—Original Article—

Role of EUS at high risk for choledocholithiasis without severe cholangitis and visible stone on cross-sectional imaging: A multicenter randomized clinical trial

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ABSTRACT

Background and Objectives: The prevalence of choledocholithiasis in the high-risk group of choledocholithiasis has been reported to be slightly more than 50% when there is no definite cholangitis. Replacement of diagnostic endoscopic retrograde cholangiography (ERC) with an EUS-first approach may be beneficial in these patients. **Materials and Methods:** In this prospective, multicenter study, patients with dilated common bile duct and serum total bilirubin levels of 1.8–4 mg/dL were randomly allocated to undergo either EUS first, followed by subsequent ERC if necessary (EUS group) or ERC only (ERC group). The primary endpoint was the incidence of negative outcomes associated with a false-negative diagnosis of the choledocholithiasis or the endoscopic procedure. The secondary endpoints were the rate of diagnostic ERC and hospital stay length related to the endoscopic procedure. **Results:** Of 90 patients who were randomly assigned, the final analysis involved 42 in the EUS group and 44 in the ERC group. The negative outcomes were not significantly different between the EUS and ERC groups (2.4% *vs.* 6.8%; $P = 0.62$). The rate of diagnostic ERC was significantly lower in the EUS group (2.4% *vs.* 47.7%; $P < 0.001$). The hospital stay length related to the endoscopic procedure was significantly shorter in the EUS group (1.8 ± 1.0 *vs.* 2.5 ± 1.2 days; $P = 0.001$). **Conclusion:** In selected high-risk choledocholithiasis patients, an EUS-first strategy significantly decreased the rate of diagnostic ERC and hospital stay but did not achieve a significant reduction in negative endoscopic procedure outcomes.

Key words: cholangitis, choledocholithiasis, endoscopic retrograde cholangiography, EUS, gallstones

Access this article online

Quick Response Code:

Website: www.eusjournal.com

DOI: 10.4103/EUS-D-20-00229

How to cite this article: Choi YH, Lee YS, Lee SH, Son JH, Ryu JK, Kim YT, *et al.* Role of EUS at high risk for choledocholithiasis without severe cholangitis and visible stone on cross-sectional imaging: A multicenter randomized clinical trial. Endosc Ultrasound 2021;10:455-62.

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Received: 2020-10-14; **Accepted:** 2021-07-12; **Published online:** 2021-11-05

INTRODUCTION

Endoscopic retrograde cholangiography (ERC) has played a pivotal role in the management of choledocholithiasis with respect to both diagnostic and therapeutic aspects.[1] However, the diagnostic role of ERC has been gradually eroded by the usage of minimally invasive modalities such as EUS or magnetic resonance cholangiopancreatography (MRCP) because ERC is a technically challenging procedure that can cause serious adverse events even when performed by experienced endoscopists.[2,3] This invasiveness of ERC makes the risk stratification of having choledocholithiasis become an essential element to consider when deciding whether an ERC-first approach is to be implemented or not.

The American Society for Gastrointestinal Endoscopy (ASGE) and European Society of Gastrointestinal Endoscopy have previously proposed treatment guidelines that involve assessing the likelihood of choledocholithiasis in patients who are considered to be at a high risk, an ERC-first approach is recommended; otherwise, minimally invasive modalities such as EUS or MRCP should be adopted as the first step to identify the stone before performing ERC.[4-6] However, even in patients at high risk for choledocholithiasis, the actual prevalence of such has been reported to be around 60% when there is no visible stone on cross-sectional imaging.[7-10] Further, while clinical cholangitis is proposed as a defining criterion suggesting a high likelihood of choledocholithiasis, its positive predictive value (PPV) was reported to fall within in a wide range of 44%–88%.[7,8] This result might be explained by the fact that prior studies were conducted retrospectively and included cholangitis of varying severity levels at varying rates. Therefore, an EUS-first approach that replaces diagnostic ERC may be beneficial even in high-risk patients unless either the grade of acute cholangitis is assessed as severe or the common bile duct (CBD) stone is visible on cross-sectional imaging. To explore this issue, we conducted a multicenter, randomized controlled trial comparing the efficacy of EUS-first and ERC-first approaches in patients at high risk for choledocholithiasis.

