Ann Med Res 2020;27(6):1668-74

Annals of Medical Research

DOI: 10.5455/annalsmedres.2020.03.287

Original Article

Endoscopic retrograde cholangiopancreatography in patients with periampullary diverticula: Technical details, classification, and timing of surgical treatment

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Abstract

Aim: Periampullary duodenal diverticula may create difficulties for selective common bile duct cannulation during endoscopic retrograde cholangiopancreatography (ERCP).

Material and Methods: For the study, the technical details and findings of ERCP and demographic features of 724 patients without duodenal diverticula and 92 patients with duodenal diverticula who underwent ERCP.

Results: The mean age was 73.09 ± 15.32 years for the 92 patients with PAD (group A) and 60,2 ± 18.85 years for the 724 patients without duodenal diverticulum (group B). Forty-eight percent of the study sample was aged over 65 years, 54.3% were female and 45.7% were male. Duodenal diverticulum was present in 11.3% of the patients. In addition, 22 (23.9%) patients in the PAD group and 155 (21.4%) patients without duodenal diverticula required a second ERCP (P = 0.583). The mean duration of hospitalization was 6.67 ± 6.23 days in patients with duodenal diverticula and 6.17 ± 5.16 days in the control group and the mean cost of hospitalization was $ 442.02 ± 512.06.

Conclusion: In conclusion, ERCP may not always be difficult in patients with a diverticulum in the periampullary region, and the difficulty of the procedure depends on the location of the papillary orifice and the type of the diverticulum. In patients with periampullary diverticula, it would be appropriate to consider surgical treatment in the presence of failed CBD cannulation and large stones that cannot be removed from the CBD.

Keywords: Common bile duct; diverticulum; endoscopic retrograde cholangiopancreatography

INTRODUCTION

Periampullary duodenal diverticula may create difficulties for selective common bile duct (CBD) cannulation during endoscopic retrograde cholangiopancreatography (ERCP). Incidentally discovered in patients during ERCP, duodenal diverticulum is usually asymptomatic, but with advanced imaging methods it can sometimes be noticed before ERCP. For the endoscopist, periampullary diverticulum (PAD) is important because it can be a source of morbidity. PAD is commonly located in the second part of the duodenum and is usually seen in the elderly. It is often caused by the progression of duodenal motility disorders. In addition, progressive weakening of intestinal smooth muscles and increased intraduodenal pressure are known as underlying etiologies for this defect (1). Periampullary diverticula are rare in patients under the age of 40 years. Although PAD usually does not cause symptoms, it may lead to the development of obstructive jaundice. This unusual occurrence of obstructive jaundice secondary to PAD is known as Lemmel syndrome (2).PAD usually consists of mucosa, submucosa, and the muscularis mucosa extending through the intestinal serosa within a radius of 3 cm from the ampulla of Vater. Depending on the type of study, the incidence of PAD is reported to be between 10% and 20% in the literature (3). Although the majority of PAD is asymptomatic, its association with various pancreaticobiliary complications is generally thought to be the result of both mechanical compression of the distal CBD and dysfunction of the sphincter of Oddi (4). In general, duodenal diverticula rarely cause bleeding, but when they do, it is difficult to make a timely diagnosis and thus, they are often fatal (5). The main purpose of our study was to compare the clinical data of patients with and without PAD, according to the PAD types and the position of the papillary orifice and to determine its effect on the cannulation of the common bile duct, if any. An additional

Received: 31.03.2020 **Accepted:** 04.05.2020 **Available online:** 12.06.2020
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purpose of this study was to describe certain technical details of ERCP in patients with duodenal diverticula and to evaluate when and how to perform surgery in patients with PAD.

