



## Digestive Endoscopy

## ASGE high-risk criteria for choledocholithiasis – Are they applicable in cholecystectomized patients?



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## ABSTRACT

**Background and aims:** The guidelines by the American Society for Gastrointestinal Endoscopy (ASGE) suggest that in patients with gallbladder in situ, endoscopic retrograde cholangiopancreatography (ERCP) should be performed in the presence of high-risk criteria for choledocholithiasis, after biochemical tests and abdominal ultrasound. There are no specific recommendations for cholecystectomized patients. The aim of this study was to evaluate the applicability of ASGE criteria for ERCP in cholecystectomized patients with suspected choledocholithiasis.

**Methods:** We conducted a retrospective study that included patients with high-risk ASGE criteria for choledocholithiasis who underwent ERCP from 2013–2016.

**Results:** We included 327 patients in our analysis – 258 with gallbladder in situ (79%) and 69 with cholecystectomy (21%). We showed that the ASGE criteria true positive rate was similar between patients with and without cholecystectomy – the prevalence of choledocholithiasis on ERCP was 71% in cholecystectomized and 70% in non-cholecystectomized. In addition, both the presence and the diameter of the CBD stone were predictors of positive ERCP in both groups. In contrast, the diameter of the CBD was predictor of positive ERCP only in non-cholecystectomized patients.

**Conclusions:** Although dilatation of the CBD was not a predictive factor for choledocholithiasis in cholecystectomized patients, the ASGE criteria true positive rate was similar to that of non-cholecystectomized patients.

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## 1. Introduction

Choledocholithiasis is a common cause of hospitalization and may lead to cholangitis and gallstone pancreatitis. The initial evaluation of suspected choledocholithiasis should include serum liver biochemical tests and transabdominal ultrasound (US) of the right upper quadrant [1]. Once the diagnosis of choledocholithiasis is confirmed, common bile duct (CBD) stones should be removed, usually by endoscopic retrograde cholangiopancreatography (ERCP) [2]. This technique is associated with high efficacy (~90%) but also with a non-negligible rate of adverse effects (~5%), including post-ERCP pancreatitis, post-endoscopic sphincterotomy bleeding, cholangitis, perforation and death (<1%) [3]. Therefore, selection of patients for ERCP is crucial, and the American Society for Gastrointestinal Endoscopy (ASGE) has published criteria that stratify

patients based on their probability of having choledocholithiasis. Patients are considered at high probability of CBD stone and require further evaluation typically with ERCP if they: (a) present with one very strong predictor (CBD stone on transabdominal US, clinical ascending cholangitis, total bilirubin (TB) superior to 4 mg/dL) or (b) present with two strong predictors (dilated CBD on ultrasound (>6 mm) and TB level 1.8–4 mg/dL) [1].

Several studies, however, have shown that the sensitivity of these criteria ranges from 55 to 89%, which means that a substantial proportion of patients classified as high risk do not in fact have CBD stones on ERCP [4,5,6] ASGE criteria only apply to patients with gallbladder in situ and there are no specific recommendations for cholecystectomized patients. Cholecystectomized patients may present with dilation of the CBD even in healthy post-cholecystectomy. If clinicians do not take this into account there will be increased unnecessary invasive investigations, morbidity, and additional costs [7].

The primary aim of this study was therefore to compare the rate of positive ERCPs between cholecystectomized patients with high likelihood for choledocholithiasis according to ASGE criteria, and

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**Table 1**  
Baseline characteristics of the patients.

	All patients	Non-cholecystectomized	Cholecystectomized
Number patients included (n)	327	258	69
Age years (mean ± SD)	70 ± 16	71 ± 17	68 ± 15
Female gender (n (%))	188 (57%)	143 (55%)	45 (65%)
CBD stone (n (%))	223 (68%)	171 (66%)	52 (75%)
CBD stone diameter mm (mean ± SD)	11.7 ± 5	11.9 ± 5	11.1 ± 5
Ascending cholangitis (n (%))	80 (24%)	70 (27%)	10 (15%)
TB > 4 mg/dL (n (%))	151 (40%)	111 (43%)	20 (29%)
TB mg/dL (mean ± SD)	4.5 ± 6.7	4.8 ± 7.4	3.2 ± 2.6
Dilation CBD > 6 mm (n (%))	292 (89%)	229 (89%)	63 (91%)
Diameter CBD mm (mean ± SD)	12 ± 4.1	11.9 ± 4.2	12.6 ± 3.9
Dilation > 6 mm + TB 1.8–4 mg/dl (n(%))	213 (65%)	173 (67%)	40 (58%)
Abnormal liver chemistry other than TB (n (%))	290 (89%)	235 (91%)	55 (81%)
Gallstone pancreatitis (n (%))	40 (12%)	34 (13%)	6 (9%)
Positive ERCP (n (%))	230 (70%)	181 (70%)	49 (71%)
Post-ERCP complications (n (%))	44 (13%)	29 (11%)	12 (17%)
Pancreatitis (n,%)	19 (6%)	14 (5%)	5 (7%)
Cholangitis (n,%)	20 (6%)	13 (5%)	7 (10%)
Bleeding (n,%)	1 ((0.3%)	1 (0.3%)	0
Perforation (n,%)	1 (0.3%)	1 (0.3%)	0
Endoscopic US (n (%))	3 (0.9%)	3 (1.1%)	0
MRCP (n (%))	54 (16%)	46 (18%)	8 (12%)

NA – Non applicable; SD – Standard deviation; CBD – Common bile duct; TB – Total bilirubin; ERCP – Endoscopic retrograde cholangiopancreatography; US – Ultrasound; MRCP – Magnetic resonance cholangiopancreatography; \* Statistically significant.

those with gallbladder in situ. The secondary aim was to identify the predictors of positive ERCP in these two sub-groups.