MATERIALS AND METHODS

Study design

This was a multicenter, prospective, randomized study designed to assess the benefits of adopting an EUS-first approach in a patient group at high risk for choledocholithiasis. The study protocol was approved by the Institutional Review (H-1705-070-854) at ClinicalTrials.gov (NCT03250286). Further, this study was conducted in accordance with the provisions of the Declaration of Helsinki, and informed written consent was obtained from all subjects after full explanation of the study protocol before their enrollment.

Patients

Study participants were recruited from two academic hospitals in Korea between July 2017 and December 2019 and were followed up with until June 2020. Patients who visited the emergency room or outpatient clinic with suspected choledocholithiasis were screened and those with naïve papillae were deemed eligible for enrollment in this study. Among the high-risk criteria for choledocholithiasis stated in the ASGE guideline, a CBD diameter of >6 mm (>8 mm in patients with previous cholecystectomy) on ultrasound (US) or computed tomography (CT) and a total bilirubin level between 1.8 and 4.0 mg/dL were used as inclusion criteria for this study. The exclusion criteria were an age of younger than 18 years, severe mental illness, severe comorbidity including end-stage renal disease, advanced chronic obstructive pulmonary disease, severe heart failure, poorly controlled blood sugar, pregnancy, suspicion of pancreatobiliary malignancy, presence of coexisting acute pancreatitis, presence of CBD stone on US or CT, severe cholangitis according to the Tokyo Guidelines 2013,[11] previous gastric surgery preventing further EUS or ERC procedures, including Billroth II or Roux-en-Y, and failure to participate in scheduled follow-up.

Enrolled patients were randomly assigned in a 1:1 ratio to undergo bile duct evaluation with either EUS followed by ERC if necessary (EUS group) or ERC only (ERC group). The study participants were enrolled consecutively at each institution without stratification. Random allocation numbers generated by an independent statistician using block randomization (block size: 6) were provided to each institution in sealed envelopes, which were only opened by the study coordinator at each site.

Intervention and follow-up

Patients allocated into the EUS group underwent EUS first to evaluate the CBD and if CBD stone or sludge was confirmed by the EUS, then subsequent therapeutic ERC was performed by the same operator

during the same session. On the other hand, if EUS imaging did not reveal CBD stone or sludge, no additional procedure was performed. Patients allocated into the ERC group underwent ERC directly for confirming and clearing the CBD simultaneously. EUS examinations were performed using a radial array echoendoscope (GF-UE260; Olympus Optical Co., Tokyo, Japan) by one of three expert endoscopists with experience performing more than 1000 EUS examinations for pancreatobiliary diseases. Previous study showed that compared to the curved linear array echoendoscope, the radial array echoendoscope did not differ in the mid-to-distal CBD delineation and was superior for the gallbladder and major papilla delineation.[12] Therefore, it was unified to use a radial array echoendoscope for EUS examination in this study. A biliary stone was defined as a concretion measuring more than 2 mm in diameter, while biliary sludge was defined as a viscous mixture of particles derived from bile measuring smaller in diameter than a biliary stone.[13] ERC procedures including sphincterotomy and stone extraction were performed in a standard manner using a video duodenoscope (TJF-260v, JF-260v, TJF-240, or JF-240; Olympus, Tokyo, Japan). All ERC procedures were performed by one of three experienced endoscopists with more than 5000-lifetime experiences in ERC, and CBD clearance was attempted using a basket or retrieval balloon or both, depending on the endoscopist's discretion. Patients in the ERC group underwent ERC procedures only as described above. After each procedure, the extension of the current hospital stay or the admission of an outpatient to the hospital was determined at the physician's discretion.

Patients were followed up with for 6 months at 3-month intervals in the outpatient department, with those who were unable to visit the outpatient clinic evaluated by phone contact. During the follow-up period, patients were assessed for symptoms potentially related to choledocholithiasis, such as abdominal pain, jaundice, fever, and clay-colored feces. If the patients were suspected to have recurred choledocholithiasis or acute cholangitis, ERC was reattempted. Hospitalization possibly related to choledocholithiasis such as that for biliary pancreatitis, cholangitis, or obstructive jaundice was also recorded.

