

The impact of periampullary diverticula on the endoscopic treatment of choledocholithiasis

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Abstract

Introduction: Periampullary diverticula (PD) are generally asymptomatic and frequently diagnosed coincidentally during endoscopic retrograde cholangiopancreatography (ERCP).

Aim: To investigate the impact of PD on procedural success in ERCP for common bile duct (CBD) stones, and possible complications.

Material and methods: Five hundred and eighty-six patients diagnosed with CBD stones by diagnostic techniques and treated by ERCP were prospectively included in the study. Periampullary diverticula presence (patients with PD were allocated to group A, and those without PD to group B), size of the diverticulum (< 2 cm or ≥ 2 cm), papillary association with the diverticulum, size and number of CBD stones, were prospectively recorded for each patient. Total extraction of CBD stones by ERCP was considered successful treatment, and inability to remove the stone(s) was defined as lack of success.

Results: Group A consisted of 478 (82%), and group B 108 patients (18%). Cannulation success at first try was 97.7% in group A, and 95.4% in group B patients ($p > 0.05$). The prevalence of stone impaction was 3.1% in group A, and 10.2% in group B ($p < 0.01$). 86.8% of group A and 81.5% of group B patients were treated endoscopically.

Conclusions: Periampullary diverticula is a contributing factor in the formation of choledocholithiasis, and in the increase in size or impaction of existing stones. However, the presence of PD does not necessarily affect the success of ERCP or the prevalence of procedure-related complications in patients with CBD stones.

Introduction

Periampullary diverticula (PD) are generally located along the medial aspect of the second portion of the duodenum. Incidence increases with age. Radiological and postmortem studies report a prevalence rate of 5%, while endoscopic prevalence is 5-32% [1, 2]. Periampullary diverticula are usually asymptomatic, but there exist studies that report an increased prevalence with choledocholithiasis and pancreatic disorders [3-5].

Several studies have demonstrated that periampullary diverticula in patients undergoing endoscopic retrograde cholangiopancreatography (ERCP) procedures have an impact on procedural success, success of cannulation, and inter- and post-procedure complications. However, these results are considered to be controversial due to the small number of patients and the differences in study designs [6, 7].

Aim

In this study, we aimed to investigate the impact of PD on procedural success of ERCP for common bile duct (CBD) stones, and procedure-related complications.

Material and methods

Five hundred and eighty-six patients who presented to the Gastroenterology Clinic of Izmir Atatürk Training and Research Hospital between September 2008 and September 2010 with clinical and laboratory findings of obstructive jaundice and who underwent ERCP with a diagnosis of CBD stone by abdominal ultrasonography, magnetic resonance cholangiopancreatography (MRCP) or endoscopic ultrasonography (EUS) were prospectively included in the study. Patients with acute cholangitis and acute pancreatitis, pregnancy, or history of gastric procedures were excluded. Patients' demographic char-

acteristics and biochemical findings (alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, serum total bilirubin and amylase levels) were recorded.

Endoscopic retrograde cholangiopancreatography procedures were performed by two physicians with 600 procedures/year/9 years experience using an Olympus TJF 145 standard therapeutic duodenoscope and a Shimadzu Opescope 50N fluoroscopy scope. Written and verbal informed consent was obtained from patients prior to the procedure. Endoscopic retrograde cholangiopancreatography was performed following 12-hour fasting under respiratory and cardiac monitoring, with 3-4% nasal O₂ administration, under sedative anesthesia (propofol 1-2 mg/kg, midazolam 0.01-0.1 mg/kg). After visualization of the papilla by the duodenoscope, cannulation was achieved with a standard sphincterotome. In cases of failure of biliary cannulation after five tries during the same session, the precut technique or cannulation by fistulotomy was attempted. The procedure was terminated upon failure of cannulation by the precut technique. A second ERCP procedure was performed on these patients within 48 h. Unsuccessful cannulation during the second procedure was considered treatment failure. Following CBD cannulation, fluoroscopic imaging was obtained with the aid of contrast agents. The location, size, number, and impaction of stones were determined. Following sufficient endoscopic sphincterotomy, stone extraction by means of an ERCP balloon was attempted. In patients where this method failed, a mechanical lithotripter was used. In cases where balloon sweeping and mechanical lithotripter failed, a plastic biliary stent (7- to 10-French diameter, 10-12 cm length, according to the location and size of stones) was placed. Complete removal of CBD stones by ERCP was considered "treatment success", and inability to remove stones was considered "treatment failure".



