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Preoperative endoscopic retrograde cholangio-pancreatography (ERCP) is a risk factor for surgical site infections after laparoscopic cholecystectomy

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A B S T R A C T

Background: We sought to examine whether preoperative endoscopic retrograde cholangio-pancreatography (ERCP) increases the risk of surgical site infections (SSI) after laparoscopic cholecystectomy.
Methods: Patients admitted to an academic hospital from 2010 to 2016, who were older than 18 and had a laparoscopic or a laparoscopic converted to open cholecystectomy for complicated biliary tract disease were included. We compared those who had a preoperative ERCP to those who did not. Our primary endpoint was the rate of SSI.
Results: A total of 640 patients were included. Of them, 122 (19.1%) received preoperative ERCP and 518 (80.9%) did not. The former had different preoperative diagnoses compared to non-ERCP patients (choledocholithiasis [35.2%–7.0%], acute cholecystitis [31.2%–76.4%], gallstone pancreatitis [20.5%–16.2%], and cholangitis [13.1%–0.4%], $p < 0.001$). The rate of SSI was higher in the preoperative ERCP group (11.5%–4.0%, $p = 0.005$). In a multivariable analysis conversion to open (OR = 2.57, 95% CI = 1.06–6.21, $p = 0.037$) and preoperative ERCP (OR = 3.12, 95% CI = 1.34–7.22, $p = 0.008$) were the only independent predictors of SSI.
Conclusion: Preoperative ERCP is associated with a threefold increase in the risk of SSI after laparoscopic cholecystectomy.

Introduction

Endoscopic retrograde cholangio-pancreatography (ERCP) is commonly performed prior to laparoscopic cholecystectomy when choledocholithiasis is proven or suspected. The immediate procedure-related complications of ERCP are well-described and include pancreatitis, bleeding, and perforation.[1,2] Preoperative ERCP for biliary drainage has been associated with an increased risk of surgical site infections in patients undergoing pancreaticoduodenectomy, presumably by allowing preoperative bacterial colonization of the biliary tract, and has been one of the most consistent independent predictors of surgical site infections following pancreaticoduodenectomy.[3–8] Given the frequent use of ERCP prior to laparoscopic cholecystectomy, we sought to examine whether ERCP is associated with an increased incidence of postoperative wound infections in patients undergoing laparoscopic cholecystectomy. We hypothesized that patients who underwent preoperative ERCP with sphincterotomy would have a higher rate of surgical site infections after laparoscopic cholecystectomy than those who did not undergo preoperative ERCP.

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Methods

Between May 2010 and July 2016, patients undergoing a laparoscopic or a laparoscopic converted to open cholecystectomy by the acute care surgery division of an academic hospital were identified using a prospectively collected database. Adult patients with complicated biliary tract disease, which was defined as a preoperative diagnosis of acute cholecystitis, choledocholithiasis, cholangitis, or gallstone pancreatitis, were included. We excluded patients who underwent planned open cholecystectomy. We also excluded patients who underwent laparoscopic cholecystectomy due to biliary colic, or asymptomatic cholelithiasis. We did not have a formal prospective algorithm for the diagnosis or management of suspected choledocholithiasis. Decisions regarding repeating liver function tests, biliary tract imaging such as magnetic resonance cholangio-pancreatography (MRCP), whether to perform an intraoperative cholangiogram (IOC), and whether or when to perform ERCP were made by the treating physicians based on their clinical suspicion for choledocholithiasis. Of note, all patients received preoperative antibiotics right before the incision. In addition, all gallbladders were placed in a retrieval bag prior to removal from the abdomen.

We collected data including baseline demographics (age, gender), comorbidities (diabetes mellitus, prior abdominal surgery, previous history of acute cholecystitis, body mass index [BMI], American Society of Anesthesiologists [ASA] class), serum liver function tests on initial presentation to the emergency department (total and direct bilirubin, alkaline phosphatase, aspartate aminotransferase [AST], alanine aminotransferase [ALT]), ERCP-related data (ERCP findings, failure to clear the common bile duct (CBD), ERCP-related complications), intraoperative data (IOC, laparoscopic CBD clearance), hospital length of stay, surgical site infections, and overall complications. The ERCP-related data, as well as the preoperative laboratory variables were not captured in the prospective database and had to be retrospectively collected by medical chart review.

