



## **Risk Factors of Stone Recurrence after Endoscopic Retrograde Cholangiopancreatography for Common Bile Duct Stones**

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**Abstract**

**Background:** Endoscopic retrograde cholangiopancreatography (ERCP) is now the gold standard for the treatment of bile duct stones. However, recurrence stones is frequent after their complete removal by endoscopic treatment.

The aim of our study is to identify predictors of recurrent common bile duct (CBD) stones after ERCP

**Materials and methods:** The present study is retrospective, descriptive and analytic, including all patients who underwent ERCP for CBD stones between January 2008 and September 2023. Recurrent CBD stone was defined as the finding of a stone at least 6 months after the initial ERCP in which complete stone extraction was performed. Factors associated with recurrent CBD stones were studied by logistic regression analysis. Statistical analysis was performed using Jamovi software.

**Results:** Among 1151 patients who underwent ERCP for lithiasis pathology, 88 patients or 7.7% had recurrent CBD stone. Mean age of the patients was 64.5 +/-13.4 years, with extremes ranging from 22 to 94 years. Sex ratio (M/F) was 0.69, with a female predominance of 59.1%. A periampullary diverticulum was found in 5.7% of patients (n=5). In univariate analysis, the risk factors for recurrent CBD stone were: older age (OR :9,9 ;IC95% : [4,49-22,04]; p<0,001), CBD diameter > 15 mm (OR : 7,36 ;IC95% : [5,51-9,8] ; p<0,001), presence of cholangitis ( OR : 2.06 ;IC95% : [1,12-3,8]; p=0,02), number of CBD stones (OR :8,61; IC95% : [6,51-11,39]; p=0,018), size of CBD stones (OR :2,51 ;IC95% : [1,43-4,39] ; p=0,001), while enlargement EST (OR :0,18; IC95% : [0,08-0,44] ; p<0,001) was a protective factor. After multivariate analysis, and adjusting for the factors studied, only older age (OR:1.96; CI95%: [1.94-2.93]; p=0.001), number of CBD stones (OR: 1.99; CI95%: [1,2-3,4]; p=0,037) and size of CBD stones (OR :4,06; IC95% : [3,51-6,72]; p=0,003) were risk factors, and enlargement EST (OR :0,31; IC95% : [0,11-0,85]; p=0,024) was protective factor.

**Conclusion:** In our study, the predictive factors for recurrent CBD stones were advanced age, the presence of impaction and a large stone.

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## Introduction

Common bile duct (CBD) stones are the most common biliary tract diseases. CBD stones may result in severe and life-threatening conditions including pancreatitis, cholangitis and sepsis which can deteriorate to death [1]. Endoscopic retrograde cholangiopancreatography (ERCP) is currently the most commonly used and preferred method for definitive treatment of CBD stones, as endoscopic sphincterotomy (EST) followed by stone extraction with balloon or basket has been used traditionally as a standard technique [2]

Although ERCP is a well-established and highly efficacious modality for definitive bile duct stones removal, with complete stones clearance rate reaching 92%– 100% [3], recurrent CBD stones after endoscopic clearance by the standard techniques is a well-known sequel of ERCP, which is defined by stones detected more than 6 months following the index ERCP [4,5], encountered in almost 10% of patients [6]. Other study reported a recurrence rate ranging from 4% to 24%, when the recurrence interval was up to 15 years period [7].

Furthermore, there are several factors associated with the CBD stones recurrence. In general, the cause of recurrence of CBDS after ERCP is caused by many factors [8-11]. How to prevent and reduce the recurrence of CBDS after ERCP has become the focus of hepatobiliary surgeons.

The aim of our study is to explore the recurrence rate and related risk factors of ERCP in patients with CBD stones, so as to provide reference for reducing the recurrence rate of CBD stones after ERCP.

## Materials And Methods

### Patients data inclusion and exclusion criteria

A retrospective case control study was conducted on 1151 patients who underwent ERCP for documented CBD stone at Endoscopic department of Mohamed V Military Hospital, Rabat, Morocco from January 2008 to September 2023.

Inclusion criteria were: 1) patients who were older than 18 years of age, 2) diagnosed with CBD stone by radiological modalities, 3) underwent ERCP procedure including EST plus stone extraction and (4) with complete clearance for CBD as defined by normal cholangiogram performed after stone extraction.