MATERIAL and METHODS

For the study, the technical details and findings of ERCP and demographic features of 724 patients without duodenal diverticula and 92 patients with duodenal diverticula who underwent ERCP in our gastroenterological surgery clinic between 2015 and 2018 were prospectively entered into a database and evaluated retrospectively. Patients with prior surgery were excluded because the cannulation technique was different from that of the normal anatomy due to surgically altered anatomy (Billroth II or Roux-en-Y anastomosis).For comparison, participants were classified into two groups; group A, which consisted of patients with periampullary duodenal diverticula (92 patients served as the reference group) and group B, patients with no periampullary duodenal diverticula (724 patients served as the control group). Liver function tests, cost, and hospital stay were evaluated and compared between the groups. The ERCP procedure was performed in accordance with generally accepted indications. Sedation was performed under conscious sedation or under general anesthesia by an anesthesiologist. Cannulation was performed as per standard techniques previously described in patients with PAD. This study was not directed to standard complications of ERCP. Every ERCP procedure was recorded on video for all PAD cases. The video recordings were reviewed and PAD classification was made. The videos were assembled with video editing programs to contribute to the ERCP practice and were prepared as part of the article (if available in the journal).

Periampullary diverticula cases were categorized as type 1, 2 or 3 according to the classification of Zhen Sun et al.: type 1, the major papilla is located inside the diverticulum; type 2, the major papilla is located on the edge of the diverticulum and type 3, major papilla is located outside of the diverticulum (6). The ERCP procedure was performed by a gastroenterology surgeon using a standard technique and duodenoscope. Surgical treatment was performed for patients with failed ERCP due to PAD and large common bile duct stones that could not be removed and the data were recorded. In this study, we aimed to evaluate the clinical data of patients with or without periampullary diverticula, the difficulty of performing ERCP based on the types of diverticulum, and the reason for surgical treatment.

Statistical analysis

The normality of distribution of continuous variables was tested using the Shapiro-Wilk test. The Mann-Whitney U test was used to compare two independent groups for non-normal data. The Chi-square test was used to investigate the relationship between two categorical variables. All statistical analyses were performed using the SPSS for Windows, version 24.0 software packages, and p values less than 0.05 were considered statistically significant.

Papillary cannulation technique

Periampullary diverticula may pose difficulties for selective CBD cannulation. Even an experienced endoscopist may not be able to successfully complete ERCP procedures in some cases. Ahmed et al. described different cannulation techniques including: a) the two devices in one-channel method, b) the reversed guidewire method, c) the double-endoscope method, d) balloon dilation of the narrow diverticular neck, e) endoclip-assisted cannulation, f) cap-assisted cannulation, g) pancreatic duct stent placement followed by pre-cut biliary sphincterotomy, h) percutaneous ultrasound-guided rendezvous technique, and j) the endoscopic ultrasonography (EUS)-guided rendezvous technique (7). Most of these techniques are established techniques. In our study, we cannulated the common bile duct with standard sphincterotomy without using the aforementioned techniques. In some cases, we cannulated using a tapered tip catheter and double-wire method. In difficult cases, if the pancreatic duct was intraoperatively cannulated with a guidewire during the procedure, cannulation was attempted by leaving the guidewire in the main pancreatic duct or inserting a stent into the pancreatic duct. If necessary, pre-cut sphincterotomy or fistulotomy was performed.

