Identifying Patients Most Likely to Have a Common Bile Duct Stone After a Positive Intraoperative Cholangiogram

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Abstract: The false-positive rates of a positive intraoperative cholangiogram (IOC) are as high as 60%. Endoscopic retrograde cholangiopancreatography (ERCP) for stone removal is required after a positive IOC. It is unclear which clinical factors identify patients most likely to have a stone after a positive IOC. This study was conducted to identify factors predictive of common bile duct (CBD) stone(s) on ERCP after a positive IOC. A retrospective review of our endoscopic database identified all ERCP and/or endoscopic ultrasound (EUS) procedures performed for a positive IOC between August 2003 and August 2009. Collected data included patient demographics; indication for cholecystectomy; IOC findings; blood tests before and after cholecystectomy, including liver function tests, complete blood count, and amylase and lipase measurements; and ERCP and/or EUS results. Patients who had a negative EUS for CBD stones and no subsequent ERCP were contacted by phone to see if they eventually required an ERCP. Univariate and multivariable analyses were performed. A total of 114 patients were included in the study. IOC findings included a single stone, multiple stones, nonpassage of contrast into the duodenum, dilated CBD, and poor visualization of the bile duct. Eighty-four percent of patients had ERCP only, 9% had EUS only, and 7% had EUS followed by ERCP. Sixty-five patients (57%) had CBD stones on ERCP or EUS. Older age, multiple stones, dilated CBD on IOC, and elevated postcholecystectomy bilirubin levels were the clinical variables with statistically significant differences on univariate analysis. On multivariable analysis, older age and elevated postcholecystectomy total bilirubin levels correlated with the presence of CBD stones on ERCP. Fifty-seven percent of patients referred for endoscopic evaluation after a positive IOC had CBD stones on ERCP. Patients with CBD stones after a positive IOC were more likely to be older with elevated postcholecystectomy total serum bilirubin levels.

Laparoscopic cholecystectomy is regarded as the treatment of choice for cholecystitis and symptomatic cholelithiasis.[1,2] An intraoperative cholangiogram (IOC) is often performed during laparoscopic cholecystectomy to determine biliary patency, integrity, and anatomy. The incidence of common bile duct (CBD) stones found on IOC after cholecystectomy ranges from 8% to 15%.[1] Unfortunately, false-positive rates for IOCs are as high as 60% in some series.[3-5] It is unclear whether these rates are due to misinterpretation of the cholangiogram, passage of the stones prior to endoscopic intervention, or nonvisualization of stones at the time of their removal.

After a positive IOC, a postoperative endoscopic retrograde cholangiopancreatography (ERCP) is indicated for stone removal.[6] ERCP is not an innocuous procedure. The complication rates for ERCP range from 2.5% to 11%.[7,8] The most common complications are post-ERCP pancreatitis, infection, and bleeding. The identification of patients most likely to have a CBD stone at the time of the ERCP is important to limit patient exposure to potential complications.

We describe a retrospective review of every ERCP and/or EUS related to a positive IOC performed at Wake Forest Baptist Medical Center in Winston-Salem, North Carolina between August 2003 and August 2009. The purpose of this study was to identify factors predictive of CBD stone(s) at the time of endoscopic evaluation after a positive IOC, thereby individualizing the intervention required for the patients to preemptively minimize or even eliminate the risks associated with postcholecystectomy ERCP. This study also describes the performance of endoscopic ultrasound (EUS) in detecting CBD stones in patients after a positive IOC. The study was approved by the Institutional Review Board of Wake Forest University Baptist Medical Center.

Methods

The following data were collected for all patients: patient demographics; indication for cholecystectomy; IOC findings; and blood tests before and after cholecystectomy, including liver function tests (LFTs; total bilirubin, direct bilirubin, transaminases, and alkaline phosphatase), peripheral white blood cell count, amylase, and lipase. The interval (in days) between the positive IOC and ERCP and/or EUS was documented.

