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Research Article

Complicated Choledocholithiasis More Common after Cholecystectomy

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Abstract

Background: Common bile duct stones following cholecystectomy are either retained from time of surgery or form de novo postoperatively. Complications of choledocholithiasis are well recognized, however there is a paucity of data regarding the pattern of presentation after surgery.

Objectives: A retrospective review was performed to assess clinical presentations of choledocholithiasis between patients with and without a prior cholecystectomy and symptom onset after surgery.

Methods: Adult patients with or without prior cholecystectomy presenting to a tertiary and secondary care setting from 2014 - 2016 with symptomatic choledocholithiasis due to isolated stone disease requiring endoscopic retrograde cholangiopancreatography during an inpatient stay were retrospectively reviewed. Patient demographics, pattern of presentation, and periprocedural data including presentation onset after cholecystectomy were compared.

Results: 258 patients without and 100 patients with prior cholecystectomy were included. There was a significant difference between the proportion of patients presenting with cholangitis (32% vs 12.6%, $p < 0.001$) as well as biliary colic (62% vs 75.1%, $p = 0.008$) between patients with and without prior cholecystectomy, respectively. Of 24 patients who presented within 3 years of surgery, 8 (33%) had acute cholangitis.

Conclusion: Higher rates of complicated biliary disease after cholecystectomy including those presenting within 3 years after surgery supports further evaluation of identifying patients predisposed to recurrent bile duct obstruction.

Keywords: *Choledocholithiasis; Cholecystectomy; Cholangitis; Complicated Choledocholithiasis*

Introduction

Gallstones are present in approximately 7% of the United States population [1] and over 436,000 laparoscopic cholecystectomies were performed in 2010 [2]. An estimated 10% to 20% of patients with symptomatic gallstones have choledocholithiasis which, in Western countries, typically is due to migration of cholesterol stones from the gallbladder [3]. Biliary obstruction from common bile duct (CBD) stones may lead to biliary colic, obstructive jaundice, or complicated disease including acute pancreatitis and cholangitis [4]. Liver function tests (LFTs) and trans-abdominal ultrasound are recommended for suspected CBD stones, however normal results do not preclude further investigation if clinical suspicion remains high [3]. Assuming patients are fit to undergo treatment, recent guidelines published by the National Institute for Health and Care Excellence (NICE) and Williams., et al. recommend that patients with CBD stones, regardless of symptoms, should be offered stone extraction and cholecystectomy if surgically appropriate [3,5]. Patients with choledocholithiasis after cholecystectomy may be asymptomatic for years, however there is a paucity of data on their sequela. The aim of this study was to compare pattern of presentation of symptomatic choledocholithiasis in patients with and without a prior cholecystectomy and evaluate time of presentation and after cholecystectomy.

Methods

The study was approved by the Institutional Review Board at Thomas Jefferson University Hospital. A retrospective chart review was conducted of patients at least 18 years of age who were hospitalized with biliary pancreatitis, acute cholangitis, or symptomatic cho-

ledocholithiasis at Methodist Hospital and Thomas Jefferson University Hospital (TJUH) between January 2014 to December 2016. The electronic medical record was reviewed to collect the following data: age, sex, race, body mass index, surgical reports including history of cholecystectomy and perioperative bile duct evaluation, presence of CBD stone or sludge, periprocedural laboratory data, and endoscopic retrograde cholangiopancreatography (ERCP) results including maximum CBD diameter and presence of periampullary duodenal diverticula.

Initially 736 adults with a diagnosis related group (DRG) for cholelithiasis, choledocholithiasis, bile duct obstruction, acute or chronic pancreatitis, or cholangitis and a Current Procedural Terminology (CPT) code for ERCP during the same admission were included (Figure 1). Diagnostic criteria for acute pancreatitis followed the Atlanta classification [6]. Acute cholangitis was defined by the presence of purulent bile or the definitive diagnostic criteria of the Tokyo Guidelines (TG13) [7].