Our primary endpoint was the rate of surgical site infections in patients with and without preoperative ERCP with sphincterotomy. We defined surgical site infections as superficial or deep incisional infections, or organ/space infections (i.e. intraabdominal abscesses). A clinical diagnosis with prescription of antibiotics was required to label a patient as positive for superficial or deep incisional surgical site infection. Organ/space infections were confirmed with imaging studies.

Statistical analysis was performed using the STATA software (version 13.1). We compared patients who had preoperative ERCP to those who did not. The numerical variables were summarized as medians and interquartile ranges (25th to 75th percentile) and the categorical ones as frequencies and percentages. We used the Mann-Whitney *U* test for the comparison of continuous variables and the chi-square or Fisher's exact test for the categorical ones as appropriate. Subsequently, we performed a stepwise logistic regression analysis to identify independent predictors of surgical site infections. We defined a p-value of less than 0.05 as statistically significant. The study was approved by out Institutional Review Board.

Results

A total of 640 patients were included. The characteristics of these patients are summarized in Table 1. Of the 640 patients, 122 (19.1%) received preoperative ERCP with sphincterotomy and 518 (80.9%) did not. Table 2 summarizes the results of the univariate analysis. The ERCP patients were older (median age 59 versus 46, $p < 0.001$) and more frequently males (54.1% versus 36.7%, $p < 0.001$). Their preoperative diagnoses were also different compared to non-ERCP patients (choledocholithiasis [35.2% versus 7.0%], acute cholecystitis [31.2% versus 76.4%], gallstone pancreatitis [20.5% versus 16.2%], and cholangitis [13.1% versus 0.4%], $p < 0.001$). They had an ASA class ≥3 more frequently than the non-ERCP patients (32.0% versus 17.6%, $p = 0.001$). Furthermore, diabetes mellitus was more common among them (17.2% versus 8.5%, $p = 0.004$), as was the previous history of acute cholecystitis episodes (9.0% versus 3.9%, $p = 0.017$). The laboratory values including AST, ALT, alkaline phosphatase, and bilirubins (both total and direct) were significantly more elevated in the ERCP group. Neither conversion to open nor the duration of surgery differed between the two groups. Even though 13 (10.7%) patients of the ERCP group had an IOC, none required intraoperative or postoperative duct clearance. On the other hand, 52 patients of the non-ERCP group had a positive IOC, which led to 6 attempts of laparoscopic CBD clearance (3 of which were successful), as well as 49 postoperative ERCPs. Of the latter, 36 identified choledocholithiasis (73.5%) and all successfully cleared the CBD.

Regarding postoperative outcomes, the overall complication rates were not different between the two groups (22.1% versus 20.8%, $p = 0.768$). However, the rate of surgical site infections was higher in the preoperative ERCP group (11.5% versus 4.0%, $p = 0.005$). There was a statistically significant difference between the two groups in the rates of both intraabdominal abscesses (4.8% versus 0.7%, $p = 0.008$) and superficial/deep incisional surgical site infections (8.7% versus 3.6%, $p = 0.03$). There was no difference in the surgical site infection rates between those with a positive and those with a negative pre-operative ERCP (10.8 versus 12.0%

Table 1
Characteristics of the population ($n = 640$).

