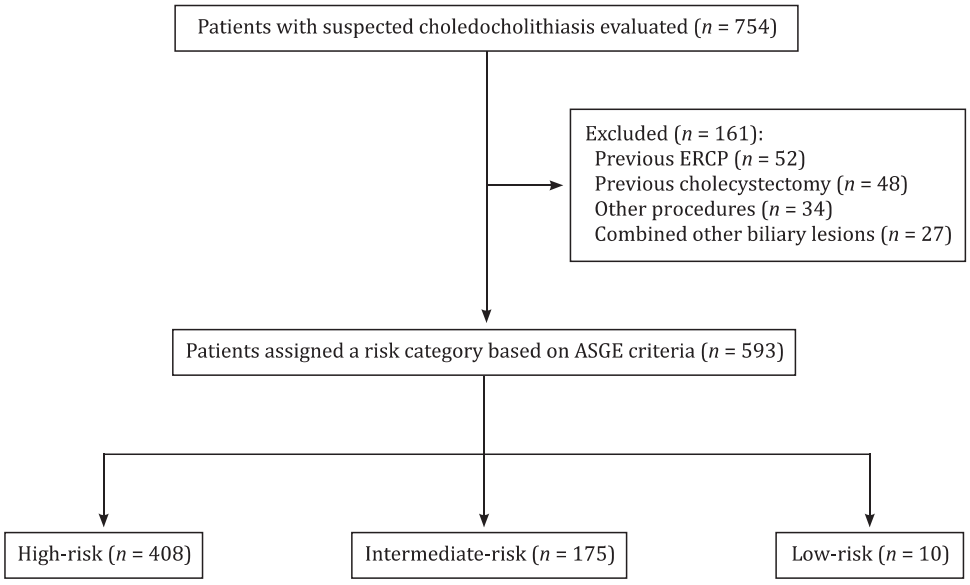

Fig. 1. Flow diagram of patients. ERCP: endoscopic retrograde cholangiopancreatography; ASGE: the American Society for Gastrointestinal Endoscopy.

Table 1
Baseline characteristics of enrolled patients for suspected choledocholithiasis.

Variables	Total (n = 583)	No choledocholithiasis on ERCP (n = 243)	Choledocholithiasis on ERCP (n = 340)	P value
Male	307 (52.7%)	128 (52.7%)	179 (52.6%)	>0.999
Age (yr)	57.55 ± 15.13	54.52 ± 14.89	59.38 ± 15.09	<**0.001**
BMI (kg/m^2)	24.56 ± 3.54	24.89 ± 3.78	24.57 ± 3.35	0.281
Total bilirubin (mg/dL)	2.57 ± 3.17	2.42 ± 2.60	2.71 ± 3.59	0.290
AST (IU/L)	212.94 ± 273.92	214.17 ± 241.35	211.92 ± 292.59	0.922
ALT (IU/L)	218.06 ± 224.41	232.90 ± 219.68	208.99 ± 230.64	0.209
ALP (IU/L)	165.94 ± 132.86	162.00 ± 128.77	166.48 ± 133.63	0.686
r-GT (IU/L)	301.53 ± 245.46	311.65 ± 243.53	294.02 ± 245.91	0.398
WBC (10^3/μL)	8.97 ± 3.94	8.93 ± 3.82	8.99 ± 4.09	0.858
CRP (mg/L)	3.58 ± 6.40	3.60 ± 5.93	3.54 ± 6.65	0.911
ERCP delay time* (days)	1.4 ± 1.2	1.4 ± 1.3	1.5 ± 1.2	0.339

* The internval between CT and ERCP procedure. ERCP: endoscopic retrograde cholangiopancreatography; BMI: body mass index; AST: aspartate aminotransferase; ALT: alanine aminotransferase; ALP: alkaline phosphatase; r-GT: gamma-glutamyl transferase; WBC: white blood cell; CRP: C-reactive protein.

Table 2
Frequency of ASGE predictors in patients with and without choledocholithiasis.