The technical aspect we aimed to demonstrate in this study was not just about the cannulation technique. A more important consideration is to perform ERCP through teamwork by maneuvers on the long and short axes with the duodenoscope positioned according to the location of the diverticulum. Such supportive technical maneuvers are more difficult in PAD than in standard maneuvers. Experience of endoscopist is crucial to determine the position and to secure the appropriate position by the duodenoscope. When the papilla orifice is not detected, attempts are made to detect the orifice by pushing the diverticulum mucosa (outward, upward, and downward) with the tip of the sphincterotome. If the papilla orifice is undetected, the interior segment of the diverticulum is carefully revised with the duodenoscope. Uncontrolled advances with the duodenoscope may cause perforation during revision because there is no serosa layer of the diverticulum. The endoscopist should determine the position with one hand and then proceed in coordination with the endoscopy nurse. Due to the motility of the duodenum, the CBD should be cannulated in a short period of time when it stays in a fixed position. For this reason, the endoscopist and the nurse should be experienced to deal with difficult PAD cases. In cases with selective CBD cannulation, we did not refrain from adequate sphincterotomy and 12 mm balloon dilation when needed. One of the factors that challenges ERCP or affects the success or failure of the procedure is the type of PAD. A type 1 PAD with papilla located at 9-12 and 12-3 o'clock position causes difficulty in selective CBD cannulation and in most cases results in failed ERCP. In case of failed cannulation, percutaneous transhepatic biliary drainage (PTBD) or EUS-guided biliary drainage (EUS-BD) has priority over surgery. In addition, when large

stones cannot be removed in these patients, they should be evaluated for surgical treatment.

RESULTS

The mean age was 73.09 ± 15.32 years for the 92 patients with PAD (group A) and 60.2 ± 18.85 years for the 724 patients without duodenal diverticulum (group B). Forty-eight percent of the study samples were aged over 65 years, 54.3% were female and 45.7% were male. Duodenal diverticulum was present in 11.3% of the patients. In addition, 22 (23.9%) patients in the PAD group and 155 (21.4%) patients without duodenal diverticula required a second ERCP (P = 0.583). The mean duration of hospitalization was 6.67 ± 6.23 days in patients with duodenal diverticula and 6.17 ± 5.16 days in the control group (P = 0.936) and the mean cost of hospitalization was $ 442.02 ± 512.06. Compared with group A, group B had a significantly higher percentage of patients aged over 65 years (P = 0.001) (Table 1). The mean age of group A was significantly higher than Group B (P = 0.001)

Table 1. Comparison of patients with or without duodenal diverticula

		group A (n=92)	group B (n=724)	P
Age groups (years)	<65	19 (20.7)	403 (56)	0.001*
	≥65	73 (79.3)	317 (44)	
Sex	M	40 (43.5)	333 (46)	0.648
	F	52 (56.5)	391 (54)	
Cholangiocellular carcinoma (suspected)	+	0 (0)	17 (2.3)	0.137
Suspected malignancy	+	2 (2.2)	30 (4.1)	0.359
Bile leakage	+	0 (0)	9 (1.2)	0.282
Need for second ERCP	+	22 (23.9)	155 (21.4)	0.583
Stent placement	+	14 (15.2)	150 (20.7)	0.215
Cholecystectomy	+	8 (8.7)	79 (10.9)	0.517
Sphincterotomy	+	87 (94.6)	681 (94.1)	0.846
Sclerotherapy	+	1 (1.1)	18 (2.5)	0.402

*Significant at 0.05 level based on Chi-square test

Table 2. Comparison of study variables in patients with or without diverticula

Variables	Group A Present (n=92)	Group B Absent (n=724)	P
Age (years)	73.09 ± 15.32	60.2 ± 18.85	0.001*
Hospital stay (days)	6.67 ± 6.23	6.17 ± 5.16	0.936
Cost (USD)	2804.69 ± 3276.14	2308.92 ± 2661.06	0.779
Number of ERCP	1.27 ± 0.61	1.17 ± 0.51	0.078
WBC x10^3 cells u/L	12.21 ± 7.2	12.27 ± 7.31	0.484
GGT (IU/L)	292.36 ± 272.97	375.52 ± 338.76	0.020*
Direct bilirubin mg/dL	2.65 ± 2.77	3.49 ± 3.76	0.153
Alkaline Phosphatase (IU/L)	228.98 ± 237.15	256.85 ± 206.94	0.050*
Alanine aminotransferase (IU/L)	180.59 ± 254.48	213.04 ± 240.29	0.010*
Aspartate aminotransferase (IU/L)	33.04 ± 27.04	41.87 ± 43.33	0.031*
Amylase (IU/L)	478.11 ± 698.04	479.87 ± 679.73	0.502

