

# Evaluation of the Causes for Repeated Endoscopic Retrograde Cholangiopancreatography in the Early Period

## Erken Dönemde Tekrarlayan Endoskopik Retrograd Kolanjiyopankreatografi Nedenlerinin Değerlendirilmesi

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### ABSTRACT

**Objective:** Endoscopic retrograde cholangiopancreatography (ERCP) is the most important invasive endoscopic procedure for the clearance of bile duct stones. Several factors may interfere with a positive outcome in the first attempt. It is important for the endoscopist and the patient to predict under which circumstances repeated intervention may be required. The aim of this study was to determine the conditions in which the need for repeated ERCP increases in patients who have undergone ERCP for bile duct stones.

**Methods:** Data collected from the procedures performed by a single endoscopist between 2005 and 2020 were analyzed retrospectively. The findings obtained from 100 cases whose bile duct stones were cleared in a single procedure were compared with those of 100 cases who required repeated ERCP in the early period. The demographic findings of the patients, laboratory examinations, difficulty of common bile duct (CBD) stones, clinical manifestation of cholangitis, anatomical and pathological conditions of the patients, factors that complicated the ERCP procedure, and consequently the effect of these factors on post-ERCP complications were investigated in both groups.

**Results:** According to the results of this study, the diameter of the CBD and the number of stones increased in elderly patients. On the other hand, the presence of stenosis, enclaved stones in the CBD, and accompanying pancreatitis increased the need for repeated ERCP in young patients. In the prediction of single and repeated ERCP using the univariate model, a significant association ( $p<0.05$ ) was observed between post-ERCP complications and age, white blood cell count, aspartate aminotransferase (AST), alanine aminotransferase, total bilirubin, direct bilirubin, width, angulation, and shape of the CBD, fever and chills, biliary pancreatitis, cholangitis, and difficult stones. In the prediction of single and repeated ERCP using the multivariate model, a significant association ( $p<0.05$ ) was observed between post-ERCP complications and AST, fever and chills, biliary pancreatitis, and difficult stones.

**Conclusion:** The need for stenting was higher in both age groups when cholangitis was present. The success rate of ERCP was not affected by a single factor, but by all clinical and pathological factors that increase the difficulty of the procedure.

**Keywords:** Bile duct angulation, cholangitis, choledocholithiasis, common bile duct stones, difficult common bile duct stones, ERCP, pancreatitis, pre-cut sphincterotomy, repeated ERCP, suppurative cholangitis

### ÖZ

**Amaç:** Bu çalışmanın amacı koledok taşı ön tanısıyla endoskopik retrograd kolanjiyopankreatografi (ERCP) işlemi yapılan hastalarda tekrarlayıcı ERCP gereksiniminin hangi durumlarda arttığına ortaya konmasıdır.

**Yöntemler:** 2005-2020 yılları arasında tek cerrahi endoskopiste ait veriler retrospektif olarak irdelendi. Tek seansta safra kanalı taşları temizlenen 100 olguyla erken dönemde ERCP tekrarı gereken diğer 100 olguya ait bulgular karşılaştırıldı. Hastaların demografik bulguları, laboratuvar incelemeleri, koledok taşlarının zorluğu, kolanjit tabloları, hastalara ait anatomik ve patolojik durumlar, ERCP işlemini zorlaştıran faktörler ve sonuç olarak her iki grupta bu sonuçların post-ERCP komplikasyonlarına etkisi araştırıldı.

**Bulgular:** ERCP ile safra kanalı taşlarının temizlenmesi en önemli invaziv endoskopik girişimdir. Bu işlemle bilindiği gibi birçok nedenden dolayı tek bir girişimde sonuç almak mümkün olmamaktadır. Bu durumun hangi durumlarda tekrar edebileceğinin tahmin edilebilmesi endoskopist ve hastalar

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için önemlidir. Bu çalışmanın sonuçlarına göre ileriki yaşlarda koledok çapı genişliği ve taş sayısı artmaktadır. Genç hastalarda ise dar koledok, anklave taşlar ve bu tabloya eşlik eden pankreatit durumlarında tekrarlayıcı ERCP olasılığının daha fazla olduğu görülmektedir. Her iki yaş grubunda bu tablolara eşlik eden kolanjit tablosunda stent koyma ihtiyacı daha fazladır. ERCP'de başarıyı tek bir faktör değil işlem zorluğunu artıran tüm klinik ve patolojik faktörler etkilemektedir.