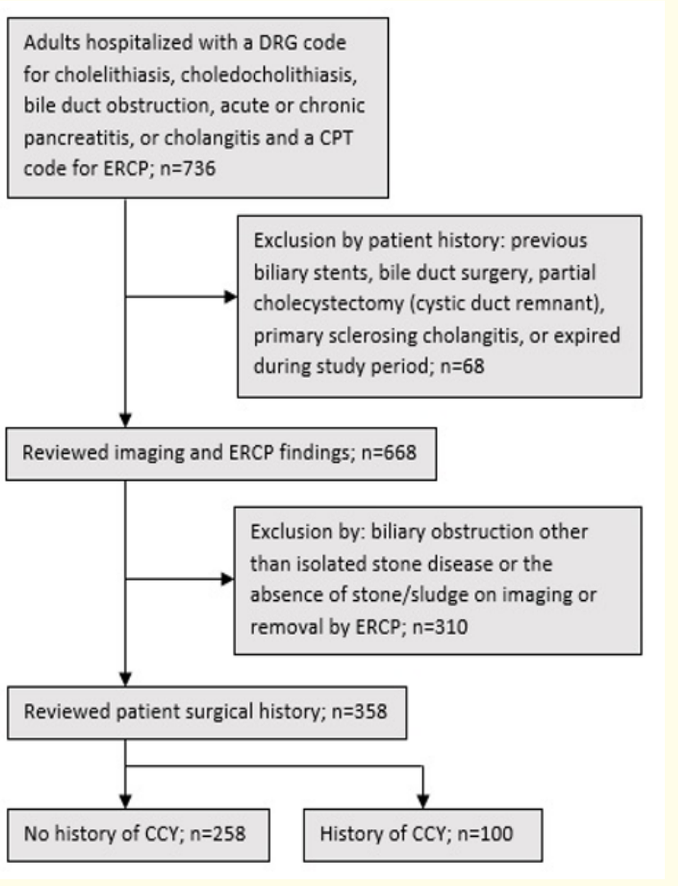

Figure 1: *Flowchart of patient selection.*

DRG: Diagnostic Related Group; CPT: Current Procedural Terminology; ERCP: Endoscopic Retrograde Cholangiopancreatography; CCY: Cholecystectomy.

68 patients were initially excluded due to a history of biliary stent placement, bile duct surgery, partial cholecystectomy with a cystic duct remnant, primary sclerosing cholangitis, or who expired during the study. Imaging and ERCP findings were reviewed and a further 310 patients were excluded based on causes of biliary obstruction other than isolated stone disease (i.e. biliary stenosis, malignancy, sphincter of Oddi dysfunction) or the absence of stone/sludge on imaging or removal by ERCP. 100 of the remaining 358 patients were determined to have had a prior cholecystectomy either by review of surgical reports or imaging. All comparisons in this review were two-tailed and differences with a p-value < 0.05 were considered statistically significant.

Results

A total of 358 patients with biliary pancreatitis, acute cholangitis, or biliary colic due to choledocholithiasis underwent ERCP between January 2014 and December 2016 and were stratified by the presence or absence of a gallbladder. Demographic and clinical data were reviewed (Table 1). 72.1% (258 of 358) of patients presented with symptomatic choledocholithiasis without a prior cholecystectomy compared to 27.9% (100 of 358) of patients with a prior cholecystectomy. Of the 258 patients without a cholecystectomy, 58.1% (150) were male and 73.3% (189) were Caucasian. The mean age was 62.4 years and mean BMI was 28.8 kg/m2. Of the 100 patients post-cholecystectomy, 66% were male, 76% were Caucasian, and had a mean age of 64.6 years and a mean BMI of 29.6. Demographics including sex (male, p = 0.174), race (Caucasian, p = 0.596), age (p = 0.352), and BMI (p = 0.299) yielded no statistical significance.

Patients		No CCY (n = 258)	Post-CCY (n = 100)	*P*-value
Sex	Male	150 (58.1%)	66 (66%)	0.174
	Female	108 (41.9%)	34 (34%)	
Race	Caucasian	189 (73.3%)	76 (76%)	0.596
	African American	34 (13.2%)	11 (11%)	
	Latino	12 (4.7%)	4 (4%)	
	Asian	20 (7.8%)	9 (9%)	
	Not Reported	3 (1.2%)	0 (0%)	
Mean Age (years)		62.4	64.6	0.352
Mean BMI		28.8	29.6	0.299
Presence of Periampullary Diverticulum		50 (19.38%)	26 (26.0%)	0.085

Table 1: *Patient demographics and clinical characteristics.*

CCY: Cholecystectomy.

There was no statistical significance in comparison of sex (Male, p = 0.174), race (Caucasian, p = 0.596), age (p = 0.352), and BMI (p = 0.299) between the two cohorts.