Predictors	Total (n = 583)	No choledocholithiasis on ERCP (n = 243)	Choledocholithiasis on ERCP (n = 340)	Odds ratio (95% CI)	P value
Very strong predictor					
Stones on CT	244 (41.9%)	49 (20.2%)	195 (57.4%)	5.32 (3.64–7.78)	<**0.001**
Clinical ascending cholangitis	184 (31.6%)	74 (30.5%)	110 (32.4%)	1.09 (0.76–1.55)	0.626
Total bilirubin > 4 mg/dL	113 (19.4%)	45 (18.5%)	68 (20.0%)	1.10 (0.72–1.67)	0.656
Strong predictor					
Dilated CBD on CT (> 6 mm with gallbladder *in situ*)	368 (63.1%)	117 (48.1%)	251 (73.8%)	3.03 (2.12–4.30)	<**0.001**
Total bilirubin 1.8–4 mg/dL	158 (27.1%)	70 (28.8%)	88 (25.9%)	0.86 (0.59–1.24)	0.434
Moderate predictor					
Abnormal LFT other than bilirubin	451 (77.4%)	202 (83.1%)	249 (73.2%)	0.55 (0.36–0.83)	**0.005**
Age > 55 yr	351 (60.2%)	130 (53.5%)	221 (65.0%)	1.61 (1.15–2.26)	**0.005**
Clinical gallstone pancreatitis	107 (18.4%)	56 (23.0%)	51 (15.0%)	0.58 (0.37–0.89)	**0.014**

Data in table are presented as the number (of patients) with percentage. ERCP: endoscopic retrograde cholangiopancreatography; CT: computed tomography; CI: confidence index; CBD: common bile duct; LFT: liver function test.

ERCP (65.0% vs. 53.5%, P = 0.005), but an abnormal liver biochemical test (other than bilirubin) and clinical gallstone pancreatitis showed a higher frequency in patients without choledocholithiasis on ERCP (73.2% vs. 83.1%, P = 0.005 and 15.0% vs. 23.0%, P = 0.014, respectively). The risk of choledocholithiasis, as shown by the odds ratio, was increased for patients with choledocholithiasis on CT (OR=5.32; 95% CI: 3.64–7.78), CBD diameter > 6 mm (OR=3.03; 95% CI: 2.12–4.30), and age > 55 year (OR=1.61; 95% CI: 1.15–2.26) (Table 2).

Performance of ASGE high- and intermediate-risk group and individual predictors

Of 408 patients in the high-risk group, 269 (65.9%) patients had choledocholithiasis on ERCP. Of 175 patients in the intermediate-risk group, 71 (40.6%) patients had choledocholithiasis on ERCP. Diagnostic accuracy of the ASGE criteria for choledocholithiasis in high-risk patients was 63.98% (79.12% sensitivity and 42.80% specificity) and in the intermediate-risk patients was 36.02% (20.88%

Table 3
Diagnostic performance of ASGE high and intermediate-risk group and predictors for choledocholithiasis.

Predictors	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
High-risk group	79.12% (74.80%–83.44%)	42.80% (36.58%–49.02%)	65.93% (61.33%–70.53%)	59.43% (52.15%–66.70%)	63.98% (60.08%–67.88%)
Stone on CT	57.35% (52.10%–62.61%)	79.83% (74.79%–84.88%)	79.92% (74.89%–84.94%)	57.23% (51.96%–62.49%)	66.72% (62.90%–70.55%)
Clinical ascending cholangitis	32.35% (27.38%–37.33%)	69.55% (63.76%–75.33%)	59.78% (52.70%–66.87%)	42.36% (37.51%–47.20%)	47.86% (43.80%–51.91%)
Total bilirubin > 4 mg/dL	20.00% (15.75%–24.25%)	81.48% (76.60%–86.37%)	60.18% (51.15%–69.20%)	42.13% (37.66%–46.59%)	45.63% (41.58%–49.67%)
Dilated CBD on CT (> 6 mm with gallbladder *in situ*) + Total bilirubin 1.8–4 mg/dL	19.41% (15.21%–23.62%)	86.83% (82.58%–91.08%)	67.35% (58.06%–76.63%)	43.51% (39.09%–47.92%)	47.51% (43.46%–51.57%)
Intermediate-risk group	20.88% (16.56%–25.20%)	57.20% (50.98%–63.42%)	40.57% (33.30%–47.85%)	34.07% (29.47%–38.67%)	36.02% (32.12%–39.92%)
Dilated CBD on CT (> 6 mm with gallbladder in situ)	73.82% (69.15%–78.50%)	51.85% (45.57%–58.13%)	68.21% (63.45%–72.96%)	58.60% (52.02%–65.19%)	64.67% (60.78%–68.55%)
Total bilirubin 1.8–4 mg/dL	25.88% (21.23%–30.54%)	71.19% (65.50%–76.89%)	55.70% (47.95%–63.44%)	40.71% (36.03%–45.38%)	44.76% (40.73%–48.80%)
Abnormal LFT other than bilirubin	73.23% (68.53%–77.94%)	16.87% (12.16%–21.58%)	55.21% (50.62%–59.80%)	31.06% (23.16%–38.95%)	49.74% (45.68%–53.80%)
Age >55 yr	65.00% (59.93%–70.07%)	46.50% (40.23%–52.77%)	62.31% (57.90%–68.01%)	48.71% (42.28%–55.14%)	57.29% (53.27%–61.31%)
Clinical gallstone pancreatitis	15.00% (11.20%–18.80%)	76.96% (71.66%–82.25%)	47.66% (38.20%–57.13%)	39.29% (34.90%–43.67%)	40.82% (36.83%–44.81%)