* Significant at 0.05 level based on Mann-Whitney U test

(Table 2). When the papillary orifice was located within the diverticulum and at 9-12 and 12-3 o'clock positions, the CBD cannulation was difficult and sometimes failed. In our study, the chances of a successful CBD cannulation were higher when the papilla orifice was located at the 5 to 7 o'clock position in the duodenal diverticulum or when it was located outside the diverticulum (types 2 and 3). Selective CBD cannulation depends on the location of the parapapillary duodenal diverticulum and its size, the number of diverticula and, most importantly, the position of the papillary orifice in relation to the PAD. ERCP procedures of all cases were recorded and assembled in the form of short videos. The classification of the duodenal diverticula was made for the current cases. The relative frequency of PAD was further classified according to the subtype: 28.8% were type 1, 51.6% were type 2, and 21.5% were type 3 (Figure 1). PAD subtypes were correlated with differences in clinical features. Fifty-four (58.8%) patients had a single PAD and 39 (41.9%) patients had a double PAD (Figure 2).

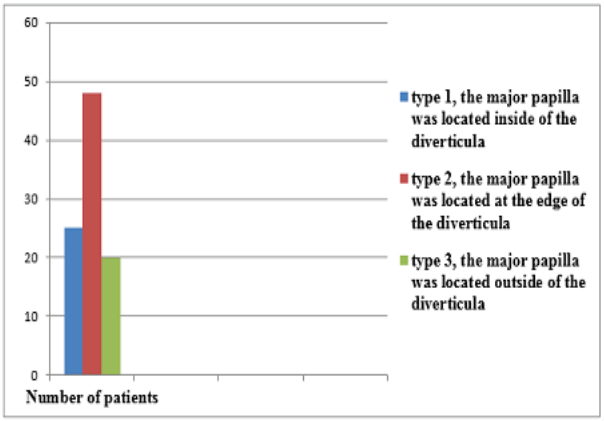

Figure 1. PAD cases were classified as type 1, 2, or 3 according to the position of the major papilla from the endoscopic view

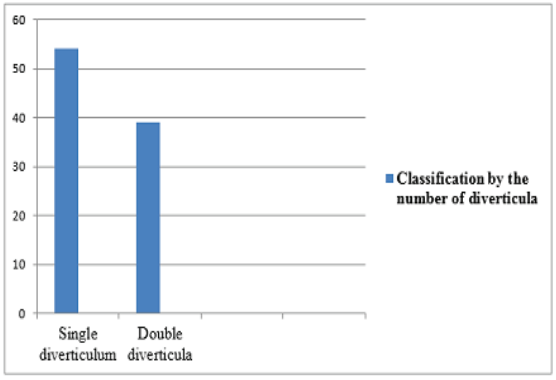

Figure 2. Number of diverticulum in the duodenum (single and double)

According to the papilla diverticulum position, 3 (3.2%) patients had a diverticulum at the 12 to 3 o'clock position, 45 (48.3%) patients at the 3 to 6 o'clock position, 41 (44%) patients at the 6 to 9 o'clock position and 4 (4.3%) patients at the 9 - 12 o'clock position (Figure 3). A second ERCP was required in 22 (23.9%) patients of group A and 155 (21.4%) patients of group B, with a non-significant difference

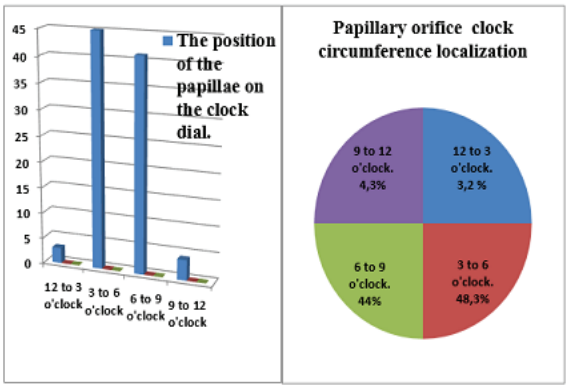

Figure 3. Localization of the papillary orifice in the periampullary duodenal diverticula