Variable	
Age (in years), median (IQR)	47 (34–63)
Body Mass Index (BMI), median (IQR)	28.5 (25.7–32.7)
Male Gender, n (%)	256 (40.0)
American Society of Anesthesiologists (ASA):	
• Class 1, n (%)	121 (18.9)
• Class 2, n (%)	388 (60.7)
• Class 3, n (%)	124 (19.4)
• Class 4, n (%)	5 (0.8)
• Class 5, n (%)	1 (0.2)
Diabetes Mellitus, n (%)	65 (10.2)
History of Abdominal Surgery, n (%)	229 (35.8)
Previous History of Acute Cholecystitis, n (%)	31 (4.8)
Elective Surgery[a], n (%)	79 (12.3)
Diagnosis:	
• Acute Cholecystitis, n (%)	434 (67.8)
• Gallstone Pancreatitis, n (%)	109 (17.0)
• Choledocholithiasis, n (%)	79 (12.4)
• Cholangitis, n (%)	18 (2.8)
Liver Function Tests on Initial Presentation:	
• Aspartate Aminotransferase (AST), median (IQR)	41 (22–182)
• Alanine Aminotransferase (ALT), median (IQR)	46 (20–182)
• Alkaline Phosphatase, median (IQR)	98 (74–148)
• Total Bilirubin, median (IQR)	0.7 (0.4–1.6)
•Direct Bilirubin, median (IQR)	0.2 (0.1–0.7)
Preoperative ERCP with Sphincterotomy, n (%)	122 (19.1)
Choledocholithiasis confirmed by preoperative ERCP, n (%)	89 (75.4)
Failure to clear the duct, n (%)	3 (3.4)
Complications of preoperative ERCP, n (%)	0
Duration of Surgery (in minutes), median (IQR)	100 (76–126)
Converted to Open, n (%)	72 (11.3)
Intraoperative Cholangiogram (IOC), n (%)	143 (22.3)
Laparoscopic Common Bile Duct Exploration, n (%)	6 (0.9)
Postoperative ERCP, n (%)	49 (7.7)
Positive Postoperative ERCP, n (%)	36 (73.5%)

IQR: Interquartile Range (25th to 75th percentile).
[a] Elective was defined as scheduled outpatient surgery.

Table 2
Comparison of patients who had a preoperative ERCP with sphincterotomy to those who did not.

Variable	Pre-op ERCP (n = 122)	No Pre-op ERCP (n = 518)	p value
Age (in years), median (IQR)	59 (41–74)	46 (32–61)	<0.001
Body Mass Index (BMI), median (IQR)	28.1 (25.8–31.4)	28.9 (25.7–32.9)	0.350
Male Gender, n (%)	66 (54.1)	190 (36.7)	<0.001
American Society of Anesthesiologists (ASA):			<0.001
• Class 1, n (%)	9 (7.4)	112 (21.7)	
• Class 2, n (%)	74 (60.7)	314 (60.7)	
• Class 3, n (%)	36 (29.5)	88 (17.0)	
• Class 4, n (%)	3 (2.4)	2 (0.4)	
• Class 5, n (%)	0	1 (0.2)	
ASA Class ≥ 3, n (%)	39 (32.0)	91 (17.6)	0.001
Diabetes Mellitus, n (%)	21 (17.2)	44 (8.5)	0.004
History of Abdominal Surgery, n (%)	43 (35.3)	186 (35.9)	0.891
Previous History of Acute Cholecystitis, n (%)	11 (9.0)	20 (3.9)	0.017
Elective Surgery, n (%)	27 (22.1)	52 (10.0)	<0.001
Diagnosis:			<0.001
• Acute Cholecystitis, n (%)	38 (31.2)	396 (76.4)	
• Gallstone Pancreatitis, n (%)	25 (20.5)	84 (16.2)	
• Choledocholithiasis, n (%)	43 (35.2)	36 (7.0)	
• Cholangitis, n (%)	16 (13.1)	2 (0.4)	
Aspartate Aminotransferase (AST), median (IQR)	143 (42–311)	32 (21–138)	<0.001
Alanine Aminotransferase (ALT), median (IQR)	186 (50–331)	36 (18–134)	<0.001
Alkaline Phosphatase, median (IQR)	142 (105–230)	91 (71–132)	<0.001
Total Bilirubin, median (IQR)	2.2 (0.8–3.8)	0.6 (0.4–1.2)	<0.001
Direct Bilirubin, median (IQR)	1 (0.3–2.6)	0.2 (0.1–0.4)	<0.001
Duration of Surgery (in minutes), median (IQR)	97 (75–139)	100 (77–124)	0.868
Converted to Open, n (%)	17 (13.9)	55 (10.6)	0.297
Intraoperative Cholangiogram (IOC), n (%)	13 (10.7)	130 (25.1)	0.001
Laparoscopic Common Bile Duct Exploration, n (%)	0	6 (1.2)	0.601
Hospital Length of Stay (in days), median (IQR)	4 (3–6)	3 (2–4)	<0.001
Any Postoperative Complication, n (%)[a]	23 (22.1)	93 (20.8)	0.768
Superficial or Deep Incisional Surgical Site Infection, n (%)[a]	9 (8.7)	16 (3.6)	0.03
Intraabdominal Abscess (organ/space surgical site infection), n (%)[a]	5 (4.8)	3 (0.7)	0.008
Any Surgical Site Infection, n (%)[a]	12 (11.5)	18 (4.0)	0.005