Exclusion criteria included: (1) a prior history of ERCP, (2) patients with biliary or duodena malignancy, (3) patients with CBD stenosis, (4) biliary stent placement and (5) patient with incomplete stone clearance at the

index ERCP procedure.

Diagnostic criteria for CBD stones recurrence [4,12-14] diagnosed with CBD stones more than six months after endoscopic stone retraction by ultrasound, computed tomography (CT), magnetic resonance imaging (MRI), magnetic resonance cholangiopancreatography (MRCP) or ERCP.

### **ERCP procedure:**

ERCP was performed with intubation. The procedures were performed using a side-viewing duodenoscopic system (Olympus or Pentax) and synchronous imaging techniques were used to confirm the location of the bile duct. Prophylactic antibiotics were routinely administered to all patients before ERCP.

The initial procedure was the classic approach using a standard sphincterotome and guidewire for patients with a normal appearing papilla. If cannulation could not be performed, the needle precut technique was applied. After cannulation of common bile duct, the procedure to apply is EST. Following EST, the guidewire is detected by cholangiography in common bile duct, which is visualized by administering a contrast product, then the intraluminal stones are removed using an endoscopic basket or endoscopic balloon. Our standard practice is to use a balloon to remove CBD stones, but for stones larger than 1 cm, we use basket. In addition, if it is impossible to extract the stone through the papilla, we perform mechanical lithotripsy or endoscopic balloon dilatation of the papilla. Finally, cholangiography was performed to ensure that there were no stones in the lumen.

### **Follow up Evaluation:**

After the endoscopic removal of CBD stones, patients were referred for follow-up one month later with liver test and abdominal ultrasound examination. If stones were present in the gallbladders, laparoscopic cholecystectomy was planned. All patients were evaluated every three months for one year. After that, according to the condition of patients' follow-up, blood biochemistry and abdominal ultrasound were performed once every 6 months. If the patient has jaundice, abdominal pain and other symptoms, abdominal ultrasound, CT and MRCP should be performed to confirm the diagnosis of CBD stones recurrence, and ERCP should be performed again in hospital

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**Data collection:**

All medical records of eligible patients were reviewed and the following parameters were collected: Demographic data (age, sex and medical history), ERCP indication (biliary pancreatitis, cholangitis or abnormal cholestatic liver enzymes) and morphological data (presence of a stone on abdominal CT, MRI or EUS).

Endoscopic findings, including the presence of periampullary diverticulum, ERCP interventions for stone extraction, as well as cholangiography findings (size and number of CBD stones, size of CBD, presence of biliary stricture) were extracted from the endoscopy reports.

**Statistical analysis**

Data were analyzed using JAMOVI software. Continuous variables that followed a normal distribution were expressed as the mean  $\pm$  SD; those that didn't were expressed as the median (lower quartile, upper quartile). Categorical variables were presented as counts and percentages.  $p < 0.05$  was considered statistically significant. Statistical significance was set at  $P < .05$ . In the determination of recurrent risk factors, logistic regression analysis, a binary logistics method, was used to calculate odds ratios (ORs) with a 95% confidence interval.

**Results****Demographics, clinical and endoscopic characteristics**

According to the exclusion and inclusion criteria, from January 2008 to September 2023, a total of 1151 patients underwent ERCP treatment in our hospital due to CBD stones. According to the diagnostic criteria of recurrence of CBD stones, 88 patients had recurrence of CBD stones, the recurrence rate was 7,7%.

The mean age was 64.5  $\pm$  13.4 years (range 22-94 year), the predominant age range was 50 to 59 (Figure1). Sex ratio (M/F) was 0.69, with a female predominance of 59.1%.

Clinical characteristics during the study period are summarized in Table 1.

Periampullary diverticulum was detected in 5 (5,7%) patients, With regard to cholangiographic findings, 31 patients (37,8%) had multiple CBD stones. 22 patients (26,8%) had large CBD stones. The median common bile duct diameter of the patients was 15 (12-17) mm. 7.3% of patients presented with CBD stricture.

The most common endoscopic intervention for stone removal was balloon extraction (67,1%) Interestingly, endoscopic papillary balloon dilation was performed in 12,2% of patients, while mechanical lithotripsy was performed in 11%. 4.9% of patients needed biliary stents.