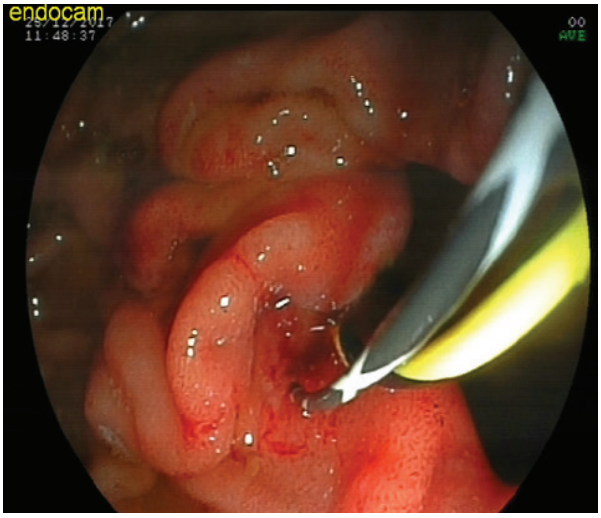

Figure 4. Tip 1 Periampullary duodenal diverticula

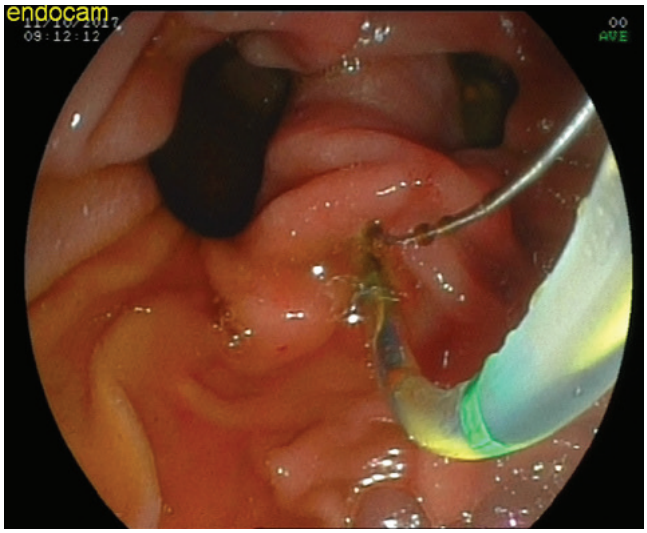

Figure 5. Tip 2 Periampullary duodenal diverticula

(P = 0.583). PAD type 1, type 2, type 3 is shown with sample images (Figure 4,5) The number of patients undergoing CBD stenting was 14 (15.2%) in the PAD group and 150 (20.7%) in the control group (P = 0.215), and a second ERCP was performed for stent removal. The reasons for a second ERCP in both groups included failed cannulation,

complementary ERCP for large stones, recurrent choledocholithiasis, and stent removal. In the PAD group, a second ERCP procedure was performed in 14 out of 22 patients for stent removal and for control of the CBD. In one of the three patients who underwent stenting, the stones were completely removed and the other two patients received choledochotomy and T-tube drainage as surgical treatment. Two of the remaining 8 patients had a successful second ERCP procedure and the CBD stones were removed.