Patients without a prior cholecystectomy included 196 (75.1%) with biliary colic, 32 (12.3%) with biliary pancreatitis, and 33 (12.6%) with acute cholangitis (Figure 2). Notably 3 of the 258 patients presented with concomitant biliary pancreatitis and acute cholangitis (N = 261). Patients with a prior cholecystectomy included 62 (62%) with biliary colic, 6 (6%) with biliary pancreatitis, and 32 (32%) with acute cholangitis. Compared to the cohort without a prior cholecystectomy, patients post-cholecystectomy had a significantly higher proportion presenting with acute cholangitis ($p < 0.001$) and less biliary colic ($p = 0.008$), whereas the proportion with biliary pancreatitis was similar ($p = 0.078$). Among post-cholecystectomy patients, a higher proportion of females presented with complicated disease (58% versus 32%; $p = 0.003$). Age ($p = 0.074$), race (Caucasian, $p = 0.308$), and BMI ($p = 0.186$) were not statistically different.

Endoscopic and clinical predictors of recurrent biliary tract disease were evaluated in patients presenting with choledocholithiasis post-cholecystectomy. Only 6 patients had clinical conditions associated with formation of sludge and microlithiasis including rapid weight loss and cirrhosis and 26% (26) of patients with a prior cholecystectomy had the presence of a periampullary diverticulum. At the time of presentation, 76% (76) of patients post-cholecystectomy had a recorded maximum common bile duct diameter of > 10 mm (range 4 - 25 mm) on ERCP or imaging including trans-abdominal ultrasound or magnetic resonance cholangiopancreatography (MRCP), compared to 21% (21) with ≤ 10 mm and 3 were not reported. Concomitantly, 87% (87) of patients had an alkaline phosphatase (ALP) greater than the hospital laboratory's upper limit of normal of 92 IU/L, and 55% (55) of patients with a total bilirubin ≥ 2.0 mg/dL. 29 of 39 patients with an ultrasound had evidence of bile duct obstruction defined by the presence of echogenic material in the CBD or CBD dilatation, giving a sensitivity of 74.4%.

Surgical reports including perioperative bile duct evaluation were obtained for 30 of the 100 patients who had a cholecystectomy. The median time from cholecystectomy to choledocholithiasis requiring ERCP was 210 days (range 6 - 5160 days) and 80% (24) presented within 3 years of surgery (Figure 3). 79.2% (19 of 24) of those patients did not undergo perioperative bile duct evaluation with intraoperative cholangiography (IOC) or ERCP at the time of cholecystectomy. 33% (8 of 24) of patients presented with acute cholangitis within 3 years of cholecystectomy which included 5 who did not undergo perioperative CBD exploration.

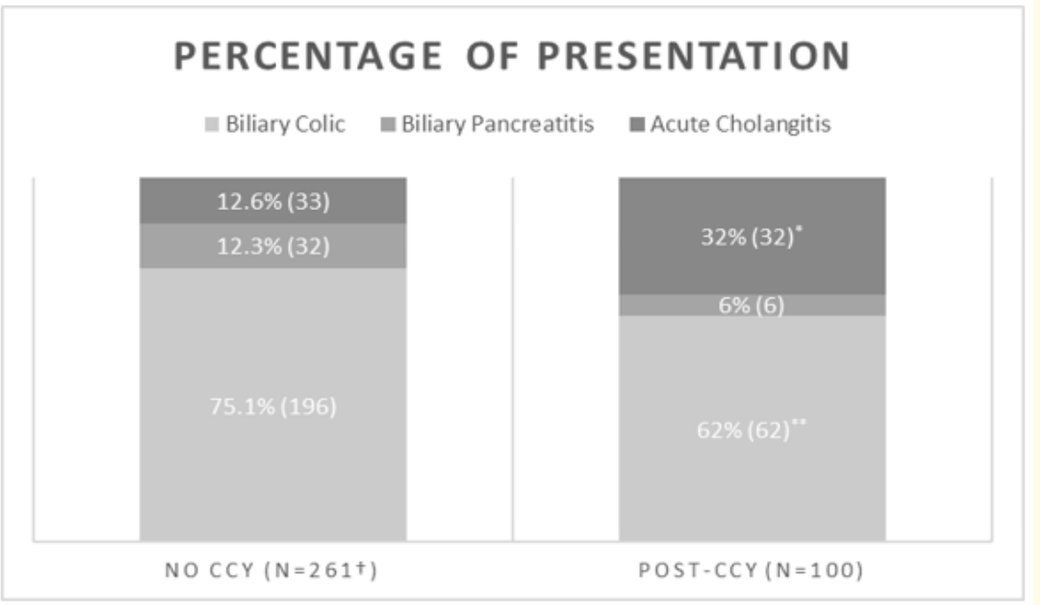

Figure 2: *Comparing clinical presentations of choledocholithiasis.*

CCY: Cholecystectomy; †: 3 of the 258 patients without cholecystectomy presented with concomitant biliary pancreatitis and acute cholangitis.