Definition and outcomes

The primary outcome was any negative outcomes related to either a false-negative diagnosis of choledocholithiasis or the endoscopic procedure. Negative outcomes associated with a false-negative diagnosis of choledocholithiasis were defined as follows: (1) diagnosis of choledocholithiasis during follow-up or (2) hospitalization for a condition likely associated with choledocholithiasis, such as biliary pancreatitis, cholangitis, or obstructive jaundice. Negative outcomes of endoscopic procedures were assessed according to the ASGE lexicon.[14]

Secondary outcomes were the rate of diagnostic ERC and hospital stay length related to endoscopy. The diagnostic ERC was defined as any ERC procedures in which no stone or sludge was removed. Hospital stay length related to endoscopy was defined as "(the date the patient can be discharged due to being free from problems related to their endoscopic procedure – the date of their endoscopic procedure) +1."

The diagnostic accuracy of EUS was analyzed by dividing cases into those where only biliary stone was regarded as a positive test result and those where biliary sludge was added as a positive test result in addition to biliary stone. The gold standard for the diagnosis of choledocholithiasis was defined as the removal of stones through ERC in the initial procedure and/or during the 6-month follow-up period.

Sample size calculation

In patients at intermediate risk of choledocholithiasis, the proportion of negative outcomes is known to be 10% in those undergoing EUS and 40% in those undergoing ERC.[15] Since patients at high risk for choledocholithiasis were the subjects of this study, the prevalence of choledocholithiasis in this study will be higher than these percentages mentioned, and we assumed that this difference will affect the rate of negative outcomes. In the previous study, all of the negative outcomes in the EUS group were related to ERC procedures performed in patients with biliary stones. Therefore, we assumed that the negative outcome of the EUS group would change in proportion to the prevalence of choledocholithiasis. In addition, in the ERC group, since the conduct of sphincterotomy was highly correlated with choledocholithiasis, it was assumed that the negative outcome was affected by the change in the prevalence of choledocholithiasis. In previous studies, the prevalence of choledocholithiasis in the high-risk group according to the ASGE guideline was 55.3%, whereas in patients at intermediate risk of choledocholithiasis,

the prevalence of choledocholithiasis was about 25%.[15,16] Based on the prevalence of choledocholithiasis in each risk group and the above assumptions, negative outcomes of the EUS group and the ERC group in patients at high risk for choledocholithiasis were predicted to occur at rates of 22.1% and 54.5%, respectively. We estimated the required sample size using the proportion of negative outcomes calculated above as the primary outcome of this study. A sample size of 40 patients in each group was required to achieve the power of 0.80 in the Chi-squared test with an alpha level of 0.05. Considering a 10% dropout rate, we decided to include a final sample size of 45 patients in each group.

Statistical analysis

Continuous variables were presented in the format mean ± standard deviation, and categorical variables were expressed as numbers. Comparisons between groups were conducted using student's *t*-test for continuous data, including hospitalization length as the secondary outcome. The Chi-square test or Fisher's exact test was used for assessing categorical data, including the primary outcome of this study and the rate of diagnostic ERC. Diagnostic accuracy was evaluated by sensitivity, specificity, PPV, negative predictive value (NPV), and overall accuracy. A $P < 0.05$ was considered to be statistically significant. Statistical analyses were carried out using SPSS version 24.0 software program (IBM Corporation, Armonk, NY, USA) and the MedCalc version 19.4.0 statistical software program (MedCalc Software Ltd., Ostend, Belgium).

RESULTS

Study population

During the study period, 1301 patients suspected to have choledocholithiasis were screened for eligibility. Among them, 90 patients were enrolled and randomly assigned to the EUS group ($n = 45$) and the ERC group ($n = 45$), respectively. Thereafter, three patients in the EUS group and one patient in the ERC group were excluded after randomization because they were lost to follow-up. Therefore, a total of 86 patients completed the 6 months of follow-up, with 42 patients in the EUS group and 44 patients in the ERC group finally analyzed [Figure 1]. The baseline characteristics of the two groups were similar [Table 1]. The number of patients undergoing cholecystectomy during the follow-up period was also similar between the EUS (16/42, 38.1%) and ERC groups (21/44, 47.7%) ($P = 0.37$).