In six patients, the operation was unsuccessful despite a second ERCP. Choledochoduodenostomy was performed in 4 of these patients as surgical treatment and the remaining two patients underwent choledochotomy, stone removal, and T-tube drainage. The reasons for surgical treatment in patients with duodenal diverticula included failed ERCP, large bile stones that could not be removed, and failed ERCP despite a second attempt. Periampullary disease was suspected in 30 (4.1%) patients with duodenal diverticula and in only 2 (2.2%) patients in the control group (P = 0.359). Post-ERCP pancreatitis (PEP), which is defined as elevated serum amylase greater than 3 times the upper limit of normal in patients with PAD, developed in 6 (6.5%) patients with PAD, two patients had moderate pancreatitis and four had mild pancreatitis. In the control group, PEP developed in 40 (5.5%) patients. One patient (1.1%) in the duodenal diverticula group and 18 (2.5%) patients in the control group had hemorrhage, with a statistically non-significant difference (P = 0.402). Perforation was not detected in the PAD group.

DISCUSSION

The aims of this study were to investigate the relationship between different types of PAD and technical success of ERCP, to determine the types of PAD based on video recordings, and to share our experience with surgical treatment after failed ERCP. The obvious limitations of the study include a single-center analysis and the retrospective design. Periampullary diverticula may not always be mentioned in the radiology reports and therefore, patients with PAD were prospectively recorded during the ERCP operation. In addition, the assessment for the ERCP indication was based on magnetic resonance cholangiopancreatography (MRCP), computed tomography (CT) findings and abdominal ultrasound reports. Radiological evaluation of the periampullary region may pose unique challenges because the CBD is dilated and has a distal blunt end. Periampullary diverticula may be confused with cystic lesions in the pancreatic head when they are filled with fluid. Radiologists should be aware of this potential pitfall. Chee Hui Ng (8) et al. carefully reviewed three cases in which lesions with a cystic appearance were initially misdiagnosed as cystic pancreatic lesion, pseudocyst or intraductal papillary mucin neoplasm. Subsequently, they reached the right diagnosis of periampullary diverticula using detailed MRCP, EUS, and CT imaging results.

In our study, ERCP and surgical treatment were performed by a single gastroenterology surgeon. The radiologic images of all cases were analyzed in detail before and after ERCP. A multidisciplinary approach was employed for all ERCP cases. Each case was discussed and information was shared with radiologists. There were no cases of misdiagnosis but two cases had suspicion of periampullary tumor and this suspicion was eliminated after ERCP. Small diverticula were not usually mentioned in radiologic reports and were recorded during the ERCP procedure.

Endoscopists do not feel comfortable with using endoscopic papillary large balloon dilation (EPLBD) with limited endoscopic sphincterotomy (ES) in patients with PAD. The cause of their anxiety in patients with PAD is the risk of various adverse events such as hemorrhage, perforation, pancreatitis, and cholangitis. Endoscopic papillary balloon dilation with ES has been widely used to extract large or difficult biliary stones (9). Complications such as bleeding and perforation have been reported to be less frequent in EPLBD + ES compared with standard ES (10). In a retrospective study by Kook Hyun Kim et al., periampullary diverticula were detected in 93 out of 223 patients. Of these PAD cases, 18 (19.3%) were type 1, 41 (44.0%) were type 2, and 34 (36.7%) were type 3. They reported that EPLBD alone and limited ES plus EPLBD were safe and effective methods for the removal of CBD stones in patients with PAD (11). In our study, mechanical lithotripsy was used for stones with a diameter greater than 12 mm. ES was performed in all cases. For larger stones, stones were removed with limited ES + EPLBD and surgical treatment was planned when stone removal failed.

Although the diagnosis and treatment success of the ERCP unit is very high, surgical treatment is indispensable for some patients. In our study, patients in whom CBD stones could not be removed through sphincterotomy and balloon dilation and the papillary orifice could not be cannulated despite a second ERCP were evaluated for surgical treatment. Stone extraction with choledochotomy and T-tube drainage were performed for patients with unsuccessful removal of CBD stones despite the use of sphincterotomy and balloon dilation. Choledochotomy, stone extraction and choledochoduodenostomy were performed for patients with choledocholithiasis in whom CBD cannulation failed during the second ERCP session because of the duodenal diverticulum.