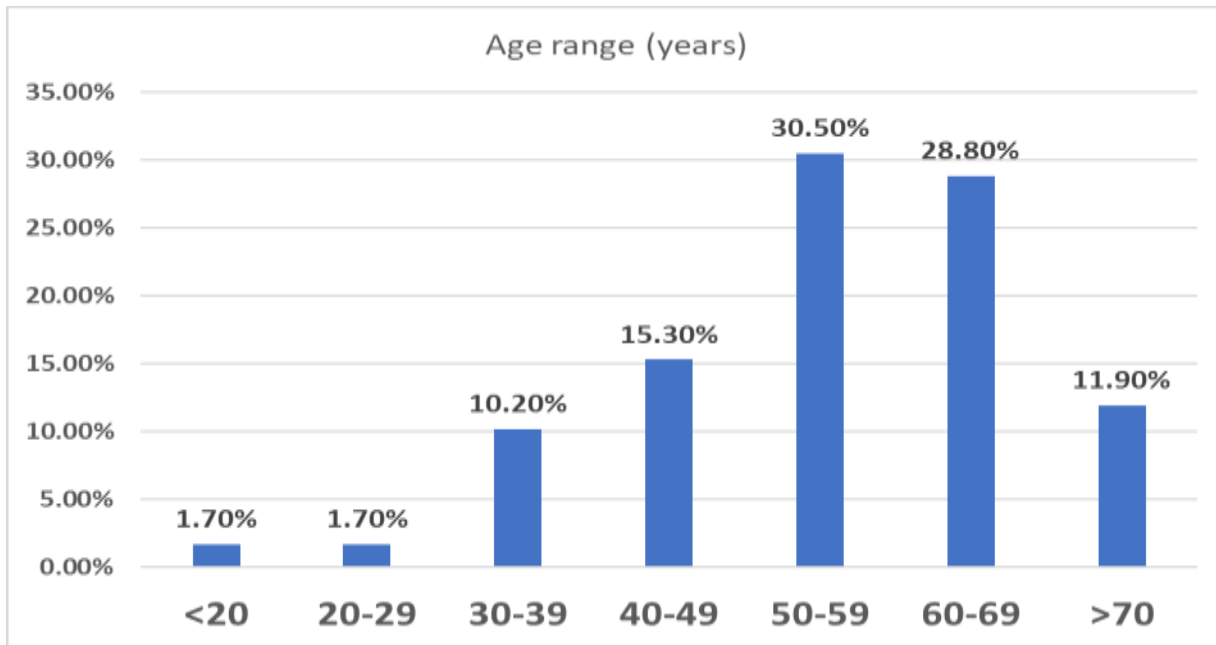


Figure 1: Patient distribution by age group

Table 1: Demographic and clinical characteristics of study population

Characteristics	Values (n=1151)
Age (years) <sup>o</sup>	64,5 ±13,4
Sex *	
Male	35 (42,7)
Female	47 (57,3)
Clinical presentation*	
Cholangitis	18 (22)
Pancreatitis	6 (7,3)

Mean +/-SD

\* Counts (percentages)

### Univariate and multivariate regression analysis

In univariate analysis, the risk factors for recurrent CBD stone were: older age (OR :37; IC95% : [10,7-127,2] ; p<0,001), female gender ( OR :9,9 ;IC95% : [4,49-22,04] ; p<0,001), CBD diameter > 15 mm (OR : 7,36 ;IC95% : [5,51-9,8] ; p<0,001), presence of cholangitis( OR : 2.06 ;IC95% : [1,12-3,8] ; p=0,02), number of CBD stones (OR :8,61; IC95% : [6,51-11,39] ; p=0,018), size of CBD stones (OR :2,51 ;IC95% : [1,43-4,39] ; p=0,001), while enlargement EST (OR :0,18; IC95% : [0,08-0,44] ; p<0,001) was a protective factor.

After multivariate analysis, and adjusting for the factors studied, only older age (OR:1.96; CI95%: [1.94-2.93]; p=0.001), number of CBD stones (OR: 1.99; CI95%: [1,2-3,4] ; p=0,037) and size of CBD stones (OR :4,06; IC95% : [3,51-6,72] ; p=0,003) were risk factors, and enlargement EST (OR :0,31; IC95% : [0,11-0,85] ; p=0,024) was protective factor. (Table 2)

**Table 2: Univariate and multivariate analyses of parameters associated with recurrent CBD stone.**

Variables	Univariate			Multivariate		
	OR	IC	p	OR	IC	p
Age	37	[10,7-127,2]	<0,001	1,96	[1.94-2.93]	0,001
Femal gender	9,9	[4,49-22,04]	<0,001			
Cholangitis	2,06	[1,12-3,8]	0,002			
CBD > 15 mm	7,36	[5,51-9,8]	<0,001			
Number of CBD stones	8,61	[6,51-11,39]	0,018	1,99	[1,2-3,4]	0,037