** P-value < 0.001; Statistically significant.*

*** P-value 0.008; Statistically significant.*

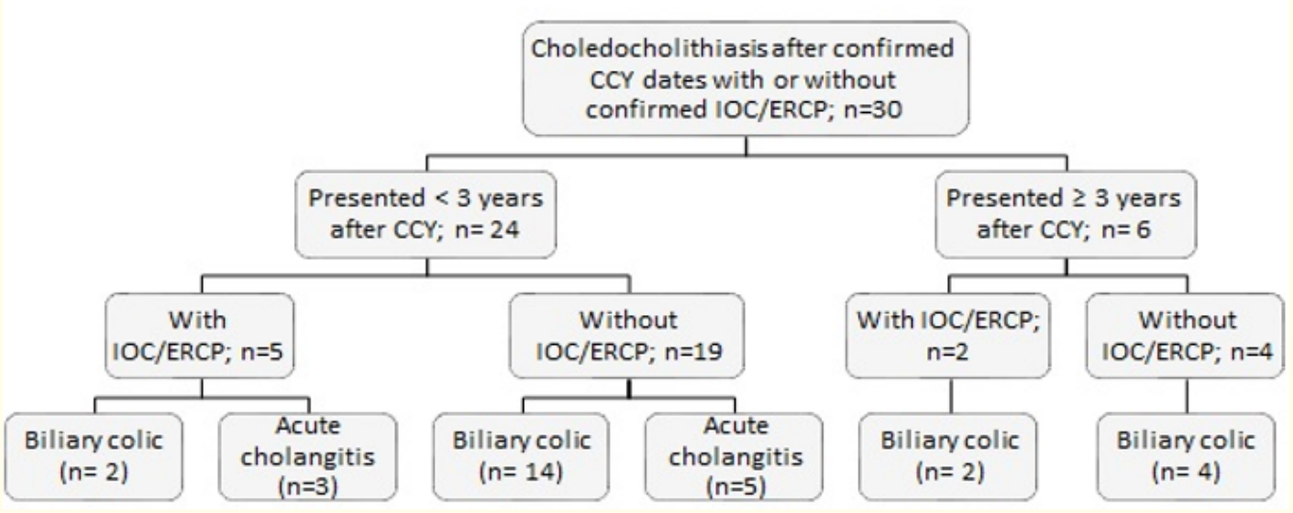

Figure 3: *Comparing pattern of presentation and time of onset in post-cholecystectomy patients who did or did not undergo perioperative bile duct evaluation with ERCP or IOC.*

CCY: Cholecystectomy; IOC: Intraoperative Cholangiography; ERCP: Endoscopic Retrograde Cholangiopancreatography.

Surgical reports including perioperative bile duct evaluation were obtained for 30 of the 100 patients who had a cholecystectomy. Clinical presentation and documentation of perioperative bile duct evaluation with IOC or ERCP was analyzed between patients who presented within or after 3 years of their cholecystectomy. 33% (8 of 24) of patients presented with acute cholangitis within 3 years of cholecystectomy which included 5 who did not undergo perioperative CBD exploration.

Discussion

Symptomatic choledocholithiasis post-cholecystectomy is not uncommon, as over a fourth of the patients in the study presented after gallbladder removal. Complications of CBD stones are well recognized, however there is a paucity of data on pattern of presentation after cholecystectomy. In an evaluation of patients in California who underwent cholecystectomy for symptomatic gallstones (including uncomplicated cholecystitis), only 4.0% had gallstone pancreatitis and 0.2% had acute cholangitis [8]. Cox., *et al.* [9] performed a retrospective review of patients presenting with symptomatic choledocholithiasis who had previously undergone laparoscopic cholecystectomy and of 61 patients, 74% (45 of 61) of patients presented with uncomplicated choledocholithiasis whereas 26% (16 of 61) presented with complicated disease including acute cholangitis and biliary pancreatitis. Our study showed a similarly high percentage of patients with complicated disease, especially acute cholangitis, than would be expected in the general population. Compared to our patients with an intact gallbladder, there was a statistically significant difference in the proportion of patients presenting with acute cholangitis (32% versus 12.6%; $p < 0.001$). In addition to presentation, laboratory data including LFTs and imaging in our patients post-cholecystectomy with symptomatic choledocholithiasis requiring ERCP were evaluated. The sensitivity for detection of choledocholithiasis was 55% for an elevated total bilirubin, 87% for an elevated ALP, and 74.4% for trans-abdominal ultrasound. Although these tests are helpful in identifying choledocholithiasis, their imperfect sensitivity coupled with the high percentage of complicated and potentially life-threatening illness post-cholecystectomy should prompt clinicians to investigate further if clinical suspicion remains high.