The indications for laparoscopic cholecystectomy were reviewed and divided into the following 5 categories: symptomatic cholelithiasis, cholecystitis, pancreatitis, gallbladder dyskinesia, and other causes. The positive findings on IOC that prompted referral for ERCP are divided into the following 6 categories: nonpassage of contrast into the duodenum, a single stone, multiple stones, dilated bile duct (>8 mm), poor visualization of the distal CBD, and palpable CBD stones at surgery. The findings on IOC were taken from the operative notes and from the record of the treating gastroenterologist. No IOC images were available to be reviewed independently. Patients with positive findings on IOC underwent ERCP and/or EUS for elevated liver enzymes pre- or postoperatively or for persistent abdominal pain, nausea, and/or vomiting.

All ERCP and EUS procedures were performed by experienced gastroenterologists at Wake Forest Baptist Medical Center. The decision to perform EUS prior to ERCP was at the discretion of the endoscopist. Patients who did not proceed to ERCP after a negative EUS were called by the principal investigator and asked if they had ongoing biliary symptoms and whether they had undergone ERCP at a different facility.

An ERCP was determined to be positive for stone(s) if the cholangiogram demonstrated filling defects consistent with stones or if stones were seen after a biliary sphincterotomy and CBD sweep. CBD stones seen on ERCP were removed using baskets or retrieval balloons. After stone removal, a cholangiogram was performed to ensure clearance of the bile duct. ERCP/EUS findings noted the presence of stone(s), whether there was a single stone or multiple stones, the size of the stone(s), and the diameter of the CBD.

Statistical Analysis

Univariate analysis was used to assess for statistically significant associations between potential clinical risk factors and whether or not a CBD stone was seen on ERCP. Continuous variables were reported as means and standard deviations if normally distributed and as medians and ranges if not normally distributed. Continuous variables were compared using *t* test or Wilcoxon rank sum test as appropriate. Categorical variables were compared using the chi-square test.

Multivariable logistic regression analysis was also performed. The variables included in the model were all those significant on the univariate analysis. Statistical analysis was performed using Intercooled Stata 8.0 for Windows (Stata Corp).

Results

A total of 114 patients were included. None of the patients had any precholecystectomy evaluation of the bile ducts with either magnetic resonance cholangiopancreatography (MRCP) or EUS. The majority of cholecystectomies were performed at outside hospitals, and later patients were transferred to our medical center for ERCP/EUS. The indications for cholecystectomy include 49 (43%) patients with symptomatic cholelithiasis, 19 (17%) with

cholecystitis, 21 (18%) with pancreatitis, 7 (6%) with gallbladder dyskinesia (based on abnormal cholescintigraphy), 1 (1%) with acute cholangitis, and 17 (15%) with no record available in our database. Of the 19 patients who had cholecystitis, 13 (68%) had calculus type, and the remaining 6 (32%) had no record of the type.

Operative notes were unavailable for review in 61 patients (54%), and, in 8 patients (7%), no indication for IOC was noted. The indication for performing an IOC was elevated liver enzymes in 20 patients, pancreatitis in 13 patients, CBD stone on preoperative abdominal ultrasound (US) in 4 patients, abnormal cystic duct anatomy in 2 patients, and CBD stone on computed tomography, CBD stone on magnetic resonance imaging, intraoperative cystic duct stone, CBD dilatation on preoperative abdominal US, gallbladder neck stone on preoperative abdominal US, and brisk outflow of bile from the cystic duct during the operation in 1 patient each. For patients who came to our institution with no operative notes, the findings noted on IOC were recorded by the gastroenterologist at the time of transfer as reported by the referring physician.

All patients had successful ERCP and/or EUS. CBD stones were confirmed in 65 patients (57%), for a false-positive IOC rate of 43%. The majority (84%) of patients underwent ERCP alone; however, a significant minority (16%) had EUS performed in addition to ERCP. The median time to ERCP and/or EUS after surgery was 4 days (range, 0-167). A single stone was identified on EUS and confirmed by ERCP in the patient who had the procedures 167 days after a positive IOC.