**Sonuç:** Klinik olarak kolanjitin eşlik ettiği durumlarda her iki yaş grubunda stentleme ihtiyacı daha yüksekti. ERCP'nin başarı oranı tek bir faktörden değil, işlemin zorluğunu artıran tüm klinik ve patolojik faktörlerden etkilenmektedir.

**Anahtar kelimeler:** Safra yolu açılanması, kolanjit, koledok taşı, birleşik safra kanalı taşı, zor safra yolu taşları, ERCP, pankreatit, precut sfinkterotomi, tekrarlayıcı ERCP, süpüratif kolanjit

## INTRODUCTION

Despite it being the gold standard for the treatment of choledochal stones, clearance of the common bile duct (CBD) stones with endoscopic retrograde cholangiopancreatography (ERCP) may not be successful in the first attempt in some patients. Although gallstones are prevalent in 15-20% of the general population, the prevalence of the choledochal stones observed concomitantly with gallstones is reported to be 3-10% in the literature (1-7). In addition to clinical evaluation, advanced imaging methods, such as ultrasonography (USG), magnetic resonance cholangiopancreatography (MRCP), and endoscopic ultrasonography (EUS) are diagnostic modalities used to diagnose bile duct stones. With a success rate of 90%, MRCP is the most accurate imaging method (6,8). The invasive ERCP procedure is widely replaced by MRCP and EUS as a diagnostic tool and is predominantly used for treatment purposes in current practice (9). The failure rate of selective CBD cannulation in ERCP varies between 5 and 15% (5,10,11). Advanced endoscopic, surgical, and percutaneous techniques may be indicated in the presence of CBD stones which cannot be removed with a standard ERCP intervention and in cases with altered biliary anatomy (6,9).

The incidence rate of CBD stones is currently increasing with advanced age due to the increasing average age and changes in food habits (5,11,12). In this age group, the prevalence of stones which cannot be cleared with a single attempt has also been increasing. In many patients, stenting is required to prevent prolonged ERCP procedure risks resulting from anatomical difficulties, such as juxtapapillary diverticulum, difficult CBD stones, and increased frequency of cholangitis. The success rate of repeated ERCP interventions were reported to be higher with more satisfactory results being achieved (6,7,13,14). The aim of this study was to determine the conditions in which the need for repeated ERCP increases in patients who have undergone ERCP for bile duct stones.

## METHODS

In this study, the files of patients who had undergone ERCP by the same endoscopist in different health institutions for CBD stones between 2005 and 2020 were retrospectively reviewed. The patients were evaluated according to age, gender, pre-procedural laboratory tests, imaging methods, anatomopathological conditions, bile duct factors, and stone conditions. Pre-procedural complaints (pain, icterus, fever, and chills), cholangitis,

and a history of biliary pancreatitis were investigated to evaluate whether they had any effect on repeated ERCP.

All laboratory tests related to biliary tract pathologies were performed. The differences between the laboratory tests of the two groups were investigated. Pre-procedural USG and MRCP examinations were performed for the detection of CBD stones. In non-emergency situations, the patients sent to our reference hospital were subjected to MRCP for a detailed detection of pancreatic and biliary tract pathologies. In patients with acute biliary pancreatitis, early ERCP was planned if findings of acute cholangitis were present, while in the absence of these findings, the procedure was delayed until the patient's general condition improved.