Fig. 1. Small diverticula

A periampullary diverticulum was defined as a > 5 mm depression of the mucosa within a 2.5-cm radius of the papilla in endoscopic imaging by a duodenoscope [8]. Patients with and without diverticula were allocated to two groups (group B and group A, respectively). Group B patients were further divided into two groups according to diverticulum diameter: those with a diameter of < 2 cm were recorded as patients with small diverticula (group I), while those with a diameter of ≥ 2 cm were recorded as patients with large diverticula (group II) (Figures 1 and 2). Patients were also stratified according to the location of the papilla – at the edge of the diverticulum or within the diverticulum.

The duration of the ERCP procedure, cannulation success, inter- and post-procedure complications (bleeding, perforation, post-procedure symptomatic pancreatitis), size and number of CBD stones, stone impaction, treatment technique (balloon only, balloon and basket, plastic stent placement, endoscopic treatment in a separate session, and surgery) were recorded and evaluated.

Statistical analysis

Statistical analysis were performed using the SPSS-17.0 package, using Student's *t*-test, χ^2 test, and Fisher's exact test.

Results

Group A (without diverticula) consisted of 478 patients (82%), group B (with diverticula) of 108 patients (18%). Mean age was significantly higher in patients with diverticula ($p = 0.0001$). There was no correlation between the groups in terms of gender ($p < 0.05$) (Table I).

Cannulation was successful during the first ERCP session in 467 patients (97.7%) in group A, and 103 patients (95.4%) in group B. There was no difference be-

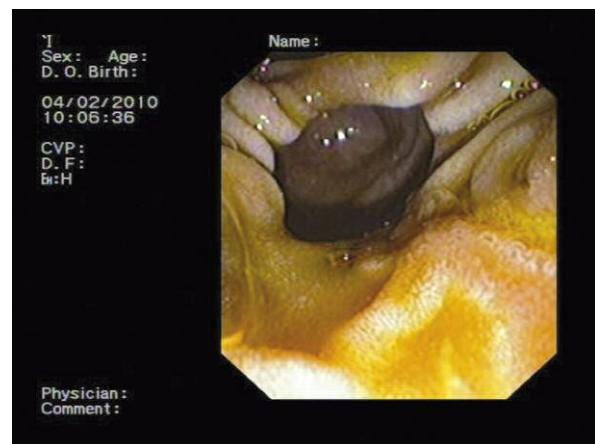


Fig. 2. Large diverticula

tween the groups in terms of cannulation technique or success ($p = 0.52$). There was also no difference between the groups in terms of the requirement for a second ERCP procedure ($p = 0.35$) (Table I).

The papilla was located at the edge of the diverticulum in 67 patients (62%), and within the diverticulum in 41 (38%). The size of the diverticulum was smaller than 2 cm in 90 patients (83.3%), and ≥ 2 cm in 18 (16.7%). Among the 18 patients with large diverticula, the papilla was located within the diverticulum in 12, and at the edge of the diverticulum in 6 ($p = 0.007$) (Table II).

There was no difference between the groups in terms of the number of CBD stones. Average stone diameter was larger in patients with diverticula compared with those without diverticula ($p = 0.001$), and the prevalence of stone impaction was higher (10.2% in group A vs. 3.1% in group B; $p = 0.003$) (Table I). Among patients with impacted stones, average size of stone was 15 ± 6 mm in group A and 22 ± 11 mm in group B patients ($p = 0.06$). There was no correlation between the size of stones and the diameter of diverticula or

location of papilla ($p = 0.174$ and $p = 0.7$, respectively) (Tables II and III).

Endoscopic stone removal was successful in 503 (86%) of the total 586 patients, and unsuccessful in 83 (14%) ($p = 0.134$). Treatment success was achieved in 415 patients (86.8%) in group A and 88 (81.5%) in group B, while attempts at stone extraction failed in 63 patients (13.2%) in group A and 20 (18.5%) in group B ($p = 0.15$). There was no correlation between success of endoscopic treatment and size of diverticula or location of papilla (81% in group I, 83% in group II; $p = 0.26$) (Table II). Endoscopic treatment was successful in 10 group A patients (67%) and 5 group B patients (45%) with impacted stones ($p = 0.25$) (Table III).

There was sphincterotome-related bleeding in 28 (4.7%) of the total 586 patients (20 (4.2%) in group A and 8 (7.4%) in group B; $p = 0.12$). No complications occurred in patients treated with the precut technique. There was no perforation. No correlation was determined between the risk of bleeding and size of diverticula or location of papilla ($p > 0.05$).