CT: computed tomography; CI: confidence index; CBD: common bile duct; LFT: liver function test.

Table 4
Comparison of diagnostic performance between CT and US in high-risk patients for suspected choledocholithiasis.

Modality	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
CT	81.67% (71.88%–91.46%)	74.42% (61.37%–87.46%)	81.67% (71.88%–91.46%)	74.42% (61.38%–87.46%)	78.64% (70.73%–86.56%)
US	21.67% (11.24%–32.09%)	97.67% (93.17%–100%)	92.86% (79.37%–100%)	47.19% (36.82%–57.56%)	53.40% (43.76%–63.03%)

CT: computed tomography; US: ultrasound; CI: confidence index; PPV: positive predictive value; NPV: negative predictive value.

sensitivity and 57.20% specificity). Other diagnostic performances of individual predictors for choledocholithiasis in the high and intermediate-risk groups are shown in Table 3.

Diagnostic performance of CT and US in patients with high-risk for suspected choledocholithiasis

Of 103 patients who underwent both CT and US in the high-risk group, the presence of choledocholithiasis on ERCP was identified in 60 (58.3%) patients. The diagnostic performance of CT or US in patients with a high risk for choledocholithiasis had an accuracy of 78.64% (81.67% sensitivity and 74.42% specificity) and 53.40% (21.67% sensitivity and 97.67% specificity), respectively (Table 4). Fig. 2 shows the ROC curves representing the diagnostic performance of CT and US in high-risk patients with suspected choledocholithiasis. The AUC of CT was 0.78 (95% CI, 0.69–0.86) and significantly higher than that of US (0.59; 95% CI, 0.53–0.65) ($P < 0.001$ by DeLong's test).

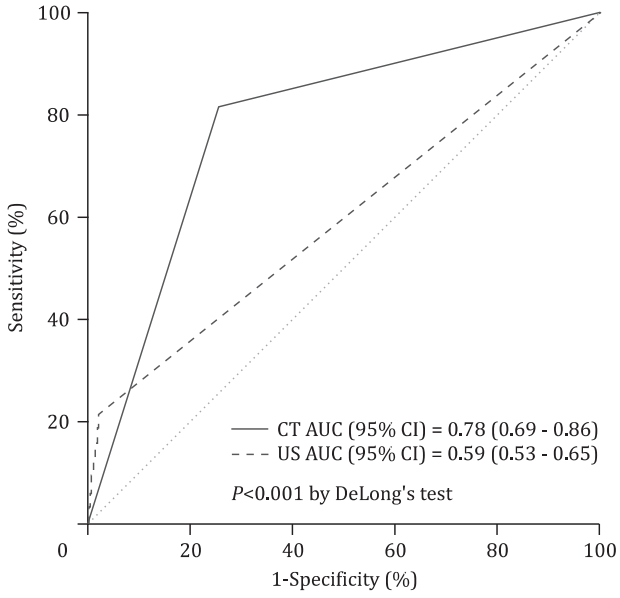

Fig. 2. Comparison of diagnostic performance between CT and US in high-risk patients for suspected choledocholithiasis CT: computed tomography; US: ultrasound; AUC: area under the curve.