The condition of the papilla, presence of juxtapapillary diverticulum, appearance of the papilla, presence of very rarely observed findings of choledochoduodenal fistula, and cannulation success were defined. Needle-knife sphincterotomy was the method of choice in patients who were unsuitable for early selective cannulation, especially in the presence of papillary protrusion. However, if cannulation was not present, the procedure was suspended to be repeated. Contrast material was administered after confirming the selective cannulation of the CBD with a guidewire or through the aspiration of bile. In the endoscopic examination, the diameter of the CBD was determined using the image of the extrahepatic biliary tract axis, and the CBD angulation was measured. Extraction of stone/sludge/pus during the procedure was also investigated. The diameter and localization of the stones were recorded. Single stones >15 mm, multiple stones <15 mm, enclaved CBD stones, distal stenosis of the CBD, and stones requiring mechanical lithotripsy were considered as difficult CBD stones. Patients with choledochoduodenal fistula, T-tube *in situ*, or intraprocedural basket impaction were also included in this group. Patients with intrahepatic stones and modified anatomy were not included in this study. All these anatomopathological factors were evaluated in both groups. These factors may be summarized as the presence of juxtapapillary diverticulum, unsuccessful cannulation, and presence of pre-cut sphincterotomy and difficult CBD stones.

Endoscopic biliary stenting was performed in cases where adequate clearing of the stones could not be achieved despite prolongation of the procedure, especially in those with concomitant cholangitis. Our first choice was a 10-F

Amsterdam-type plastic stent. However, in patients with severe cholangitis, a dilated CBD, and multiple stones, we preferred a pigtail stent.

Procedural complications included inadequate ERCP, difficult CBD stones, residual stones, and cholangitis. Two groups were formed with 100 patients each, who were selected consecutively; the single ERCP group, in which the initial attempt of stone clearance was successful and repeated ERCP was not required in the early period, and the repeated ERCP group, in which a second procedure was required within a month of the initial procedure due to inadequate stone clearance, stenting, failed cannulation, or basket impaction.

### Statistical Analysis

Descriptive statistics of the data used the mean, standard deviation, median, minimum, maximum, frequency, and ratio values. The distribution of variables was determined with the Kolmogorov-Smirnov test. The independent-samples t-test and Mann-Whitney U test were used for the analysis of continuous independent data. The chi-square test was conducted for the analysis of categorical independent data, and Fisher's Exact test was used when the chi-square test criteria were not achieved. The effect levels of the factors were investigated with univariate and multivariate logistic regression analyses. SPSS v. 27.0 software package was used in all statistical analyses.

## RESULTS

Of the total 200 cases, 128 were female, and 72 were male. The age of patients in the repeated ERCP group were significantly higher ( $p < 0.05$ ) than that of patients in the single ERCP group (Table 1).

There was no significant difference in gender distribution between the repeated and single ERCP groups ( $p > 0.05$ ). Similarly, the rate of complaints in terms of pain, jaundice, and the presence of gallstones were not significantly different between the two groups ( $p > 0.05$ ). The repeated and single ERCP groups did not differ significantly in terms of the duration of complaints ( $p > 0.05$ ). The length of complaints did not differ with regard to the number of ERCPs (Table 2).

Compared to the single ERCP group, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were significantly higher in repeat ERCP group ( $p < 0.05$ ). The gamma glutamyl transferase, alkaline phosphatase, amylase, and indirect bilirubin levels showed a significant difference between the two groups ( $p < 0.05$ ). However, the repeated and single ERCP groups did not differ significantly in terms of the number of gallstones ( $p > 0.05$ ). Although juxtapapillary diverticulum was commonly observed in the repeated ERCP group, the difference was not significant between the groups (Table 2).

Compared to the single ERCP group, the presence of pre-procedural biliary pancreatitis and the prevalence of difficult CBD stones were significantly higher in the group with repeated ERCP ( $p < 0.05$  for both). Additional factors other than the size and

number of stones, including age, presence of fever and chills, biliary pancreatitis, cholangitis, white blood cell (WBC), AST, ALT, and total and direct bilirubin levels were also increased with the difficulty of the procedure ( $p < 0.05$ ) (Table 2).