<b>size of CBD stones enlargement EST</b>	4,06	[3,51-6,72]	<b>0,003</b>	4,06	[3,51-6,72]	<b>0,003</b>
	0,31	[0,11-0,85]	<b>0,024</b>	0,31	[0,11-0,85]	<b>0,024</b>

## Discussion

ERCP represents treatment modality of choice for CBD stone removal. However, CBDs are likely to recur within 6 months of ERCP treatment, which has become a difficult problem for clinicians.

The recurrence rate of CBD stones in our study was 7.7%, similar to previous retrospective studies reporting a recurrence rate between 2% and 22% [15]. Therefore, investigating risk factors for CBD stone recurrence after ERCP is an important measure to reduce the recurrence of stones after ERCP.

Several studies reported advanced age as a risk factor for recurrence of CBD stones after endoscopic treatment [16,17]. This association is mainly related to the increase gallstone formation with age [1]., lack of physical activity and greasy diet in elderly patients, as well as decreased duodenal papillary sphincter function with age, bile duct wall tension and insufficient bile duct motility, and poor bile drainage [17].

Women are more susceptible to cholelithiasis, associated with increased estrogen levels and reduced exercise. Reductions in gallbladder muscle contraction retard cholestasis and contribute to cholesterol crystal formation. However, several studies demonstrate that there was no significant association between gender and recurrence of CBD stones. This finding was similar to that reported in the present study [18,19].

Previous studies have suggested that multiple stones ( $\geq 2$ ) are risk factors for CBD stones recurrence after ERCP [9,20-22]. In this study, we found that multiple stones are independent risk factors for the recurrence of CBD stones after ERCP. This may be explained by the fact that multiple stones mechanically damage the duodenal sphincter, leading to its dysfunction. Eventually, pressure in the bile duct decreases, and intestinal bacteria and contents easily return to the common bile duct, ultimately leading to stone recurrence [17].

Large stones cause further dilatation of the bile ducts and impair their function, leading to difficulties in bile excretion and can easily cause cholestasis and bacterial infections [23]. In our study, mean stone size was not a risk factor for recurrence.



Studies suggest that the recurrence rate of CBD stones after ERCP is 19.5% when CBD diameter > 15 mm compared with 4.9% when CBD diameter is < 10 mm [24,25]. The possible reason is that the dilated bile duct has a dysfunction, leading to poor bile drainage and cholestasis. At the same time, secondary bacterial infections also provide the core of stone formation [17]. In this study, we found that CBD diameter > 15 mm was a risk factor in univariate analysis, but was not statistically significant in multivariate analysis.

The prevalence of peri-ampullary diverticula in general population is about 20%. The existence of a peri-ampullary diverticulum is related to the recurrence of CBD stones after ERCP [26], which may be related to mechanical compression of the peri-ampullary diverticulum and secondary infection of residual food in the diverticulum, leading to biliary obstruction and accelerating choledocholithiasis formation. In our study, a peri-ampullary diverticulum was detected in 5.7% of our patients, and unlike other studies, was not a risk factor for recurrence of CBDs.

In a retrospective study conducted in 2021, they might postulate that the size of EST could affect the efficacy of balloon and basket in complete stone extraction. However, as ERCP examinations were performed by an experienced gastroenterologist with a high volume of procedures, it can be assumed that EST is uniform across the patient cohort (including patients whose stones were removed by balloon or basket) and that variation in EST size was negligible [27]. In our study, EST enlargement was a protective factor against CBD recurrence.

Although patients' clinical data were analyzed in detail and risk factors for CBDS recurrence after ERCP were thoroughly investigated, this retrospective study still has limitations. First, it is a retrospective study conducted at a single institution. Second, although we included a large number of patients in the entire cohort, the sample size of patients with recurrent CBD stones is relatively small. Third, we did not analyze the composition of the stone.

In conclusion, in our cohort the prevalence of CBD stone recurrence after ERCP and stone removal was 7,7%. Interestingly, we could, by multivariate analysis, identify both risk and protective factors for CBD stone recurrence. In our study, the predictive factors for recurrent CBD stones were advanced age, presence of impaction and a large stone and enlargement EST was protective factor. Further studies on larger cohort of patients are warranted to confirm our results.

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