Diagnostic performance of EUS and MRCP for suspected choledocholithiasis but negative CT finding

EUS and MRCP were performed in 105 (30.9%) and 120 (35.4%) patients out of 339 patients with negative CT findings of choledocholithiasis. Among 105 patients, EUS revealed choledocholithiasis in 55 (52.4%) patients, and 50 (90.9%) patients were confirmed to have choledocholithiasis on ERCP. Among 120 patients, MRCP revealed choledocholithiasis in 32 (26.7%) patients, and 27 (84.4%) patients were confirmed to have choledocholithiasis on ERCP. The diagnostic performance of EUS and MRCP in patients with suspected choledocholithiasis but negative CT finding had an accuracy of 90.91% (93.15% sensitivity and 88.13% specificity and 82.76% (73.03% sensitivity and 92.94% specificity), respectively (Table 5). Fig. 3 shows the ROC curves representing the diagnostic performance of EUS and MRCP in patients with suspected choledocholithiasis but negative CT finding. The AUC of EUS (0.91; 95% CI: 0.86–0.96) was not significantly higher than that of MRCP (0.83; 95% CI: 0.78–0.88) ($P = 0.347$ by DeLong's test).

Table 5
Comparison of diagnostic performance between EUS and MRCP in patients with suspected choledocholithiasis but negative CT finding.

Modality	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Accuracy (95% CI)
EUS	93.15% (87.36%–98.95%)	88.13% (79.88%–96.39%)	90.67% (84.08%–97.25%)	91.23% (83.88%–98.57%)	90.91% (86.00%–95.81%)
MRCP	73.03% (63.81%–82.25%)	92.94% (87.50%–98.39%)	91.55% (85.08%–98.02%)	76.70% (68.53%–84.86%)	82.76% (77.15%–88.37%)

EUS: endoscopic ultrasound; MRCP: magnetic resonance cholangiopancreatography; CI: confidence index; PPV: positive predictive value; NPV: negative predictive value.

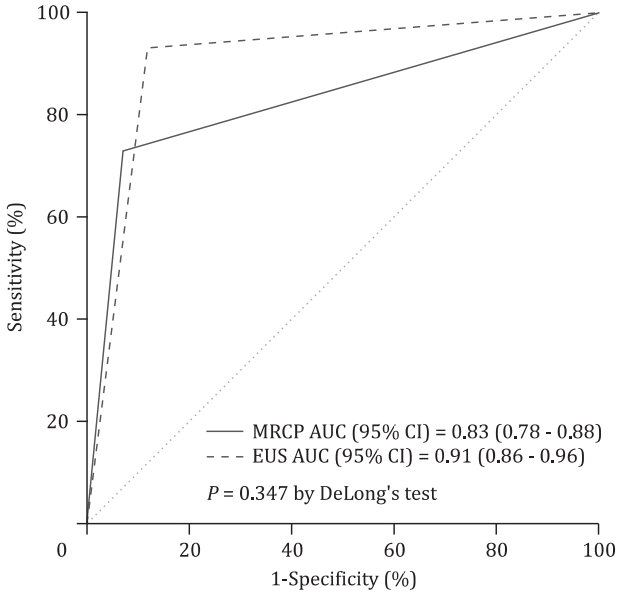

Fig. 3. Comparison of diagnostic performance between MRCP and EUS in patients with suspected choledocholithiasis but negative CT finding. MRCP: magnetic resonance cholangiopancreatography; EUS: endoscopic ultrasound; CT: computed tomography; AUC: area under the curve.

Discussion

To date, ERCP is an effective procedure for removing choledocholithiasis in most cases. However, the major concerns of ERCP are procedure related adverse events and even deaths due to its invasiveness [3,4]. Therefore, current ASGE guideline suggests using a risk-stratified approach based on clinical, laboratory, and imaging based on US results to accurately select and minimized adverse events of ERCP. Based on the ASGE guideline, high-risk patients (>50%) are recommended proceeding direct treatment by ERCP and intermediate-risk patients (10%–50%) are recommended less invasive preoperative procedures such as EUS and MRCP [5].