Similarly, when we compared the two groups according to the anatomical structure of the biliary system and disease-related variables, the width of the CBD and the number of V-type CBDs were significantly higher in the repeated ERCP group than in the single ERCP group ( $p < 0.05$ ). Moreover, CBD angulation was significantly smaller in the repeated ERCP group compared to that in the single ERCP group ( $p < 0.05$ ) (Table 3).

The single and repeated ERCP groups did not show a significant difference in terms of the intraprocedural complications ( $p > 0.05$ ). Intraprocedural and post-ERCP complications are presented in Table 3. During the procedure, only 14 of the 200 patients had minimal hemorrhage that did not require blood transfusion. The

**Table 1. Demographic status, complaints, blood test results, and the number of ERCPs of the sample**

		Mean $\pm$ SD/n-%
Age		61.1 $\pm$ 16.5
Gender	Female	128/64.0%
	Male	72/36.0%
<b>Complaint</b>		
Pain		194/97.0%
Jaundice		142/71.0%
Fever-chills		62/31.0%
Biliary pancreatitis		55/27.5%
Cholangitis		118/59.0%
Gallstone		136/68.0%
Duration of complaint		16.8 $\pm$ 28.4
WBC ( $\mu\text{L} \times 10^3$ )		10.6 $\pm$ 4.1
AST (U/L)		211.1 $\pm$ 219.3
ALT (U/L)		271.9 $\pm$ 226.4
GGT (U/L)		521.6 $\pm$ 381.1
ALP (U/L)		453.8 $\pm$ 323.2
Amylase (U/L)		343.6 $\pm$ 685.3
Total bilirubin mg/dL		5.5 $\pm$ 4.1
Direct bilirubin mg/dL		4.1 $\pm$ 3.3
Indirect bilirubin mg/dL		1.4 $\pm$ 1.5
Number of ERCPs	1	100/50.0%
	2	73/36.5%
	3	24/12.0%
	4	2/1.0%
	5	1/0.5%

SD: standard deviation, WBC: white blood cell, AST: aspartate aminotransferase, ALT: alanine aminotransferase, GGT: gamma glutamyl transferase, ALP: alkaline phosphatase, ERCP: endoscopic retrograde cholangiopancreatography

cases that developed hemorrhage were managed using balloon tamponade and injection control. Basket impaction developed in three of our patients, of whom two were treated endoscopically and one was treated by open surgery.

The complication rate was significantly higher in the repeated ERCP group than in the single ERCP group ( $p < 0.05$ ) (Table 3). Post-procedural pancreatitis was detected in a patient of the single ERCP group and in five cases of the repeated ERCP group. In addition, the repeated ERCP group comprised 16 patients who developed cholangitis requiring temporary or early ERCP intervention. However, mortality was not observed in these patients.

Imaging performed under endoscopy generally revealed three different types of CBD courses. The straight course was mainly seen in the young patients with a smaller number of stones, V-type angulation was observed in 71 patients, and the S-type CBD course was predominantly observed in elderly patients with larger and more stones (Table 4).

In the prediction of single and repeated ERCP using the univariate model, a significant association was observed between post-

ERCP complications and age, WBC, AST, ALT, total bilirubin, direct bilirubin, width of CBD, angulation of CBD, fever and chills, biliary pancreatitis, cholangitis, difficult stones, and shape of the CBD ( $p < 0.05$ ). In the prediction of single and repeated ERCP using the multivariate model, there was a significant association between post-ERCP complications and AST, fever and chills, biliary pancreatitis, and the presence of difficult stones ( $p < 0.05$ ) (Table 5).

