Original Article

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Factors Affecting Recurrent Choledocholithiasis After Endoscopic Biliary Sphincterotomy: A Cross-Sectional Study

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Abstract

Aim: The purpose of this study was to identify and analyze factors associated with the recurrence of common bile duct stones (CBDS) following endoscopic interventions, aiming to provide insights into predictors and characteristics of CBDS recurrence after endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (EST) procedures.

Methods: The study was designed as a single-center, cross-sectional study. Clinical data were collected from 271 patients with CBDS who underwent ERCP between June 2019 and December 2022. According to the diagnostic criteria for CBDS recurrence, patients were categorized into recurrence and non-recurrence groups. The assessment of predisposing risk factors for recurrent bile duct stones included various variables such as age, sex, gallbladder status, presence of periampullary diverticulum (PAD), number and diameter of bile duct stones, bile duct diameter, pre-cutting, and early complications.

Results: A total of 271 patients were included in the study. CBDS recurrence occurred in 25 patients (9.2%), with a median of 18 months after ERCP and EST. Notable findings included that patients with recurrent CBDS had larger common bile duct diameters (7.5±4.5 mm vs 13±1.7 mm, p=0.037). Choledocholithiasis was more common in patients with a choledochal duct diameter ≥1.5 cm (3% vs 48%, p=0.00001). Recurrent choledocholithiasis was frequent in patients with larger stone sizes (7.3±6.5 mm vs 13.5±4.3 mm, p=0.04). The presence of PAD was correlated with a higher recurrence risk (23% vs 44%, p=0.013). The time to stone recurrence after the index ERCP and EST was 18.273±2.021 months. There was no significant difference in recurrence between patients with ≥2 CBDS and those with a single stone (41% vs 44%, p=0.35).

Conclusion: Larger bile duct diameter, choledochal stone size, initial stone size, and the presence of PAD emerged as crucial indicators of recurrence risk. These findings contribute to our understanding of the prediction and management of CBDS recurrence after ERCP and EST procedures.

Keywords: Endoscopic retrograde cholangiopancreatography, endoscopic biliary sphincterotomy, common bile duct stone, recurrence, periampullary diverticulum

Introduction

Gallstones represent a prevalent issue within the digestive system (1). Approximately 10-20% of individuals with gallstones also exhibit common bile duct stones (CBDS), whereas a staggering 95% of patients diagnosed with CBDS concurrently possess gallstones (2). Following the pioneering work of Kawai in 1974, endoscopic sphincterotomy (EST) has emerged as the foremost technique for eradicating CBDS through endoscopic retrograde cholangiopancreatography (ERCP). The success rate of ERCP hovers around 98%, coupled with a clearance rate of up to 95% (3). Reports suggest that the recurrence rate of CBDS following endoscopic treatment ranges from 4% to 25% (4).

Even after cholecystectomy, stones may recur, with biliary stasis and gallbladder bacteria implicated as the primary culprits for CBDS recurrence. While dilated common bile ducts, large or multiple stones, and the presence of periampullary diverticulum (PAD) have been proposed as predictors of CBDS recurrence after endoscopic stone removal (5,6), consistent definitions remain elusive due to study design variations. Referred

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to as a belated complication after successful ERCP and biliary tract stone extraction, CBDS recurrence has spurred essential research into the identification of its predictors. Several studies (7-9) have consistently underscored specific factors associated with heightened recurrence probabilities. For instance, an enlarged common bile duct increases the risk because of its potential to harbor residual stones or facilitate stone reformation. Larger stones, which are more laborious to completely extract during the initial procedure, can lead to recurrence. Correspondingly, the presence of multiple stones and PAD has been associated with elevated recurrence risk (8-10). These collective findings substantiate the pivotal role of these predictors in shaping CBDS recurrence following endoscopic stone removal procedures.

We aimed to assess the recurrence rate of symptomatic CBDS in patients who have undergone ERCP and EST for CBDS while also examining the associated factors.