However, recent study showed that only 55.3% (99/179) patients who met the ASGE high-risk criteria had choledocholithiasis on a subsequent confirmatory test. The overall accuracy of the ASGE guideline in this study was 62.1% (47.4% sensitivity and 73.0% specificity) [6]. Similarly, recently a large Chinese cohort study demonstrated that in patients with high-risk probability criteria, the positive predictive value of the guideline was 64% and specificity was 74% [8]. A Spanish study also showed that choledocholithiasis was detected in 59.6% of patients in the high-risk group, with an accuracy of 59.0% (85.5% sensitivity and 24.3% specificity) [11]. The abdominal US suggested by the ASGE guideline is easy to perform, but it is operator dependent and influenced by clinical factors, including obesity and bowel gas. Therefore, sometimes it cannot be used to evaluate the entire CBD. Therefore, the reported sensitivity of US for the detection of choledocholithiasis is only 22%–58% [5,12]. Recently published reports for validation of the ASGE guideline also showed a wide range of US sensitivity from 21.8% to 55.9% [6,9,11,13]. Therefore, our study was designed to answer the question of whether the ASGE guideline based on CT can show better diagnostic performance for detecting choledocholithiasis due to the higher sensitivity of CT compared to US and which option is better if the CT findings are negative.

In our CT-based study, a total of 58.3% (340/583) patients had confirmed choledocholithiasis during ERCP. In subgroup analysis, stones were detected in 65.9% of high-risk patients, with an accuracy of 63.98% (79.12% sensitivity and 42.80% specificity) and 40.6% of intermediate-risk patients, with an accuracy of 36.02% (20.88% sensitivity and 57.20% specificity) according to ASGE criteria. Although we validated the probability of having choledocholithiasis in the both high-risk (>50%) and intermediate-risk (10%–50%) groups, the results were not as satisfactory as we hoped. Still, more than one-third of the patients, even those in the high-risk group defined by the ASGE guideline, had to undergo unnecessary diagnostic ERCP. These suboptimal results were most likely due to the use of a strict definition of choledocholithiasis, as only definite filling defects on cholangiogram, excluding sludge, confirmed by an endoscopic view. In fact, from the results that include sludge, approximately 69.8% of these patients showed positive findings during the ERCP examination. In addition, our center is a tertiary institution with a large number of interventional procedures or one-stage operations; therefore, there is a possibility that the ratio of negative finding during the ERCP will relatively increase.

Nonetheless, ASGE guideline based on CT showed better diagnostic performance than US in our subgroup analysis. We evaluated 103 patients in the high-risk group who underwent both CT and US; in this analysis, CT showed a fair and US failed to show an accuracy. CT had significantly higher diagnostic performance than that of US.

The significance of the ASGE predictors was slightly different for each study. Stones on US and CBD dilatation in the Turkish study and stones on US, ascending cholangitis, and CBD dilatation in the Spanish study were independent risk factors for choledocholithiasis [9,11]. In the Japanese study, stones detected by imaging (OR=3.98; 95% CI: 2.3–6.8) and bilirubin level of 1.8–4.0 mg/dL (OR=1.9; 95% CI: 1.0–3.4) were independent predictors [14]. Another study suggested that two predictors such as stones detected by US, bilirubin level >4 mg/dL in combination with CBD dilatation are preferred over the ASGE criteria [8].

In our study, the presence of stones on CT, CBD dilatation >6 mm, and age >55 years were significant predictors of choledocholithiasis. The result of the imaging finding was generally consistent, but there were discrepancies in clinical and biochemical results in each study. It is important to remember that patients with acute cholecystitis have elevated liver function test and sometimes bilirubin can elevate above 4 mg/dL [15], which can be conflicting for the diagnosis of choledocholithiasis. We did not rule out patients with acute cholecystitis alone, and this could have reduced the importance of clinical and biochemical predictors for detecting choledocholithiasis. Therefore, systematically well-established guideline for patients with acute cholecystitis alone is required.

Interestingly, as previously reported by other studies [8,11,13,16], gallstones pancreatitis decrease the possibility of choledocholithiasis in our study. It may be that our patients had relatively small choledocholithiasis. Therefore, gallstones pancreatitis more occurred as the stones passed through the papilla.

According to ASGE guideline, EUS or MRCP as less invasive options was recommended for evaluation of patients who fail to identified as having choledocholithiasis [5]. Although, the development of EUS and MRCP have improved the detection of stones in bile duct and improved patient safety, it is unclear which modality is superior for detecting choledocholithiasis [17–19].