**Table 2. Comparison of demographic status, complaints, and blood test results of the single and repeated ERCP groups**

		Single ERCP	Repeated ERCP	p
		Mean $\pm$ SD/ n-%	Mean $\pm$ SD/ n-%	
Age		57.8 $\pm$ 17.5	64.4 $\pm$ 14.9	0.007 <sup>m</sup>
Gender	Female	70/70.0%	58/58.0%	0.077 <sup>x</sup>
	Male	30/30.0%	42/42.0%	
<b>Complaint</b>				
Pain		99/99.0%	95/95.0%	0.097 <sup>x</sup>
Jaundice		67/67.0%	75/75.0%	0.213 <sup>x</sup>
Fever-chills		21/21.0%	41/41.0%	0.002 <sup>x</sup>
Biliary pancreatitis		35/35.0%	20/20.0%	0.018 <sup>x</sup>
Cholangitis		51/51.0%	67/67.0%	0.021 <sup>x</sup>
Gallstone		70/70.0%	66/66.0%	0.544 <sup>x</sup>
Complaint duration		13.4 $\pm$ 10.8	20.2 $\pm$ 38.5	0.076 <sup>m</sup>
WBC ( $\mu$ Lx10 <sup>3</sup> )		9.8 $\pm$ 3.7	11.4 $\pm$ 4.3	0.004 <sup>m</sup>
AST (U/L)		258.7 $\pm$ 268.6	163.5 $\pm$ 141.4	0.002 <sup>m</sup>
ALT (U/L)		321.2 $\pm$ 249.0	222.6 $\pm$ 190.1	0.001 <sup>m</sup>
GGT (U/L)		517.2 $\pm$ 393.7	526.0 $\pm$ 370.1	0.782 <sup>m</sup>
ALP (U/L)		441.5 $\pm$ 314.0	466.2 $\pm$ 333.3	0.327 <sup>m</sup>
Amylase (U/L)		467.2 $\pm$ 870.5	219.9 $\pm$ 394.1	0.164 <sup>m</sup>
Total bilirubin mg/dL		4.7 $\pm$ 3.6	6.2 $\pm$ 4.6	0.006 <sup>m</sup>
Direct bilirubin mg/dL		3.6 $\pm$ 3.3	4.6 $\pm$ 3.3	0.013 <sup>m</sup>
Indirect bilirubin mg/dL		1.3 $\pm$ 1.0	1.6 $\pm$ 1.9	0.269 <sup>m</sup>

<sup>m</sup>Mann-Whitney U test, <sup>x</sup>chi-square test (Fisher's Exact test), SD: standard deviation, WBC: white blood cell count, AST: aspartate aminotransferase, ALT: alanine aminotransferase, GGT: gamma glutamyl transferase, ALP: alkaline phosphatase, ERCP: endoscopic retrograde cholangiopancreatography

**Table 3. Comparison of CBD anatomical features, stones, and procedure-related parameters of the single and repeated ERCP groups**

		Single ERCP	Repeat ERCP	p
		Mean $\pm$ SD/n-%	Mean $\pm$ SD/n-%	
CBD width		12.3 $\pm$ 4.3	15.2 $\pm$ 5.0	0.000 <sup>m</sup>
CBD width	<10 mm	44/44.0%	22/22.0%	0.001 <sup>x</sup>
	10-20 mm	46/46.0%	53/53.0%	
	>20 mm	10/10.0%	25/25.0%	
CBD angulation		288.9 $\pm$ 38.7	273.7 $\pm$ 36.9	0.001 <sup>m</sup>
CBD angulation	<250°	20/20.0%	32/32.0%	0.008 <sup>x</sup>
	250°-300°	32/32.0%	41/41.0%	
	⇒300°	48/48.0%	27/27.0%	
Number of gallstones	Several	58/58.0%	50/50.0%	0.467 <sup>x</sup>
	Single	3/3.0%	5/5.0%	
	None	39/39.0%	45/45.0%	
Stone difficulty	Sludge	28/28.0%	3/3.0%	0.000 <sup>x</sup>
	<10 mm	50/50.0%	24/24.0%	
	10-14 mm single stone	9/9.0%	21/21.0%	
CBD shape	8-12 mm multiple stones	13/13.0%	52/52.0%	0.042 <sup>x</sup>
	Straight	7/7.0%	6/6.0%	
	V-type	27/27.0%	44/44.0%	
ERCP complication	S-type	66/66.0%	50/50.0%	0.128 <sup>x</sup>
	(-)	95/95.0%	88/88.0%	
	(+)	5/5.0%	12/12.0%	
Post-ERCP complication	Hemorrhage	5/5.0%	9/9.0%	0.000 <sup>x</sup>
	Basket impaction	0/0.0%	3/3.0%	
	(-)	99/99.0%	79/79.0%	
Pancreatitis	(+)	1/1.0%	21/21.0%	0.000 <sup>x</sup>
	Cholangitis	0/0.0%	16/16.0%	