Primary outcome

The number of patients with negative outcomes related to false-negative diagnosis of choledocholithiasis was zero in the EUS group and one in the ERC group, respectively. Repeat ERC during the follow-up period was performed in two patients of the EUS group but was not associated with choledocholithiasis and was associated with benign biliary stricture [Table 2].

Endoscopic adverse events occurred in one patient in the EUS group and three patients in the ERC group. The one patient in the EUS group experienced mild post-ERC pancreatitis after stone removal, while the three patients in the ERC group experienced adverse events, including mild post-ERC pancreatitis ($n = 3$) and moderate cholangitis ($n = 1$), with one patient developing both simultaneously. In this patient, stones or sludge was not detected at initial ERC; however, stone-related symptoms developed after said ERC procedure. Therefore, repeat ERC was performed and

Table 1. Baseline characteristics of patients

Variable	EUS group (*n*=42), *n* (%)	ERC group (*n*=44), *n* (%)
Age (years), mean±SD	65±17	62±17
Sex (male)	23 (54.8)	30 (68.2)
History of cholecystectomy	5 (11.9)	5 (11.4)
Gallstones (initial imaging)	17 (40.5)	19 (43.2)
Total bilirubin (mg/dL), mean±SD	2.9±0.8	2.8±0.7
CBD diameter (mm), mean±SD	9.9±3.0	9.4±2.5

SD: Standard deviation; ERC: Endoscopic retrograde cholangiography; CBD: Common bile duct

Table 2. Events occurring during the 6- months follow-up period in patients who initially had no bile duct stones or sludge

Variable	EUS group (*n*=19)	ERC group (*n*=22)
Patients lost to follow-up	0	0
Repeated ERC resulting in the diagnosis of bile duct stone	0	1
Repeated ERC for reasons other than bile duct stone	2*	1†
Hospitalization due to biliary pancreatitis, cholangitis, or obstructive jaundice	0	0

*Both were benign common bile duct stricture, †Repeated ERC for endoscopic retrograde gallbladder drainage for percutaneous transhepatic gallbladder drainage tube removal. ERC: Endoscopic retrograde cholangiography

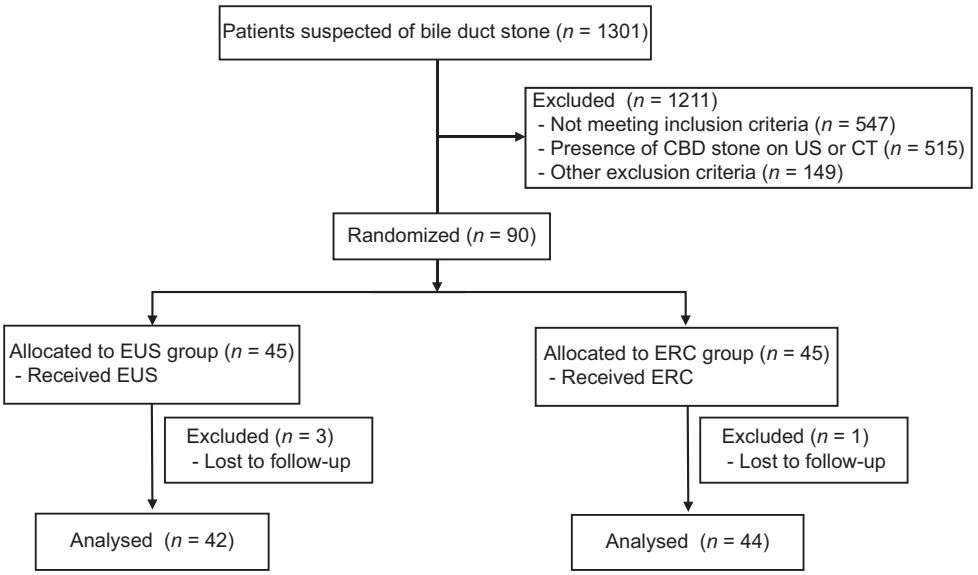

Figure 1. Flowchart of enrolled patients

the CBD stone was finally removed. Of the other two patients who developed mild post-ERC pancreatitis, one patient had biliary sludge and the other did not have any stones or sludge [Table 3].