A recent meta-analysis of the diagnostic accuracy of EUS and MRCP showed that both modalities provide good diagnostic accuracy, with sensitivity of 97% (range, 91%–99%) and specificity of 90% (range, 83%–94%) for EUS and sensitivity of 87% (range, 80%–93%) and specificity of 92% (range, 87%–96%) for MRCP [19]. Another systemic review also showed similar accuracy of 93.3% for EUS and 89.7% for MRCP [17]. Our study showed comparable EUS sensitivity of 93.15% but relatively low MRCP sensitivity of 73.03% in patients with suspected choledocholithiasis but negative CT finding. Actually, the sensitivity of MRCP seems to diminish depending on the stone size [20,21]. The sensitivity of MRCP was 67%–100% for stones >10 mm, 89%–94% for stones 6–10 mm, and 33%–71% for stones <6 mm [22]. Taken together, our cohort may have relatively small stones less than 6 mm, leading to a possibility of a negative finding in MRCP as well as CT. On the contrary, EUS remains highly sensitive for stones smaller than 5 mm, and its performance does not seem adversely affected by decreasing stone size [21,23]. However, EUS and MRCP also have some limitations including high cost for both, interference caused by metallic implants, claustrophobia, lack of rapidity for MRCP and operator dependency, a more-invasive nature, and limited availability in some facilities for EUS.

Our study showed a higher presence of stones in the EUS group when compared to the MRCP group in patients with suspected choledocholithiasis but negative CT finding. The accuracy of EUS was also higher than MRCP, however, the overall diagnostic performance of EUS and MRCP compared by AUC was not significantly different. Therefore, the choice of diagnostic modality should be based on the available resources, experience of the physician, contraindications for patients, and the cost associated with each modality, if choledocholithiasis suspected but CT findings are negative.

One of the major limitations of our study was that the data were obtained from a retrospective study performed on a single tertiary center. This study was performed by skilled endoscopists in highly experienced institute, however, the result may be different according to the skill and experience of the physicians. Therefore, this may limit the generalizability of our results. Second, the retrospective nature of our study makes it difficult to evaluate CBD sludge clearly. Therefore, we did not consider it choledocholithiasis; however, sludge can cause abdominal pain, cholangitis, and pancreatitis [6]. Third, we did not consider age when defining the CBD dilatation, but mild CBD dilatation related to advancing age has been reported [24], and the definition of cholangitis is also not consistent for each study. Fourth, time elapsed between CT and ERCP could increase the spontaneous migration of small choledocholithiasis through the ampulla. However, we had a mean interval of 1.4 days between CT and ERCP; therefore, the possibility of spontaneous stones migration was minimized.

In conclusion, CT-based ASGE guideline showed better diagnostic performance than US for predicting choledocholithiasis. The diagnostic option of EUS or MRCP in patients with suspected choledocholithiasis but negative CT finding showed comparable diagnostic performance. Therefore, the choice of the diagnostic modality may be based on the available resources, experience of the physician, contraindication, and the cost associated with each modality.

Contributors

LHW proposed the study. LHW and STJ performed the research and wrote the first draft. PDH, LSS, SDW, LSK and KMH collected the data. JJH and MJE analyzed the data. All authors contributed to the design and interpretation of the study and to further drafts. LHW is the guarantor.

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Ethical approval

This study was approved by the institutional review board of Soonchunhyang University Bucheon Hospital, and written informed consent was obtained from all patients.

Competing interest

No benefits in any form have been received or will be received from a commercial party related directly or indirectly to the subject of this article.