<sup>m</sup>Mann-Whitney U test, <sup>x</sup>chi-square test (Fisher's Exact test) SD: standard deviation, CBD: common bile duct, WBC: white blood cell count, AST: aspartate aminotransferase, ALT: alanine aminotransferase, GGT: gamma glutamyl transferase, ALP: alkaline phosphatase, ERCP: endoscopic retrograde cholangiopancreatography

## DISCUSSION

In this study, the age of the patients was significantly higher in the repeated ERCP group than in the single ERCP group. There are two possible reasons for this: First, the prevalence of problematic stones increases as the median age increases. In a study investigating the effectiveness and reliability of ERCP in patients  $\geq 85$  years, larger stones were detected in the elderly group (15). In some studies, the total clearance of stones was significantly limited in the elderly population (8,15,16). Second, in elderly patients, procedures are often delayed until second intervention to avoid the complications of prolonged ERCP and anesthesia (17).

Although a higher number of repeated ERCP procedures are performed in the elderly, non-significant differences in gender, patient complaints, and duration of the complaints were expected. Especially, fever and chills, elevated WBC, and increased total and direct bilirubin values were found to be significantly higher when

evaluated together. These findings represent cholangitis cases, which constitute the most common ERCP group. Cholangitis is a systemic infection with a high mortality rate that requires emergency treatment (6,18,19). In this condition, complaints of pain, fever, and jaundice (Charcot's triad) are accompanied by lethargy and shock (Reynolds' pentad), which is termed as acute obstructive suppurative cholangitis, and requires emergency biliary decompression (6,18,20). The aim of the treatment in cholangitis is to achieve biliary decompression and save the life of the patient, which explains the increased number of stenting procedures in this group. However, the stenting procedure itself is a risk factor for repeated ERCP interventions (6,17,21).

In our study, compared to the single ERCP group, the cholestasis enzyme levels were significantly higher in the repeated ERCP group. The increase in these values is a predictor of the need for ERCP and the presence of CBD stones. However, these factors do not have a predictive value in estimating the difficulty of the procedure and whether a repeated intervention may be necessary.

Juxtapapillary diverticulum was more commonly observed in the repeated ERCP group. There are many studies demonstrating that recurrent CBD stones develop more frequently in the presence of diverticula. Moreover, cholangitis, pancreatitis, and deformation in the choledochal axis are highly prevalent when a duodenal diverticulum is present (2-4,13).

It is generally accepted that ERCP is more challenging in cases with acute pancreatitis. The presence of enclaved CBD stones and a duodenal diverticulum is highly prevalent in cases of acute biliary pancreatitis (7). Increased pressure at the distal end of the CBD due to the developing edema may cause biliary tract obstruction and cholangitis. In case of acute pancreatitis, if there is an obstructing stone that causes acute cholangitis, early ERCP should be planned. Otherwise, unnecessary interventions may increase the severity of pancreatitis. The pathology of such cases should be demonstrated using MRCP or EUS (6,22-24). In late-stage biliary pancreatitis cases, the presence of stones should be investigated with MRCP. Difficulty of CBD cannulation during ERCP increases in patients with acute pancreatitis, and if accompanied by an enclaved stone, stone clearance becomes complicated. The frequency of pre-cut sphincterotomy is high in these patients, which further increases the risk of post-ERCP complications.