The primary outcome of this study, which was the total negative outcomes associated with either a false-negative diagnosis of choledocholithiasis or the endoscopic procedure, occurred in one patient in the EUS group and three patients in the ERC group. However, there was no statistically significant difference in the occurrence of the primary outcome between the two groups (risk ratio: 0.67; 95% confidence interval [CI]: 0.36–1.22; absolute risk difference: −4.4%; 95% CI: −4.3–13.2; $P = 0.62$) [Table 4].

Secondary outcomes

The rate of diagnostic ERC was significantly lower in the EUS group (2.4%) than in the ERC group (47.7%) ($P < 0.001$). The mean hospital stay length related to endoscopy in the EUS group (1.8 ± 1.0 days) was significantly shorter than that in the ERC group (2.5 ± 1.2 days) ($P = 0.001$) [Table 4].

The sensitivity and NPV of EUS for choledocholithiasis were 100% in both cases, regardless of whether the positive EUS test was defined as stone alone or including sludge. Separately, the specificity and the PPV of EUS for choledocholithiasis were 87.5% and 85.7%, respectively, when just a stone was the outcome of interest of a positive diagnostic test, and higher than 79.2% and 78.3% when a stone or sludge was set as the outcome of interest of positive diagnostic test. Finally, the overall diagnostic accuracy of EUS for choledocholithiasis was 92.9% when just a stone was set as the outcome of interest of a positive diagnostic test and 88.1% when sludge was included as the outcome of interest of a positive diagnostic test [Table 5].

Table 3. Procedure-related adverse events

Variable	EUS group (*n*=42)	ERC group (*n*=44)	*P*
Patients with adverse events, *n* (%)	1 (2.4)	3 (6.8)	0.62
Total number of adverse events (*n*)	1	4	
Post-ERC pancreatitis	1	3	0.62
Cholangitis	0	1	>0.99
Severity (*n*)			
Mild	1	3	0.62
Moderate	0	1*	>0.99

*Cholangitis was classified as of moderate severity because it accompanied by complicated liver cyst, requiring interventional radiology (percutaneous catheter drainage). ERC: Endoscopic retrograde cholangiography

DISCUSSION

To our knowledge, this is the first prospective, randomized controlled study to compare EUS-first and ERC-first strategies deployed in patients at high risk for choledocholithiasis. Existing guidelines recommend using an ERC-first strategy in patients at high-risk group for choledocholithiasis.[5,6] However, previous retrospective studies have reported that more than one-third to nearly one-half of patients at high risk for choledocholithiasis undergo a diagnostic ERC procedure

Table 4. Summary of study outcomes

Variable	EUS group (*n*=42), *n* (%)	ERC group (*n*=44), *n* (%)	Risk ratio (95% CI)	*P*
Primary outcome				
Patients with negative outcomes*	1 (2.4)	3† (6.8)	0.67 (0.36-1.22)	0.62
Secondary outcomes				
Diagnostic ERC	1 (2.4)	21 (47.7)	0.38 (0.27-0.53)	<0.001
Hospital day related to endoscopy (days), mean±SD	1.8±1.0	2.5±1.2	NA	0.001
Other outcomes				
Patients with bile duct stones	18 (42.9)	17 (38.6)	1.09 (0.71-1.67)	0.69
Patients with bile duct stones or sludge	21 (50.0)	23 (52.3)	0.96 (0.63-1.45)	0.83

*Endoscopy-related adverse events plus false negatives for bile duct stones during the initial examination, †Five negative outcomes occurred in three patients. CI: Confidence interval; NA: Not applicable; SD: Standard deviation; ERC: Endoscopic retrograde cholangiography

Table 5. Diagnostic yield of EUS according to sludge evaluation

	Positive diagnostic test	
	Bile duct stones in EUS	Bile duct stones or sludge in EUS
Sensitivity	100 (81.5-100)	100 (81.5-100)
Specificity	87.5 (67.6-97.3)	79.2 (57.9-92.9)
PPV	85.7 (63.6-97.0)	78.3 (56.3-92.5)
NPV	100 (83.9-100)	100 (82.4-100)
Accuracy	92.9 (80.5-98.5)	88.1 (74.4-96.0)