Table 1 shows ERCP and EUS findings. Of the 10 patients who had no stone seen on EUS, 1 patient had an ERCP, which confirmed the presence of a stone. The ERCP was performed because there was some concern that the entirety of the bile duct was not visualized by EUS due to a periampullary diverticulum. All other patients were contacted by telephone. None had symptoms of biliary colic or required an ERCP after the EUS. Of the 8 patients with stones seen on EUS, 7 patients underwent subsequent ERCP at our center, and 1 patient was lost to follow-up. Six of the 7 patients investigated at our center had CBD stone(s) on ERCP; 1 patient had no stones at the time of the procedure. Being conservative and assuming that the 1 patient with a positive EUS for a CBD stone who was lost to follow-up was a false-positive, the sensitivity and specificity of EUS for detecting CBD stones in patients with a positive IOC in this study were 100% and 83%, respectively.

A comparison of clinical factors in patients with or without confirmed CBD stones on ERCP or EUS is shown in Table 2. In our study, patients with confirmed CBD stones were more likely to be older, have multiple stones or a dilated duct on IOC, and have an elevated total serum bilirubin postcholecystectomy. There was no significant difference in indication for cholecystectomy, precholecystectomy laboratory values, or days between positive IOC and ERCP and/or EUS in patients with or without confirmed CBD stones.

Table 1. ERCP and EUS Findings

Procedure(s)	
ERCP only, n (%)	96 (84)
EUS only, n (%)	10 (9)
EUS followed by ERCP, n (%)	8 (7)
ERCP Findings (n=104)	
No stones, n (%)	40 (38)
Stone(s), n (%)	64 (62)
Median CBD diameter on ERCP, mm (range)	10 (5-20)
CBD dilated on ERCP, n (%)	45 (58)
EUS Findings (n=18)	
No stones, n (%)	10 (56)
Stone(s), n (%)	8 (44)
Median CBD diameter on EUS, mm (range)	8 (4-18)
CBD dilated on EUS, n (%)	7 (44)

CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound.

Table 3 shows the results of the multivariable logistic analysis. Patients with a positive IOC who were older and had elevated postcholecystectomy serum bilirubin levels were more likely to have a stone seen on ERCP than those who were younger and had normal bilirubin levels.

Discussion

This is the largest study to date detailing ERCP findings after a positive IOC. In our study, 38% of patients (40 of 104 patients) who underwent postoperative ERCP for a positive IOC did not have CBD stones. A study by Frossard and colleagues indicated that spontaneous migration of CBD stones (especially those less than 8 mm in diameter) occurred in up to 21% of patients.[9] Spontaneous migration of stones into the duodenum and microlithiasis appeared to be the most likely explanations for negative ERCP results in our study. Overall, these data are consistent with prior reports indicating low rates of stone recovery on a postoperative ERCP.[3,10,11] Confirmation of microlithiasis would require crystal analysis of bile for calcium bilirubinate. This could not be accomplished in our study due to its retrospective design.

IOC is mainly performed for 2 reasons: to detect choledocholithiasis and/or to confirm the integrity of the biliary system after the procedure.[12] Systematic reviews by Ford and colleagues and Sajid and colleagues indicate

Table 2. Comparison of Patient Demographics, Indications for Cholecystectomy, IOC Findings, and Laboratory Values

	CBD Stones on ERCP or EUS		
	No stones (n=49)	**Stones (n=65)**	***P* value**
Median Age, years (SD)	52 (13-93)	56 (14-92)	.03
Gender, n (%)			
Male	15 (32)	27 (42)	.27
Female	32 (68)	37 (58)	.34
IOC Findings, n (%)			
Nonpassage of contrast into the duodenum	7 (16)	7 (11)	.478
Single stone	19 (42)	26 (41)	.868
Multiple stones	12 (27)	30 (47)	.033
Dilated bile duct	0 (0)	5 (11)	.006
Poor visualization of the distal CBD	2 (4)	1 (2)	.365
Median Postcholecystectomy Laboratory Values			
AST, U/L	88	66	.35
ALT, U/L	111	102	.78
ALP, U/L	132	154	.17
Total bilirubin, mg/dL	1.12	1.65	.02
Direct bilirubin, mg/dL	0.85	0.5	.22
WBC count, ×1000	8.6	8.8	.89
Amylase, U/L	52	58	.82
Lipase, U/L	39	41	.66
Any Postoperative Liver Function Test Abnormality, n (%)	29 (88)	41 (82)	.47