Table I. Comparison of patients with and without diverticula

Parameter	Group A	Group B	Value of p
Patients, n (%)	478 (82)	108 (18)	
Age, mean \pm SD [years]	62 \pm 17	74 \pm 11	< 0.001
Gender (M/F)	193/285	41/67	> 0.05
Cannulation success, n (%)	467 (97.7)	103 (95.4)	> 0.05
Cannulation type, n (%):			
Standard cannulation	471 (98.5)	106 (98.1)	> 0.05
Precut	7 (1.5)	2 (1.7)	> 0.05
Maximum stone diameter, mean \pm SD [mm]	12 \pm 7	15 \pm 8	< 0.01
Number of stones, n (%):			
1	253 (52.9)	49 (45.4)	> 0.05
2	66 (13.8)	17 (15.7)	> 0.05
3	34 (7.1)	8 (7.4)	> 0.05
> 3	125 (26.2)	34 (31.5)	> 0.05
Stone impaction, n (%)	15 (3.1)	11 (10.2)	< 0.01
Repeat ERCP, n (%):	92 (19.2)	30 (27.8)	> 0.05
Cannulation failure	11 (12)	5 (16.7)	> 0.05
Desaturation	5 (5.4)	0	> 0.05
Failure to extract stone	30 (32.6)	14 (46.7)	> 0.05
Residual stone	46 (50)	11 (36.7)	> 0.05
Complication (bleeding), n (%)	20 (4.2)	8 (7.4)	> 0.05
Treatment success, n (%)	415 (86.8)	88 (81.5)	> 0.05
Treatment failure, n (%)	63 (13.2)	20 (18.5)	> 0.05

Table II. Comparison of patient results according to size of diverticula

Parameter	Group I	Group II	Value of p
Patients, n (%)	90 (83%)	18 (17%)	
Age, mean \pm SD [years]	74 \pm 11	78 \pm 7	< 0.05
Gender (M/F)	36/54	5/13	> 0.05
Location of Papilla, n (%):			
Papilla at edge of diverticulum	61 (67.8)	6 (33.3)	< 0.01
Papilla within diverticulum	29 (32.2)	12 (66.7)	< 0.01
Size of stone, mean \pm SD [mm]	14 \pm 8	16 \pm 9	> 0.05
Stone impaction, n (%)	8 (8.8)	3 (16.6)	> 0.05
Cannulation type, n (%):			
Standard cannulation	90 (100)	16 (88.9)	> 0.05
Precut	0	2 (11.1)	
Treatment success, n (%)	73 (81)	15 (83)	> 0.05
Treatment failure, n (%)	17 (19)	3 (17)	> 0.05

Table III. Results of patients with stone impaction

Parameter	Group A	Group B	Value of p
Patients, n (%)	15 (3.1)	11 (10.2)	< 0.05
Age, mean \pm SD [years]	61 \pm 23	80 \pm 10	< 0.01
Gender (M/F)	4/11	5/6	> 0.05
Size of stone, mean \pm SD [mm]	15 \pm 6	22 \pm 11	> 0.05
Treatment success, n (%)	10 (67)	5 (45)	> 0.05
Treatment failure, n (%)	5 (33)	6 (55)	> 0.05

Discussion

Periampullary diverticula are usually acquired lesions. They are quite uncommon under the age of forty, and their prevalence increases with age. Advanced age contributes to the development of PD due to weakening of regional connective tissue [9]. A prevalence of 5-32% has been reported in patients undergoing duodenoscopy, and prevalence increases with age and with female gender [1, 4, 10]. In a study on 350 patients, Zoepf *et al.* reported a PD incidence of 12.5%, and higher average age of patients with PD compared to those without PD [3]. A study by Panteris *et al.* conducted on 601 patients reported a PD incidence of 20.7% and a mean age of 72 years [6]. In both studies, although PD was more prevalent in female patients, the difference was non-significant when compared with patients without PD. We also found a PD prevalence of 18.4% within our patient population, and the mean age of patients with PD was significantly higher than patients without diverticula ($p < 0.001$).