Clinical predictors to identify patients at higher risk of developing complicated choledocholithiasis were evaluated in patients post-cholecystectomy. The sub-analysis revealed a statistically significant higher proportion of females presenting with acute pancreatitis or cholangitis compared to uncomplicated disease. Overall, a limited number of patients post-cholecystectomy had medical conditions associated with an increased risk of recurrent bile duct stones after cholecystectomy including prolonged fasting and/or rapid weight loss, pregnancy, sickle cell anemia, liver cirrhosis, solid organ transplantation/cyclosporine medication, or the presence of duodenal diverticula [10-12]. Although the association is unclear, the elevated morbidity and mortality associated with complicated choledocholithiasis, coupled with the lack of identifiable comorbid conditions encourages for further evaluation of patients at higher risk of complications secondary to CBD stones.

Bile duct stones are defined by their site of origin but their classification post-cholecystectomy is controversial. Characteristics including morphology and composition have been utilized to determine origin, but given the possibility of stone migration from the gallbladder and accumulation of biliary sludge, others have used time after cholecystectomy. Residual common bile duct stones have been defined as secondary stones missed at the time of cholecystectomy and may be identified up to no more than 2 to 3 years after surgery [13-15]. 80% (24 of 30) of post-cholecystectomy patients who had confirmed cholecystectomy dates presented with symptomatic choledocholithiasis within 3 years of surgery. Notably 33% of them presented with acute cholangitis but most did not undergo perioperative bile duct evaluation including IOC or ERCP.

In attempt to define a group of patients who had primary common duct stones with higher certainty, Saharia., *et al.* [13] conducted a review of patients who presented with symptomatic choledocholithiasis at least two years from time of cholecystectomy. Including only patients whose collected stones had the morphologic appearance of a primary mud stone described by Madden [16], the average time between cholecystectomy and presentation was 12 years [13]. Conversely, in the study published by Cox., *et al*. [9], all patients had secondary CBD stones determined by morphology and the median time from laparoscopic cholecystectomy to presentation was 4 years (range 6 days to 18 years). Although the separation between residual and recurrent stones is unclear, these studies suggest that patients with residual stones become symptomatic earlier than those who form CBD stones de novo post-operatively. The high prevalence of early onset in our study raises concern for patients developing complications from residual CBD stones in the absence of perioperative bile duct evaluation at time of cholecystectomy.

There were several limitations to this study. The retrospective nature precluded evaluation of other established risk factors for recurrent biliary stone formation after cholecystectomy given limited data collection on patients' surgical history as most had procedures at an outside hospital. While percentage of disease onset may have been disproportionate as data collection on patients with recent cholecystectomy was readily accessible, a significant number who presented within 3 years remained. Although several patients included presented at a secondary care center, patients with complicated disease are more likely to be transferred to a tertiary referral hospital, therefore potentially skewing the pattern of presentation. Future prospective, multi-centered studies are recommended to further investigate pattern of illness and clinical predictors of recurrent choledocholithiasis.

Conclusion

Cholecystectomies are often performed to prevent complications of choledocholithiasis, however recurrence is still observed. Despite not having well-defined criteria on determining the origin of common bile duct stones, a significant number of post-cholecystectomy patients presented with complicated choledocholithiasis within 3 years of surgery. Given the high rate of acute cholangitis, the absence of clinical predictors of recurrent biliary disease, and the limited sensitivity of diagnostic screening, further attempts at identifying patients at higher risk for complications of residual common bile duct stones should be made.

Disclosure

No contributions or funding to the research or manuscript have been made. The authors have no ethical conflicts to disclose. The authors have no conflicts of interest to declare.

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