IQR: Interquartile Range (25th to 75th percentile).
[a] 89 (13.9%) of the patients missed their follow-up appointment. The percentages shown reflect the rates among the 551 patients who attended their follow-up visits.

respectively, p = 0.872). Preoperative ERCP patients had a longer hospital length of stay (median of 4 versus 3 days, p < 0.001). Lastly, we compared the 122 patients who had a preoperative ERCP to the 52 patients who underwent either intraoperative (n = 3) or postoperative (n = 49) ERCP. There was no difference in surgical site infections (11.5% versus 2.2% respectively, p = 0.11) or median hospital length of stay (4 versus 3 days respectively, p = 0.271).

In the multivariable analysis, conversion to open (odds ratio = 2.57, 95% confidence interval = 1.06–6.21, p = 0.037) and preoperative ERCP with sphincterotomy (odds ratio = 3.12, 95% confidence interval = 1.34–7.22, p = 0.008) were the only independent predictors of surgical site infections. The results of the multivariable analysis are summarized in Table 3.

Discussion

This study shows that patients who undergo preoperative ERCP with sphincterotomy are three times more likely to develop either a wound infection or an intraabdominal abscess after laparoscopic cholecystectomy than patients who do not, even controlling for a number of important factors including diagnosis. To our knowledge this is the first study that shows an association between ERCP and surgical site infections after laparoscopic cholecystectomy. Given the frequency of both procedures, understanding the relationship between pre-operative ERCP and post-operative infectious complications may influence algorithms for the management of known or suspected choledocholithiasis and allow the adoption of patterns of care that minimize the risk of infection.

Preoperative endoscopic biliary drainage has already been linked to increased rates of surgical site infections after pancreaticoduodenectomy.[3–8] The presumed mechanism is that by eliminating the mechanical barrier of the sphincter of Oddi, there is ascending colonization of the biliary tree by bacteria of the gastrointestinal tract.[9,10] However, despite the evidence that ERCP is a risk factor for such infections after pancreaticoduodenectomy, there has been an absence of similar literature for laparoscopic

Table 3
Multivariable analysis to find independent predictors of postoperative surgical site infections.

Variable	Odds Ratio	95% Confidence Interval	p value
American Society of Anesthesiologists (ASA) Class ≥ 3	1.96	0.86–4.51	0.112
Choledocholithiasis (Compared to Acute Cholecystitis)	0.36	0.08–1.69	0.197
Diabetes Mellitus	1.97	0.75–5.20	0.169
Laparoscopic Converted to Open	2.57	1.06–6.21	0.037
Preoperative ERCP with Sphincterotomy	3.12	1.34–7.22	0.008

Variables that were removed from the stepwise logistic regression, because of p-values>0.2 included: age, gender, BMI, emergent (versus elective) surgery, previous episodes of acute cholecystitis, and other diagnoses (gallstone pancreatitis and cholangitis).

cholecystectomy.[11–13] Afaneh and colleagues concluded that a high ASA score, along with acute cholecystitis and intraoperative complications, are independent risk factors for postoperative complications after laparoscopic cholecystectomy. However, they did not report on the use of ERCP in their patient population and they only examined total complications, rather than surgical site infections.[12] A recent study by Donkervoort and colleagues showed that conversion to open and preoperative ERCP are independent predictors of intraabdominal abscesses, but failed to show that ERCP is also associated with wound infections.[13]