Methods

Compliance with Ethical Standards

Our study received authorization from the University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital Ethics Committee (protocol no: 166, date: 07.04.2023) and adhered to the Declaration of Helsinki. Informed consent was secured from each participant.

Study Design

This study adopts a cross-sectional design, with data sourced from the University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital database covering the years 2019 to 2022. EST and stone extraction were performed on 271 patients diagnosed with gallstones and established CBDS. The CBDS diagnosis was validated using magnetic resonance cholangiopancreatography, or ERCP. The inclusion criteria encompassed patients with biliary stones who had not previously undergone ERCP treatment. Stone number, diameter, and CBD diameter were confirmed by fluoroscopic imaging. EST was performed on all 271 patients, and as appropriate, CBD clearance was achieved using a balloon or basket. The confirmation of PAD presence was based on duodenoscopy images. Only patients in whom CBD was entirely and successfully cleared of stones were considered for the study. Patients with CBD strictures, periampullary and biliary tract cancer, intrahepatic duct stones, or CBDS identified via cholangiography were excluded. Recurrent CBDS, defined as occurrences at least 6 months after endoscopic extraction (11,12), were tracked along with symptomatic recurrences and cholecystectomy history during follow-up.

Statistical Analysis

The data obtained were subjected to analysis using SPSS 15.0 (Statistical Package for Social Sciences). Descriptive statistics were employed, expressing the data as the mean and standard deviation. The measurement parameter's normal distribution was verified using the "Kolmogorov-Smirnov test". For group comparisons, the "Independent groups t-test" was used for parametric data, whereas the "Mann-Whitney U test" addressed non-parametric data. Qualitative data comparisons employed the Pearson chi-square test. A p-value of ≤0.05 was deemed significant, with a confidence interval of 95%.

Results

A total of 271 patients who had not undergone any previous procedure and were treated with ERCP + EST because of choledocholithiasis during the study period were included in the study (Table 1). There were 159 female patients (59%) and 112 male patients (41%) with a female-to-male ratio of 1.4:1. The median age of the patients during the first ERCP (index ERCP) was 63.6±17.2 years. CBDS recurrence was observed in 25 patients (9.2%) at least 6 months after endoscopic treatment.

Clinical indicators of CBDS recurrence exhibited variability (Figure 1), encompassing pain (96%), jaundice

Table 1. Parameters associated with recurrent choledocholithiasis

	Non-recurrent CBDS	Recurrent CBDS (%)
Patients	246	25 (9.2)
Gender (male/female)	101/145	11/14
Age (mean ± SD, years)	63.6±17.2	65.2±15.6

CBD: Common bile duct, CBDS: Common bile duct stone, ERCP: Endoscopic retrograde cholangiopancreatography, EST: Endoscopic sphincterotomy, SD: Standard deviation

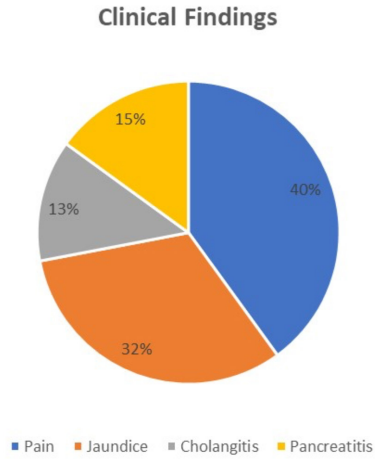

Figure 1. Clinical findings of recurrent choledocholithiasis

(76%), pancreatitis (36%), cholangitis (24%), or a combination thereof. Pain and jaundice were the most frequent clinical manifestations. Parameters linked to recurrent choledocholithiasis were meticulously assessed (Table 2).