References

[1] Peng WK, Sheikh Z, Paterson-Brown S, Nixon SJ. Role of liver function tests in predicting common bile duct stones in acute calculous cholecystitis. Br J Surg 2005;92:1241–1247.
[2] Ko CW, Lee SP. Epidemiology and natural history of common bile duct stones and prediction of disease. Gastrointest Endosc 2002;56:S165–S169.
[3] Loperfido S, Angelini G, Benedetti G, Chilovi F, Costan F, De Berardinis F, et al. Major early complications from diagnostic and therapeutic ERCP: a prospective multicenter study. Gastrointest Endosc 1998;48:1–10.
[4] Masci E, Toti G, Mariani A, Curioni S, Lomazzi A, Dinelli M, et al. Complications of diagnostic and therapeutic ERCP: a prospective multicenter study. Am J Gastroenterol 2001;96:417–423.
[5] 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.
[6] Adams MA, Hosmer AE, Wamsteker EJ, Anderson MA, Elta GH, Kubiliun NM, et al. Predicting the likelihood of a persistent bile duct stone in patients with suspected choledocholithiasis: accuracy of existing guidelines and the impact of laboratory trends. Gastrointest Endosc 2015;82:88–93.
[7] Ebrahim M, Sorensen LT, Jorgensen LN, Kalaitzakis E. Current clinical algorithms for predicting common bile duct stones have only moderate accuracy. Dig Endosc 2018;30:477–484.
[8] He H, Tan C, Wu J, Dai N, Hu W, Zhang Y, et al. Accuracy of ASGE high-risk criteria in evaluation of patients with suspected common bile duct stones. Gastrointest Endosc 2017;86:525–532.
[9] Kuzu UB, Ödemiş B, Dişibeyaz S, Parlak E, Öztaş E, Saygılı F, et al. Management of suspected common bile duct stone: diagnostic yield of current guidelines. HPB (Oxford) 2017;19:126–132.
[10] Suarez AL, LaBarre NT, Cotton PB, Payne KM, Coté GA, Elmunzer BJ. An assessment of existing risk stratification guidelines for the evaluation of patients with suspected choledocholithiasis. Surg Endosc 2016;30:4613–4618.
[11] Nárvaez Rivera RM, González González JA, Monreal Robles R, García Compean D, Paz Delgadillo J, Garza Galindo AA, et al. Accuracy of ASGE criteria for the prediction of choledocholithiasis. Rev Esp Enferm Dig 2016;108:309–314.
[12] Einstein DM, Lapin SA, Ralls PW, Halls JM. The insensitivity of sonography in the detection of choledocholithiasis. AJR Am J Roentgenol 1984;142:725–728.
[13] Magalhães J, Rosa B, Cotter J. Endoscopic retrograde cholangiopancreatography for suspected choledocholithiasis: from guidelines to clinical practice. World J Gastrointest Endosc 2015;7:128–134.
[14] Sethi S, Wang F, Korson AS, Krishnan S, Berzin TM, Chuttani R, et al. Prospective assessment of consensus criteria for evaluation of patients with suspected choledocholithiasis. Dig Endosc 2016;28:75–82.
[15] Gouveia C, Loureiro R, Ferreira R, Oliveira Ferreira A, Santos AA, Santos MPC, et al. Performance of the choledocholithiasis diagnostic score in patients with acute cholecystitis. GE Port J Gastroenterol 2018;25:24–29.
[16] Tranter SE, Thompson MH. Spontaneous passage of bile duct stones: frequency of occurrence and relation to clinical presentation. Ann R Coll Surg Engl 2003;85:174–177.

[17] De Castro VL, Moura EG, Chaves DM, Bernardo WM, Matuguma SE, Artifon EL. Endoscopic ultrasound versus magnetic resonance cholangiopancreatography in suspected choledocholithiasis: a systematic review. Endosc Ultrasound 2016;5:118–128.
[18] Lee YT, Chan FK, Leung WK, Chan HL, Wu JC, 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;67:660–668.
[19] Meeralam Y, Al-Shammari K, Yaghoobi M. Diagnostic accuracy of EUS compared with MRCP in detecting choledocholithiasis: a meta-analysis of diagnostic test accuracy in head-to-head studies. Gastrointest Endosc 2017;86:986–993.
[20] Zidi SH, Prat F, Le Guen O, Rondeau Y, Rocher L, Fritsch J, et al. Use of magnetic resonance cholangiography in the diagnosis of choledocholithiasis: prospective comparison with a reference imaging method. Gut 1999;44:118–122.
[21] Kondo S, Isayama H, Akahane M, Toda N, Sasahira N, Nakai Y, et al. Detection of common bile duct stones: comparison between endoscopic ultrasonography, magnetic resonance cholangiography, and helical-computed-tomographic cholangiography. Eur J Radiol 2005;54:271–275.
[22] Tse F, Barkun JS, Romagnuolo J, Friedman G, Bornstein JD, Barkun AN. Nonoperative imaging techniques in suspected biliary tract obstruction. HPB (Oxford) 2006;8:409–425.
[23] Aubé C, Delorme B, Yzet T, Burtin P, Lebigot J, Pessaux P, 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.
[24] Benjaminov F, Leichtman G, Naftali T, Half EE, Konikoff FM. Effects of age and cholecystectomy on common bile duct diameter as measured by endoscopic ultrasonography. Surg Endosc 2013;27:303–307.