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CBD, common bile duct; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; IOC, intraoperative cholangiogram; SD, standard deviation; WBC, white blood cell.

no concrete evidence to support or reject the use of IOC during cholecystectomy.[12,13] As the interpretation of IOC depends on the reviewer, the accuracy of results can at times be in doubt.[14] In this context, biliary endoscopists are left to decide whether to proceed with ERCP and its inherent complications or pursue confirmatory imaging or clinical markers (eg, LFTs).

In our study, none of the IOC findings accurately predicted the presence or absence of CBD stones, which is similar to findings in prior studies.[2] However, on multivariate analysis, patients who were older and had an elevated postcholecystectomy total serum bilirubin level were significantly more likely to have a CBD stone on ERCP. A study by Varadarajulu and colleagues identified abnormal LFTs as 1 of the variables that predicted the presence of CBD stones.[1] LFTs were shown to predict CBD stones in other studies, particularly in patients undergoing ERCP preoperatively.[15-17] Of all the LFTs analyzed in our data, only total serum bilirubin after the cholecystectomy predicted stones on ERCP (*P* value of .02 on univariate analysis).

Ammori and colleagues advocate a wait-and-see policy for patients with small stones on IOC or follow-up with less invasive techniques, such as EUS or MRCP.[11] Those with definite CBD stones found on follow-up imaging would then undergo ERCP. The accuracy of both tests, particularly EUS, in the evaluation of CBD stones is greater than 95%.[18-21] Our results agreed with those of the study by Ammori and colleagues regarding follow-up of patients who had negative EUS findings.[11]

EUS avoids the risk of pancreatitis seen with ERCP and can be very accurate in detecting CBD stones, even small ones in nondilated ducts.[22] EUS can be performed immediately before ERCP under the same sedation, avoiding the need for a second visit. In our study, we looked at the sensitivity and specificity of EUS for detecting CBD stones. The results showed that EUS had a high sensitivity (100%) and specificity (83%) for detecting a retained CBD stone, rendering it a useful screening study to perform before ERCP.

There are several limitations of this study, including the study's retrospective design; the use of nonstandardized IOCs, with the subjects being referred from different hospitals with different imaging technologies; and the prolonged time period between positive IOC and endo-

Table 3. Estimated Odds Ratios Based on the Multivariable Logistic Regression Model*

Variable	Odds Ratio	95% CI
Age	1.028	1.005-1.051
Multiple stones seen on IOC	2.738	0.932-8.047
Postcholecystectomy total bilirubin	1.359	1.005-1.837

*Although significant in univariate analysis, the variable "dilated bile duct on IOC" was not included in this model because only 6 patients had this diagnosis.

IOC, intraoperative cholangiogram.

scopic imaging. As the patient numbers were small in our study, a larger study, performed prospectively, comparing EUS to ERCP for identifying CBD stones is the obvious next step. We have plans to initiate such a study at our institution in the near future.

Summary

In our 6-year retrospective analysis, 57% of the patients referred for ERCP after a positive IOC during laparoscopic cholecystectomy had confirmed CBD stone(s) on ERCP/EUS. Patients with CBD stones after a positive IOC were more likely to be older and have an elevated total serum bilirubin postcholecystectomy. We recommend using safer and less invasive imaging, such as EUS, in younger patients with normal LFTs and/or normal ducts and going straight to ERCP in elderly patients with abnormal LFTs and/or dilated ducts.

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