PEP is the most common and potentially the most serious complication of ERCP and may lead to morbidity (12, 1). Compression of the CBD, ampullary dysfunction or impaired biliary flow from the papillary orifice may cause pancreatic biliary disease and possibly pancreatitis. This process is also supported by the proliferation of bacteria within the diverticulum. Although the majority of patients with PAD are asymptomatic, it is associated with an increased incidence of choledocholithiasis and

pancreatitis as reported in the current literature. There is controversy as to whether pancreatitis originates from PAD or associated biliary stones (13, 14). Previous studies have reported patients with PAD whose recurrent pancreatitis episodes were treated with ES (15). The incidence of pancreatitis in patients with PAD undergoing ERCP is similar to the incidence of post-ERCP pancreatitis in the literature. Mild and moderate cases of PEP were treated medically in our study.

The ERCP procedure may not always be successful in patients with duodenal diverticula. The experience of the endoscopist is important for successful biliary cannulation. Very rarely, uncontrolled maneuvers with the duodenoscope for papillary positioning may cause perforation of the diverticulum. In the case of periampullary diverticulum, bleeding, inflammation or perforations occur in only 5% of patients presenting with symptoms (16). Perforation is a rare complication, but is associated with an overall mortality rate of 1.0-1.5%. In a study by Rabie (17) et al. involving 10 patients with PAD with post-ERCP perforation, management was conservative in 5 patients, conservative and percutaneous cholecystostomy in one patient, conservative with percutaneous drainage collection in one patient, and 3 patients underwent laparotomy. They stated that early recognition and timely management of the condition was the only way to avert a fatal outcome (17, 18). However, with the development of endoscopic devices and techniques, endoscopic closure has been reported to be a safe and effective treatment. When endoscopic treatment fails or in the event of clinical deterioration, urgent surgical treatment should be considered (19). In our study, perforation did not occur during ERCP in patients with PAD.

Bleeding after ERCP may cause adverse events. The reported incidence of bleeding varies between 0.3% and 2.0%, and in 30% of these patients, bleeding is seen immediately after the procedure. Delayed bleeding may occur up to 2 weeks after the procedure. Well-recognized risk factors for bleeding after ES include coagulopathy use of anticoagulants within 3 days of sphincterotomy, cholangitis prior to ERCP, bleeding during initial sphincterotomy, and low endoscopist ERCP case volume. In contrast, factors not associated with increased risk of bleeding include use of aspirin (acetylsalicylic acid) or non-steroidal anti-inflammatory drugs, ampullary tumor, longer duration of sphincterotomy, and prolongation of previous sphincterotomy (20,21). Re-bleeding after initial successful endoscopic hemostasis occurs in about one-fifth of patients. To avoid the need for angiographic or surgical hemostasis, it is reasonable to consider placement of fully-covered metal stents (22, 23) in patients with unsuccessful conventional interventions. The cause of life-threatening risk is related to the position of the diverticulum and the difficulty in the localization of a bleeding point within the diverticulum (24). None of our patients experienced serious bleeding. In one patient, intraoperative bleeding was stopped using a conventional intervention.

CONCLUSION

In conclusion, ERCP may not always be difficult in patients with a diverticulum in the periampullary region, and the difficulty of the procedure depends on the location of the papillary orifice and the type of the diverticulum. The overall complication rates in patients with diverticula are similar to those without diverticula. A significant factor affecting the success of ERCP is the ability of the endoscopist to work on both the long and short axes by looking at the duodenal papilla en-face and appropriately positioning the duodenoscope in patients with PAD. In patients with periampullary diverticulum, surgical treatment should be considered in the presence of large stones that cannot be removed from the CBD despite other techniques.

Competing interests: The authors declare that they have no competing interest.

Financial Disclosure: Supported by Inonu University BAP unit.

Ethical approval: Kahramanmaras provincial health directorate has been approved by scientific study evaluation members.13511907-601.99-E.14724.

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