Pre-cut access to the CBD is more efficient in cases with enclaved CBD stones. Although these stones are typically difficult to treat, it is possible to easily remove the stone and perform selective cannulation through the efficient sphincterotomy. Pre-cut sphincterotomy can be successfully performed in patients undergoing ERCP, especially in experienced hands. It is required in 10% of all cases (13,25,26). If cannulation cannot be performed in patients with a pre-cut sphincterotomy, extending the duration of ERCP increases the rate of post-procedural complications (25). Pavlides et al. (26) reported a 78% success rate in cannulation when they repeated ERCP within an average of four days in 89 cases for whom successful selective cannulation could not be achieved despite the pre-cut procedure.

**Table 4. Stone-related and local anatomical changes and ERCP complications**

		Mean $\pm$ SD/n-%
CBD width		13.8 $\pm$ 4.9
CBD width	<10 mm	66/33.0%
	10-20 mm	99/49.5%
	>20 mm	35/17.5%
		281.3 $\pm$ 38.5
CBD angulation	<250°	52/26.0%
	250-300°	73/36.5%
	>300°	75/37.5%
Number of gallstones	Several	108/54.0%
	Single	8/4.0%
	None	84/42.0%
Stone difficulty	Sludge	31/15.5%
	<10 mm	74/37.0%
	10-14 mm single stone	30/15.0%
	8-12 mm multiple stones	65/32.5%
Shape of CBD	Straight	13/6.5%
	V-type	71/35.5%
	S-type	116/58.0%
ERCP complication	(-)	183/91.5%
	(+)	17/8.5%
	Hemorrhage	14/7.0%
	Basket impaction	3/1.5%
Post-ERCP complication	(-)	177/88.5%
	(+)	22/11.0%
	Pancreatitis	6/3.0%
	Cholangitis	16/8.0%

SD: standard deviation, ERCP: endoscopic retrograde cholangiopancreatography, CBD: common bile duct

**Table 5. Univariate and multivariate analyses of the relationship between repeated ERCP and variables related to the patients' demographic status, complaints, and blood test results**

	Univariate model			Multivariate model		
	OR	95% Confidence interval	p	OR	95% Confidence interval	p
Age	1.03	1.01-1.04	0.005	-	-	-
WBC	1.00	1.00-1.00	0.007	-	-	-
AST	1.00	1.00-1.00	0.005	1.00	0.99-1.00	0.008
ALT	1.00	1.00-1.00	0.003	-	-	-
Total bilirubin	1.10	1.02-1.19	0.014	-	-	-
Direct bilirubin	1.10	1.00-1.20	0.048	-	-	-
CBD width	1.15	1.07-1.23	0.000	-	-	-
CBD angulation	0.99	0.98-1.00	0.006	-	-	-
Fever-chills	2.61	1.40-4.88	0.003	3.36	1.47-7.63	0.004
Biliary pancreatitis	0.46	0.92-0.88	0.019	0.34	0.15-0.80	0.013
Cholangitis	1.95	1.10-3.46	0.022	-	-	-
Stone difficulty	3.20	2.29-4.48	0.000	3.45	2.33-5.11	0.000
CBD shape	1.73	1.06-2.83	0.030	-	-	-
Post-ERCP complication	36.3	3.5-200	0.002	6.02	1.32-27.03	0.020
CBD width	2.25	1.46-3.47	0.000			
CBD angulation	0.58	0.40-0.84	0.003			

Forward logistic regression. OR: odds ratio, WBC: white blood cell count, AST: aspartate aminotransferase, ALT: alanine aminotransferase, CBD: common bile duct, ERCP: endoscopic retrograde cholangiopancreatography

In the current study, patients with difficult CBD stones had a significantly higher requirement for repeated ERCP, as expected. In addition, the presence of choledochoduodenal fistula, a wide CBD, and use of mechanical lithotripsy during the procedure increased the number of repeated ERCPs (27). It should be kept in mind that most elderly patients have a wide CBD and a high number of stones, often accompanied by cholangitis (2-4,15,18,19,28). The presence of large and difficult stones in ERCP complicates stone removal. In such cases, repeated ERCP may be undertaken by performing sphincterotomy and stenting (5). It is extremely important to perform adequate sphincterotomy and ensure adequate stone clearance to reduce the number of repeated ERCPs and minimize residual and recurrent stones in the late period (5,28).