Data are presented as (95% CI). CI: Confidence interval; PPV: Positive predictive value; NPV: Negative predictive value

and the need to revise the risk classification system has been raised accordingly.[7,16] Despite these previous reports, though, no prospective studies have yet been attempted to find which subgroups of patients at high risk for choledocholithiasis benefit from replacing diagnostic ERC with an EUS-first approach. Therefore, we conducted the present randomized study in patients who met the criteria of dilated CBD and had total bilirubin level of 1.8–4.0 mg/dL from among the high-risk criteria in the 2010 ASGE guideline, without biliary stones in CT and severe cholangitis. Although the EUS-first strategy did not achieve a significant reduction in the negative outcomes in this study, it significantly reduced the length of the hospital stay and rate of diagnostic ERC. In addition, the NPV of EUS in this study was 100% and there was no negative outcome due to a false-negative diagnosis of choledocholithiasis in the EUS group. Furthermore, all five endoscopic procedure-related adverse events in this study were related to ERC, and four out of the five adverse events were post-ERC pancreatitis. Taking these results into account, an EUS-first strategy can be applied in patients at high risk for choledocholithiasis according to the criteria used in this study, especially those patients with risk factors of post-ERC pancreatitis such as female sex, young age, and a history of pancreatitis.[17,18]

Since the risk stratification criteria for likelihood of choledocholithiasis of the 2010 ASGE guideline were originally intended for symptomatic patients with confirmed gallbladder stones, the inclusion criteria were not completely consistent with the subjects of our study.[4] However, in real clinical practice, ERCP may be determined after only CT scan without US, and radiolucent gallstones may not be seen. In addition, *de novo* CBD stones are more common in patients with Asian descent.[19] Since EUS was scheduled in half of study population, the additional US to check for gallbladder stones for study enrollment was judged to be a waste of time and cost. Thus, to present a comprehensive management covering all of the actual clinical situations mentioned above, this study enrolled patients regardless of gallbladder stones in the imaging findings. Looking at the characteristics of patients enrolled in this study, there was no significant difference in the proportion of patients undergoing cholecystectomy between the two study arms, and the prevalence of choledocholithiasis in this study was similar to that of previous studies using the 2010 ASGE guideline criteria.[16] Therefore, the impact of enrolling patients regardless of gallbladder stones is considered to be negligible.

The prevalence of choledocholithiasis in this study was 51.2%. This is similar to that of 55.3% in a previous study conducted according to the 2010 ASGE guideline's high-risk criteria for choledocholithiasis, excluding cholangitis.[16] In another study, including patients with very strong predictors of choledocholithiasis per the 2010 ASGE guideline, including (1) cholangitis, (2) CBD stone on US, and (3) total bilirubin level of >4 mg/dL, the prevalence of choledocholithiasis in the high-risk group was 71.5%.[20] As such, it can be seen that there are significant differences in the prevalence of choledocholithiasis depending upon the presence or absence of three very

strong predictors of choledocholithiasis. Looking at the specificity and PPV evaluated for the predictors of choledocholithiasis in previous retrospective studies, the three very strong predictors of choledocholithiasis in the 2010 ASGE guideline showed specificity of 84%–97% and PPV of 44%–91%, whereas the inclusion criteria of this study, CBD dilatation and total bilirubin level of 1.8–4 mg/dL, triggered relatively low specificity of 61%–63% and low PPV of 54%–66%.[7,16,20] Therefore, considering these relatively low specificity and PPV of the high-risk criteria defined in this study and that the prevalence of CBD stone in this study was about 50%, the high-risk group established in this study would be appropriate to redefine as the intermediate-risk group and to receive the EUS-first strategy. Accordingly, we suggest an algorithm for choledocholithiasis management with modified high-risk criteria [Figure 2]. Changes in risk stratification for choledocholithiasis similar to what we have suggested are partly reflected in the 2019 ASGE guideline published while this study was ongoing.[5] However, this change to the 2019 ASGE guideline is based on the data of retrospective studies and there is no randomized study supporting the recommendations.[5,7,16,21] We believe that the current randomized study can provide good evidence for future risk stratification of choledocholithiasis.