## 2. Material and methods

### Patient selection

We conducted a retrospective analysis that included all patients with high-risk criteria for choledocholithiasis who underwent ERCP from January 2013 to December 2016.

High-risk criteria were defined according to ASGE guidelines as CBD stone on transabdominal US, clinical ascending cholangitis, total bilirubin (TB) superior to 4 mg/dL or dilated CBD on ultrasound (>6 mm) plus TB level 1.8–4 mg/dL. All ERCP were performed in the same center by 3 endoscopists with experience of having done more than 200 ERCP prior to the beginning of the study.

Exclusion criteria were: history of liver transplantation or other biliary surgery, known liver disease including primary sclerosing cholangitis, suspicion of pancreaticobiliary malignancy, previously placed endobiliary stent or sphincterotomy, history of biliary stricture, ERCPs without deep biliary cannulation and incomplete data.

Clinical charts were reviewed for patient demographics, presence of CBD stone on US, diameter of the CBD stone, CBD diameter, TB level, presence of ascending cholangitis, ERCP findings and ERCP related complications.

Because this retrospective research involved analysis of existing data and individual subjects cannot be identified in any way, the study was exempted from IRB approval by the ethics committee.

### Variable definitions

The presence of CBD stone (and size) and CDB dilation (and diameter) were described according to the radiologist's transabdominal US reports. Ascending cholangitis was defined as the presence of fever, jaundice and right upper quadrant abdominal pain. TB level was measured in mg/dL and the last level available before ERCP was considered. Positive ERCP was defined as the presence of stones, stone material or filling defect in cholangiography.

### ERCP Technique

Olympus duodenoscopes TJF-145 were utilized. Every patient signed an informed consent for the procedure. The duodenoscope was inserted in the second portion of the duodenum followed by biliary cannulation with a sphincterotome using guidewire technique. Biliary sphincterotomy was carried out based on the clinical decision of the endoscopist, followed by bile duct sweeping using a stone extractor balloon. When necessary, mechanical lithotripsy was performed to fragment stones prior to removal. In the end of the procedure an occlusion cholangiogram was performed. In the case of residual lithiasis, a biliary 7 or 10 Fr double pigtail plastic stent was placed.

### Statistical analysis

The statistical analysis was performed using the Statistical Package for Social Sciences (SPSS) program version 20 (IBM Corporation, Armonk, NY). Categorical variables are summarized as frequencies and percentages and continuous variables as means and standard deviation. Chi-square test or Fisher's exact test and Student's t test were used to compare non-continuous and continuous data, respectively.

A p value < 0.05 was considered statistically significant.

## 3. Results

During the study period, 327 patients met the inclusion criteria. The mean (± standard deviation) age was 70 ± 16.3 years, 188 (57%) were female and 69 (21%) had previous cholecystectomy. On presentation, 223 (68%) had CBD stone on US, 131 (40%) had TB > 4 mg/dL, 80 (24%) had ascending cholangitis and 213 (65%) had CBD > 6 mm and BT 1.8–4 mg/dL. The baseline characteristics of the patients are summarized in Table 1.

A positive ERCP was present in 70% (230/327) of patients with high-risk criteria (70% (181/258) non-cholecystectomized and 71% (49/69) cholecystectomized; p = 0.86).

In non-cholecystectomized patients with high-risk criteria, presence of CBD stones, size of CBD stone and diameter of the CBD were predictors of positive ERCP. In cholecystectomized patients,

**Table 2**  
Predictors of positive ERCP in cholecystectomized and non-cholecystectomized patients.

	Cholecystectomized			Non-cholecystectomized		
	Positive ERCP	Negative ERCP	p	Positive ERCP	Negative ERCP	p
Age (mean)	68,3 years	65,7 years	0.507	73,2 years	64,9 years	<0.01 <sup>a</sup>
CBD stone (%)	84%	55%	0.012 <sup>a</sup>	71%	55%	0.013 <sup>a</sup>
Size CBD stone (mean)	12,2 mm	7 mm	0.007 <sup>a</sup>	12.1 mm	10.1 mm	0.036 <sup>a</sup>
Ascending cholangitis (%)	16%	10%	0.498	30%	21%	0.115
TB > 4 mg/dL (%)	27%	35%	0.482	42%	46%	0.504
BT (mean)	3.3 g/dL	2.9 g/dL	0.643	6 g/dL	4.3 g/dL	0.094
Dilation > 6 mm (%)	92%	90%	0.806	90%	85%	0.165
Dilation (mean)	12.9 mm	11.6 mm	0.183	12.4 mm	10.8 mm	0.014 <sup>a</sup>
Dilation >6 mm + TB 1.8–4 mg/dl (n(%))	61%	50%	0.391	68%	65%	0.667
Abnormal liver chemistry other than TB	85%	70%	0.141	89%	94%	0.132
Gallstone pancreatitis	12%	0	0.101	12%	15%	0.548
Post-ERCP complications	14%	25%	0.309	9%	15%	0.165

CBD – Common bile duct; TB – Total bilirubin; ERCP – Endoscopic retrograde cholangiopancreatography.