An increase in the diameter of CBD is detected in proportion to the increasing difficulty and size of CBD stones. The increase in the width of CBD is greater in elderly patients when the diameter of the stone is large, the stone is enclaved, or the number of stones is high, all of which contribute to the possibility of repeated ERCP. The width of CBD is also a significant factor in the recurrence of CBD stones in the long-term. In many studies, post-ERCP follow-up results have demonstrated that CBD width was a significant factor in the long-term recurrence of CBD stones (6,7,28).

In studies concerning the shape and angulation of the CBD, significant results have been obtained, especially regarding recurrent CBD stones. It was reported that late-stage recurrent

stones are more frequently observed, mainly in the S-type CBD structure (28-30). In our study, the need for repeated ERCP attempts was increased by the location, size, and number of stones, rather than the shape of the CBD or the presence of cholangitis.

In the literature, papillary hemorrhage (1.4%) and retroperitoneal duodenal perforation (0.69%) were reported as the most frequent complications observed during invasive ERCP (6,31,32). Among our cases, complications encountered during the procedure were like those reported in the literature. The frequency of mechanical lithotripsy and related complications increase with difficult CBD stones. The most important and challenging complication was basket impaction. In two of our patients, this complication was resolved by the repeated endoscopic intervention, while the remaining patient required open surgery. In case a large stone is detected during the pre-procedural examination, a lithotripter basket should be used while seeking other appropriate solutions to prevent complications (6,7,13,14).

In our study, compared to the single ERCP group, the complication rate in the repeated ERCP group was significantly higher. The most common post-ERCP complication is pancreatitis, with a prevalence of 1.6-15.7% (3,11,33,34). Etiological factors of this complication include the use of electrocauterization in sphincterotomy, edema in the sphincter of Oddi and the pancreatic sphincter, pre-cut sphincterotomy, increased hydrostatic pressure in the pancreatic duct due to excessive contrast injection, and contamination of the

pancreatic ductal system with duodenal content (26,32). All these etiological factors increase with repeated ERCP and naturally result in a significantly higher rate of post-ERCP complications. Biliary septic complications, including cholangitis and cholecystitis are also observed in the post-ERCP period (1,5,32,35-37). The clinical follow-up of these patients is very important, since cholangitis may develop frequently in patients with difficult CBD stones due to inadequate sphincterotomy, overlooked stones, and non-functioning stenting.

### Study Limitations

The study had some limitations. The present study was conducted with ERCP records of a single endoscopist which may cause bias due to personalization of the data. Additionally, there might have been some patients who had undergone repeated ERCP in a different center that we missed during the study period. On the other hand, the most important strength of this study that to the best of our knowledge, this is the first study in the literature to include such a large number of patients with a noticeable amount of data and follow-up period.

ERCP is the gold standard in gallstone treatment; therefore, it should be considered as the first-line treatment. However, due to its invasive nature, its risk of complications is high, even in experienced hands. Along with experience, pre-procedural patient selection is a very important factor for reducing complications (34,36).

### CONCLUSION

ERCP is the most important, invasive, endoscopic procedure for the clearance of bile duct stones. It is known that several factors may interfere with a positive outcome in the first attempt. It is important for the endoscopist and the patient to be able to predict under which circumstances a repeat intervention may be required. The diameter of the CBD and the number of stones was increased in elderly patients. On the other hand, the presence of stenosis, enclaved stones in the CBD, and accompanying pancreatitis increased the need for repeated ERCP in young patients. The need for stenting was higher in both age groups when cholangitis was present. The success rate of ERCP was not affected by a single factor, but by all clinical and pathological factors that increase the difficulty of the procedure.

**Ethics Committee Approval:** Ethical approval was not sought for the present study because this study did not involve a prospective evaluation, did not involve laboratory animals, and only involved the records of ERCP procedures of different health centers at which Dr. Murat Akaydin had been working.

**Informed Consent:** Retrospective study.

**Peer-review:** Internally peer-reviewed.

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