In cases of suspected choledocholithiasis there is debate about when to perform immediate ERCP, when to pursue advanced imaging such as MRCP or endoscopic ultrasound and preoperative duct clearance if positive, and when to move directly to cholecystectomy with IOC, followed by intraoperative CBD exploration or postoperative ERCP.[14–17] The optimal treatment option has been vigorously debated in the literature, but a consensus has yet to be reached. In our study, approximately one fourth of those who underwent a preoperative ERCP with sphincterotomy had no choledocholithiasis. Although there were no immediate ERCP-related complications, this additional unnecessary procedure may have contributed to the longer length of stay in the pre-operative ERCP group, and to a higher than needed rate of post-operative infection. More liberal use of MRCP could potentially decrease the number of unnecessary ERCPs, however, some studies have questioned the accuracy and utility of MRCP in this setting.[18–20] Some authors suggest that in patients with a high suspicion for choledocholithiasis immediate ERCP is more efficient.[21,22] On the other hand, other studies have shown that MRCP decreases the need for subsequent ERCPs in up to 50% of the patients that would have otherwise undergone an ERCP.[23–25] Our study cannot settle this debate, but may inform it in several ways. First, it suggests that beyond the immediate risk of complications, the additional cost, and the additional hospital time, a non-therapeutic preoperative ERCP may have further negative downstream effects on infectious complications after subsequent cholecystectomy. Secondly, it is known that in the setting of preoperatively confirmed choledocholithiasis the vast majority of surgeons opt for ERCP to clear the duct before proceeding with a laparoscopic cholecystectomy.[26] Our study suggests that this widely accepted practice may increase the risk of post-operative infection. At the same time, even though we found an association between ERCP and surgical site infections, we need to emphasize that ERCP might not be the actual cause. However, we did control for multiple potential confounders in the multivariable analysis and ERCP was an independent predictor of surgical site infections.

It is unknown how preoperative ERCP compares to postoperative ERCP or laparoscopic common bile duct exploration with regard to infectious complications. In our study, there were higher rates of infection with preoperative ERCP than with intraoperative or post-operative clearance, but these were not statistically significant as our cohort was severely underpowered for this comparison. While infection is not the only factor to be considered when determining the optimal pathway to both cholecystectomy and resolution of choledocholithiasis, whatever algorithm is adopted by individual surgeons or institutions, our study suggests that the risk of post-operative infection should be considered.

Aside from sequencing procedures to minimize infectious risks, it is possible that broader perioperative antibiotic coverage for patients who have undergone a preoperative ERCP might reduce infectious complications. This has been demonstrated in the literature on surgical site infections in patients undergoing pancreaticoduodenectomy after preoperative biliary stenting. Additional research needs to be conducted to examine whether this would indeed lead to a decrease in surgical site infections after laparoscopic cholecystectomy.

Our study has a number of limitations. Even though we used a prospectively collected database to identify our eligible patients, we had to retrospectively review charts, in order to capture variables of interest. As a result, this study has limitations that derive from its retrospective nature and there could be unaccounted confounders that led to the decision to pursue pre-operative versus post-operative ERCP. Additionally, as we have already mentioned, there was no formal prospective algorithm for the diagnosis or management of suspected choledocholithiasis. Third, an inevitable limitation of our study was the fact that our outcome of interest had a low incidence in our patient population, with only 30 patients (5.4% of the entire population) developing surgical site infections. The finding that conversion to open cholecystectomy was associated with infectious complications is in line with the existing literature and provides some reassurance that our other findings may be broadly applicable. Lastly, one could argue against the inclusion of patients with multiple different preoperative diagnoses. We opted to include all patients with complicated biliary tract disease since we felt that best mirrored the clinical reality of caring for such patients, and increased the statistical power given the rarity of the studied outcome. We controlled for these diagnoses in our logistic regression model and found that the association of preoperative ERCP with surgical site infection remained strong.

Conclusions

Preoperative ERCP is associated with an increased risk of surgical site infections in patients undergoing laparoscopic cholecystectomy for complicated biliary tract disease. Preoperative ERCP with sphincterotomy should be selectively used only in patients with a clear indication.

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Conflicts of interest

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