<sup>a</sup> Statistically significant.

presence of CBD stone and size of the CBD stone were the only of positive ERCP – Table 2.

Ascending cholangitis, TB > 4 mg/dL, dilation > 6 mm + TB 1.8–4 mg/dl, abnormal liver chemistry other than TB and gallstone pancreatitis were not significantly different between positive and negative ERCP in either group (all  $p > 0.05$ ).

Complete removal of the CBD stone was achieved in 93.9% of patients (normal occlusion cholangiogram at the end of the procedure). Post-ERCP complications occurred in 13% of the patients – 17% cholecystectomized and 11% non-cholecystectomized ( $p = 0.17$ ). Endoscopic US and Magnetic Resonance Cholangiopancreatography (MRCP) were performed before ERCP in 0.9% and 16% of the patients, respectively.

#### 4. Discussion

ASGE guidelines provide assistance to clinicians in the evaluation of suspected choledocholithiasis. However, many studies have criticized them for lack of accuracy, resulting in unnecessary procedures to some patients, which are associated with risks, including a not negligible mortality rate [7,5,6].

In cholecystectomized patients, dilation of the CBD may be seen in healthy post-cholecystectomy patients and clinicians who do not take this into account may recommend additional unnecessary and costly diagnostic evaluations [8]. We therefore conducted a retrospective analysis of 327 patients at high risk of choledocholithiasis and who underwent ERCP. 258 patients had gallbladder in situ and 69 patients were cholecystectomized. The true positive rate was 70% overall, and it was not significantly different between patients with gallbladder in situ (70%) and cholecystectomized patients (71%). This means that approximately 30% of the patients did ERCP with negative findings, and, contrary to our predictions, there was no significant difference between the two groups.

The presence of CBD stones and its size were predictive of a positive ERCP in both groups, but dilation was only significant in patients with gallbladder in situ. This may be interpreted by the fact that dilation of the CBD is a combined criteria with bilirubin and although dilation is seen in healthy post-cholecystectomy patients, bilirubin levels are not increased in this group.

The size of the CBD stone is currently not taken into account in ASGE criteria, but it was a predictor of positive ERCP in both groups in our study. This may be explained by the hypothesis that as size decreases the likelihood of spontaneous stone passage increases. A retrospective study with 221 patients who undergone MRCP and ERCP suggest that for patients with stones measuring 2 mm or less, surgery with intraoperative cholangiography to

confirm duct clearance could be a suitable alternative avoiding unnecessary ERCPs [9]. This should be validated in a prospective trial.

In our study, only eight cholecystectomized patients performed MRCP before ERCP and endoscopic US was not performed in any patient. MRCP and endoscopic US have similar sensitivity and specificity above 90% for the diagnosis of CBD and the choice of which test to use should depend on availability, costs and contra-indications to each test [10]. In two randomized trials in patients with intermediate probability for CBD stones, the management strategy MRCP-first decreased the need for subsequent ERCPs, but not complications; and EUS-first strategy (with selective ERCP in patients with confirmed stones) was safer [11]. 10/5/2018 2:30:00 PM There are no randomized trials for MRCP/EUS in high risk patients before ERCP since it is recommended without additional work up but a retrospective database study showed greater length of hospital stay, higher radiology dosages, and a trend towards higher hospital charges [12]. Once again, these considerations in cholecystectomized patients may be different with no evidence in what should be the diagnostic algorithm in this group of patients.

The described complication rate of ERCP ranges widely depending on patient selection. In our study, the rate of pancreatitis, bleeding and perforation were similar to those described in the literature [3]. However, the cholangitis rate was superior (0.5–5% described in the literature vs 6% in our study). This may be explained by an outbreak in multidrug-resistant organisms in our institution, including carbapenem-resistant Enterobacteriaceae; this duodenoscope-transmitted infections are not attributable to recognized breaches of standard reprocessing protocols [13].

Two limitations of this study relate to its retrospective nature and the fact that only high risk patients were included. Therefore, sensitivity and specificity of the ASGE criteria could not be calculated.

In conclusion, our study demonstrated that ASGE criteria for the diagnosis of choledocholithiasis have some limitations (approximately 30% of the patients performed ERCP with no demonstration of CBD stones), but it showed that there is no difference in true positive ERCP between cholecystectomized vs non cholecystectomized groups. ASGE criteria can be used in cholecystectomized and non-cholecystectomized patients but may need revision based on prospective studies to further decrease the number of diagnostic ERCPs in both groups.

#### Conflict of interest

Non declared

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