Upon comprehensive evaluation of all patients who underwent ERCP + EST, those with recurrent CBDS showcased a broader common bile duct (7.5±4.5 mm vs 13±1.7 mm, p=0.037). Furthermore, recurrent choledocholithiasis was notably prevalent in individuals with a common bile duct diameter of 1.5 cm or more (3% vs 48%, p=0.00001). A similar pattern was observed with larger choledocholithiasis stone sizes, which correlated with an elevated occurrence of recurrent choledocholithiasis (7.3±6.5 mm vs 13.5±4.3 mm, p=0.04). Patients with PAD exhibited heightened susceptibility to recurrent choledocholithiasis (23% vs 44%, p=0.013). The mean interval between the index ERCP + ES and stone recurrence was 18.273±2.021 months. Notably, the recurrence rate showed no significant difference between patients harboring two or more CBDS and those with a solitary stone (41% vs 44%, p=0.35). Among patients who experienced recurrent stones post-index ERCP + ES, 8% had undergone cholecystectomy.

Discussion

ERCP, in conjunction with EST, is internationally acknowledged as the primary approach for the extraction of CBDS due to its minimally invasive nature. While ERCP is a highly effective and safe non-surgical intervention, complications, whether minor or major, can still manifest. A notable delayed complication of EST is the recurrence of CBDS (13). Recurrence rates following ERCP typically vary between 2-22% (12,14). However, a challenge arises when recurrent CBDS appear six months or more after ERCP, introducing complexities for medical practitioners. Despite diverse reports on the recurrence rate of choledocholithiasis post-ERCP, statistics often oscillate between 4% and 24%. Nevertheless, the connection between these risk factors and optimal therapeutic strategies remains enigmatic. Previous observational studies that evaluated patients post-EST have highlighted risk factors for recurring bile duct stones, yet their association with recommended treatments lacks clarity. These risk factors, such as multiple CBDS, larger stone sizes (exceeding 1 cm), and concurrent balloon dilation or stent insertion during ERCP, can be considered moderate risk predictors for primary CBD stone recurrence (11,15).

Table 2. Parameters associated with recurrent choledocholithiasis

Factors	Non-recurrent CBDS 246 (%)	Recurrent CBDS 25 (%)	P-value
PAD	56 (23)	11 (44)*	0.013ᵗ
CBD Diameter (mean ± SD, mm)	7.5±4.5	13±1.7*	0.037ᵗ
CBD Diameter ³1.5 cm	7 (3)	12 (48)*	0.0000ᵗ
Number of CBDS ³2	100 (41)	11 (44)	0.35ᵗ
Widest diameter of CBDS, mean ± SD (mm)	7.3±6.5	13.5±4.3*	0.04ᵗ
Recurrence time, mean ± SD (months)	-	18.273±2.021	-
Cholecystectomy	-	2 (8)	-

*p≤0.05, ᵗStudent's t-test
CBD: Common bile duct, CBDS: CBD stone, ERCP: Endoscopic retrograde cholangiopancreatography, EST: Endoscopic sphincterotomy, PAD: Periampullary diverticulum, SD: Standard deviation

In line with existing literature, our study revealed a recurrence rate of choledocholithiasis of 9.2% following ERCP and EST. Notably, stone size, CBD dilation, and the presence of a PAD emerged as risk factors for stone recurrence during the initial assessment. Intriguingly, a CBD diameter exceeding 1.5 cm was identified as a risk factor for recurrence. The precise mechanism behind CBD dilation remains uncertain; a reduction in bile hydrostatic force and disruption of normal CBD motility may render patients more susceptible to recurring stone formation (16). While CBD diameter is already acknowledged as a risk factor for CBD stone recurrence, a definitive "cut-off" diameter remains undefined, as various diameters correlate with distinct recurrence rates. For instance, Pereira Lima et al. (17) demonstrated that patients with a CBD diameter of 15 mm or more faced a four-fold higher risk of recurrence compared to those with a diameter of 10 mm or less. Patients with a CBD diameter ≥15 mm exhibited a recurrence risk of 46%, whereas those with a diameter ≤12 mm exhibited a 20% risk (5). Numerous studies underscore the significant correlation between CBD diameter and CBDS recurrence (4,6,18,19). There is consensus that a CBD diameter ≥15 mm signifies a high-risk factor for recurrent CBDS.