The sensitivity and specificity of EUS for choledocholithiasis in this study were 100% and 87.5%, respectively, thus being similar to those of previous studies.[22] As shown in Table 5, when sludge was considered as the outcome of interest in a positive diagnostic test in addition to a stone, the diagnostic performance of EUS was deteriorated. Therefore, it would be better to consider only the stone as the outcome of interest in a positive diagnostic test, while

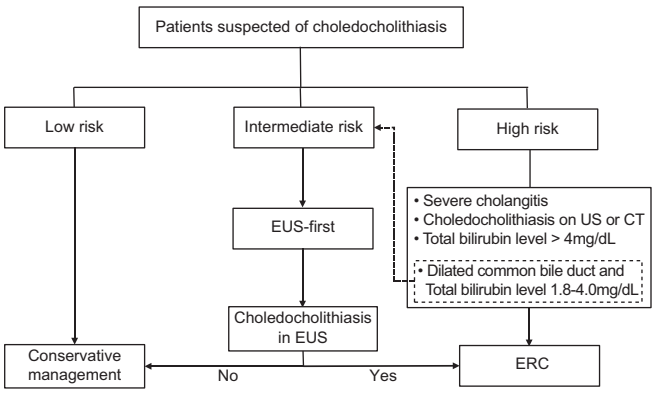

Figure 2. Choledocholithiasis management algorithm with modified high-risk criteria

when only sludge is found during EUS, we can consider simply observing such without moving to conduct ERC. However, this result should be interpreted with caution because only a small number of patients showed only sludge without stone during EUS in this study.

Even after the presence of CBD stone is excluded by EUS, the migration of cholecystolithiasis to the CBD and recurrence of acute cholangitis before elective cholecystectomy may be of concern. However, the above situation was also considered as a negative outcome of this study, and no case of acute cholangitis was triggered by the migration of cholecystolithiasis. EUS has another advantage in that it can identify radiolucent stones by observing the gallbladder as well. It seems that if CBD stone is not observed during EUS, it may not be necessary to perform ERC even if cholecystolithiasis is apparent. Performing further studies regarding the efficacy of cholecystectomy in these patients would be interesting.

Since the patients who did not undergo cholecystectomy after removal of the CBD stone were included in this study, the risk of new passage of stones from gallbladder to CBD could be counted as a false negative diagnosis of the initial examination, and the negative outcome may be overestimated. To minimize this confounding effect, we limited the follow-up period to 6 months. According to a study reported by Lai *et al.*, the recurrence rate of biliary complications within 6 months in patients who underwent ERC for clearance of CBD stones did not differ regardless of cholecystectomy, and the cumulative recurrence rates were very low.[23]

This study has several limitations. First, the negative outcomes of this study occurred less frequently than as suggested by the initial hypothesis. This is presumed to be because ERC procedures were performed by experts and patients received outpatient or emergency room-based procedures, so mild abdominal pain after discharge was not included in the negative outcome. Due to this lower incidence rate of negative outcomes relative to the assumption, it is possible that there was no statistically significant difference in the negative outcome between the EUS and ERC groups. Second, the distinction between biliary stones and sludge during EUS is often ambiguous and subjective. However, in this study, ERC was also performed in patients with only sludge found during EUS, and because there were no negative outcomes after ERC in these patients, the distinction between stone and

sludge would not have had a significant impact on the outcome of this study. Third, no analysis was conducted in terms of cost-effectiveness in this study. It is still necessary to prove whether the EUS-first strategy is practical despite the additional burden of EUS by the reduction of ERC sessions and hospital stay length.

CONCLUSION

In a selected group at high risk for choledocholithiasis, an EUS-first strategy lessened the rate of diagnostic ERC and hospitalization stay length but did not reduce the occurrence of negative outcomes related to the endoscopic procedure or the false-negative diagnosis of choledocholithiasis. Downward revision of the high-risk group to the intermediate-risk group for choledocholithiasis defined in this study should be considered.

Clinical trial registration

This study was registered at: ClinicalTrials.gov, with No. NCT03250286.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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