There is conflicting evidence regarding the impact of periampullary diverticula on the success of ERCP cannulation; some authors report an impact [11, 12], others a lack of impact [2, 6, 8, 13]. Lobo *et al.* reported a cannulation success rate of 62.4% in patients with PD, and 92.7% in those without PD [11]. In another study, the reported success rate was 95.4% in patients with PD, and 98.9% in patients without PD [3]. This difference might be attributed to the definition of treatment success (e.g., if failure to cannulate during the initial ERCP session was considered treatment failure or if alternative cannulation attempts such as the precut technique were not used). We determined that the presence of diverticula or the size of the diverticulum has no effect on cannulation success. In the majority of previously published studies, patient groups are not homogeneous [3, 6, 8]. Any condition invading the papilla (periampullary tumors, pancreatic cancer invasion, etc.) has a negative impact on cannulation success and increases the risk of procedure-related complications. We only enrolled patients in whom CBD stones had been diagnosed by non-invasive (ultrasonography or MRCP) or minimally invasive (EUS) methods, on whom ERCP had been performed. We believe that the team performing the ERCP procedures being highly experienced, the procedures being performed under sedative anesthesia administered by a specialist, as well as the diversity and adequacy of the equipment at hand (fine-tipped sphincterotome, thin guide wire, needle knife with and without guide, etc.), contributed to the similar and high rate of cannulation in both patient groups. Furthermore, the presence of diverticula might

result in the dysfunction of the sphincter of Oddi [14], which would reduce resistance against the sphincterotome, thereby enhancing cannulation success. Periampullary diverticula might affect cannulation success through anatomical damage to the location of the papillary ostium [3, 11, 12]. In the study by Zoepf *et al.*, the location of the papilla in patients with failed cannulation was inside the diverticulum in 62.5% and outside the diverticulum in 25% [3]. In another study, the location of the papilla was inside the diverticulum in 62% and outside the diverticulum in 22% of patients with failed cannulation [11]. We could not establish any correlation between the location of the papilla and cannulation success. The relatively high rate of cannulation success in our cohort might be attributed to the extra-diverticular location of the papilla in the majority of our patients. The location of the papillary ostium may differ according to the size of the diverticulum. This might inhibit deep cannulation by a standard sphincterotome, or restrict safe sphincterotomy after cannulation [7] since a large diverticulum or the papilla being located within a large diverticulum would theoretically make cannulation more difficult due to the luminal defect, and also facilitate sphincterotomy-related complications [2, 3, 7]. In the study by Zoepf *et al.*, papillary location was 54.9% within the diverticulum and 37.7% at the edge of the diverticulum, while the incidence of bleeding was 8.8% in the patient group and 4.8% in the control group ($p < 0.05$). In our study, there was no difference between the groups in terms of sphincterotomy-related bleeding ($p > 0.05$). This discrepancy might be attributed to the majority (62%) of our group B patients having an extra-diverticular papillary location. We could not establish a relationship between bleeding and the presence of diverticula, the size of the diverticulum or papillary location. We thus conclude that in patients undergoing ERCP for CBD stones, the presence of diverticula has no impact on procedure success or the development of complications.

Periampullary diverticula, besides creating external compression on the bile duct and thus inhibiting biliary drainage, cause bile stasis through anatomical dysfunction of the papilla or the sphincter of Oddi. This has a major impact on the development of CBD stones [11, 12, 14-19]. However, the size and impaction of stones are not specified in previously published studies. Large or impacted stones may in fact not only have an impact on the success of the procedure, but may also restrict endoscopic success through the prevention of complete stone removal. In the group with diverticula in our study, although both the rate of stone impaction and the average size of the largest stone was higher than the group without diverticula ($p < 0.01$), there was no difference

between the groups in terms of endoscopic treatment success ($p > 0.05$). Lobo *et al.* reported successful cannulation in the presence of biliary stones. In this study on 30 patients, 11 (36.6%) were treated surgically, 12 endoscopically, 6 were administered stents and 1 received no treatment [8]. In another recent study, 28 of 30 patients with choledocholithiasis and diverticula were treated endoscopically [8]. In our study, there was no difference between patient groups in terms of endoscopic treatment success ($p > 0.05$). The lower rate of treatment failure in our study, besides the experienced ERCP team, might be due to developments in equipment used for stone extraction with ERCP and the increased availability of this equipment.

Conclusions

Periampullary diverticula have a major impact on the formation of choledocholithiasis, and in the increase in size or impaction of existing stones. However, the presence of periampullary diverticula in patients with biliary stones does not affect the success of ERCP, the prevalence of procedure-related complications, or the rate of endoscopic treatment success in the hands of experienced physicians. The negative impact of periampullary diverticula on the therapeutic procedure might be related to the increased incidence, and comorbidities, with age.

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