PAD and dilated bile ducts devoid of residual obstruction present challenging risk factors. PAD could potentially contribute to cholangitis and recurrent biliary stone formation (14,20). The presence of a diverticulum in the bile duct is believed to impede the canal or sphincter, leading to slower biliary emptying compared to those without PAD. This delay likely contributes to recurring bile duct stone formation, as evidenced in the literature (20). Our study, akin to prior literature, included patients with PAD, revealing a substantial recurrence rate of typical choledochal stones within the periampullary duodenum. Although the precise mechanism within the diverticulum remains elusive, both stone formation

and CBDS recurrence are evident, establishing PAD as a significant risk factor (21,22).

Literature has long examined the correlation between the number and size of stones in the biliary tract. The prevailing theory suggests an escalated risk of CBDS recurrence with larger stone diameters and increased stone numbers (6,14). For instance, Deng et al. (6) found that a stone diameter below 10 mm is an independent risk factor for recurrence. In congruence with this, our study also underscores that patients with larger stone diameters are more predisposed to recurrent CBDS. However, stone quantity and recurrence didn't exhibit statistical significance. Furthermore, research suggests that having over two stones is a noteworthy risk factor for CBDS recurrence (18).

Recurrence of CBDS may sometimes be asymptomatic, occasionally detected during assessments or radiological evaluations unrelated to the issue. Yet, symptomatic CBDS presents with cholangitis, severe pancreatitis, obstructive jaundice, or biliary colic (23). Our study reveals an escalating prevalence of recurrent choledochal stones associated with discomfort, jaundice, pancreatitis, cholangitis, or a combination of these symptoms. Among these, pain and jaundice were the most frequent. Various studies have established links between endoscopic or surgical treatments for choledocholithiasis and factors like bacterial infection, abnormal biliary anatomy, inflammation, and other related variables.

Study Limitations

Our study has some limitations. The cross-sectional design hinders the establishment of causal relationships between the identified factors and recurrent choledocholithiasis. A single-center study may introduce selection bias and limit generalizability. The relatively short follow-up period may underestimate the true recurrence rate, and retrospective data collection may result in incomplete information. However, the study's substantial sample size, comprehensive assessment of various risk factors, and focus on clinically relevant outcomes enhance its value in elucidating factors influencing choledocholithiasis recurrence after ERCP + ES procedures

Conclusion

The risk factors contributing to recurrent choledocholithiasis remain partially understood and exhibit variation across different studies. Nonetheless, it is theoretically feasible to identify patients at significantly heightened risk of stone recurrence, enabling more vigilant monitoring, early intervention, and potential preventive measures. This strategic approach holds promise for mitigating the occurrence of delayed complications and recurrent stones. Notably, complications, specifically the potential for bile duct stone recurrence following endoscopic stone removal and routine bile duct clearance, may arise. The initial manifestation of stones and anatomical attributes such as choledochal diameter and the presence of PAD appear to correlate with stone characteristics encompassing size and count.

Ethics

Ethics Committee Approval: Our study received authorization from the University of Health Sciences Turkey, Istanbul Haseki Training and Research Hospital Ethics Committee (protocol no: 166, date: 07.04.2023) and adhered to the Declaration of Helsinki.

Informed Consent: Informed consent was secured from each participant.

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Authorship Contributions

Surgical and Medical Practices: N.D., B.Y., Concept: N.D., B.Y., Design: N.D., B.Y., Data Collection or Processing: N.D., Analysis or Interpretation: N.D., B.Y., Literature Search: N.D., B.Y., Writing: N.D., B.Y.

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