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Complications increase in which type of duodenal diverticulum? A retrospective cohort study

Hangi duodenal divertikül tipinde komplikasyonlar artar? Retrospektif kohort çalışma

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Abstract

Aim: In endoscopic retrograde cholangiopancreatography (ERCP), a diverticulum increases complications such as perforation and pancreatitis. We must know which type of diverticulum increases the complications to develop a strategy. The aim of this study is to examine the safety of the ERCP procedure in terms of diverticulum types.

Methods: A total of 864 patients aged 65 years and over who underwent ERCP from January 2010 to November 2019 were identified and analyzed in this retrospective cohort study. Demographic findings, indications, successful cannulation rates and complications were compared between groups with and without duodenal diverticula.

Results: Of the patients who underwent ERCP, 56.4% were female. The mean age of all patients was 77.39 (65-90) years. The most common indications were common bile duct stones (92.1%). Other indications included cholangitis (1.4%), sphincter Oddi dysfunction (1.6%), pancreatitis (2.1%), Mirizzi syndrome (2.7%), postoperative gallbladder fistula (0.7%), periampullary tumor formation (0.57%) and biliary stenosis (0.23%). Among all patients, 848 (98.1%) had no complications, 2 (0.34%) developed pancreatitis, 1 (0.17%) developed cholangitis and bleeding occurred in 1 (0.17%) patient in the group without a duodenal diverticulum. Among patients with a type I diverticulum, 4 (12.9%) had pancreatitis and 3 (9.6%) had bleeding. One patient (1.16%) had pancreatitis, 1 (1.16%) had cholangitis and 2 (2.33%) had bleeding among the type II group, while in the type III group, 1 (0.64%) had pancreatitis and 1(0.64%) had a perforation. Mortality was seen in 2 (0.23%) patients. A total of 5 (0.57%) periampullary tumors were detected in the study.

Conclusion: Our study revealed that patients with a duodenal diverticulum experience more complications than the normal population. Among them, the rate is insignificantly increased in those with a type I duodenal diverticulum. Further studies are needed on this subject.

Keywords: Endoscopic retrograde cholangiopancreatography, Duodenum, Diverticulum, Pancreatitis

Öz

Amaç: ERCP prosedüründe divertikül oluşumu perforasyon ve pankreatit gibi komplikasyonları artırır. Hangi tip divertikülün komplikasyonları artırdığını bilmeli ve bunun için bir strateji geliştirebilmeliyiz. Bu çalışmanın amacı, ERCP işleminin güvenliğini divertikül türleri açısından incelemektir.

Yöntemler: Ocak 2010'dan Kasım 2019'a kadar ERCP prosedürü uygulanan 65 yaş ve üstü 864 hasta retrospektif bir kohort çalışmasında belirlendi ve analiz edildi. Duodenal divertikülü olan ve olmayan gruplar arasında demografik bulgular, endikasyonlar, başarılı kanülasyon oranları ve komplikasyonlar karşılaştırıldı.

Bulgular: ERCP uygulanan hastaların %56,4'ü kadındı. Tüm hastaların ortalama yaşı 77,39 (65-90) yıldı. En yaygın endikasyonlar %92,1 ile safra kanalı taşlarıdır. Diğer endikasyonlar arasında %1,4 kolanjit, %1,6 sfinkter Oddi disfonksiyonu, %2,1 pankreatit, %2,7 Mirizzi sendromu, %0,7 postoperatif safra kesesi fistülü, %0,57 periampullar tümör oluşumu ve %0,23 ile safra darlığıdır. 864 hastanın 848'inde (%98,1) komplikasyon görülmedi. Duodenal divertikülü olmayan grupta 2 (%0,34) pankreatit, 1 (%0,17) kolanjit ve 1 (%0,17) kanama meydana geldi. Tip I grupta 4 (%12,9) hastada pankreatit ve 3 (%9,6) hastada kanama görüldü. Tip II grupta 1 (%1,16) hastada pankreatit, 1 (%1,16) hastada kolanjit ve 2 (%2,33) hastada kanama meydana geldi. Tip III grupta 1 (%0,64) hastada pankreatit ve 1 (%0,64) hastada perforasyon gelişti. Mortalite 2 (%0,23) hastada görüldü. Çalışmada toplam 5 (%0,57) hastada periampuller tümör tespit edildi.

Sonuç: Sonuç olarak, bu çalışmada duodenal divertikülü olan hastaların normal popülasyona göre daha fazla komplikasyon yaşadıkları gösterilmiştir. Ancak duodenal divertikül tipleri arasında özellikle tip 1 duodenal divertikülü olanların daha fazla komplikasyon yaşadığı görüldü, ancak istatistiksel olarak anlamlı değildi. Bu durum bize bu konuda yeni çalışmalara ihtiyaç olduğunu gösteriyor.

Anahtar kelimeler: Endoskopik retrograd kolanjiyopankreatografi, Duodenal, Divertikül, Pankreatit

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Introduction

A periampullary duodenal diverticulum (PAD) is a clinico-anatomic formation with the papillae residing at the edge of or within a 2.5 cm radius around the diverticulum in the duodenum. Although this formation is found incidentally in radiological imaging studies, it may present many difficulties in ERCP due to its pathological status. Various publications have shown that PAD causes many diseases including common bile duct (CBD) stones due to its anatomic character. In studies dealing with PAD, it is found in 9-32.8% of the patients. The wide range indicates the heterogeneity of the study group [1]. Boix et al. [2] divided the PAD into types based on its anatomic position: The ones where the papillae are inside the diverticulum are Type I (Figure 1), the ones where the papillae reside on the edge of the diverticulum are Type II (Figure 2) and the ones with papillae located around the diverticulum are Type III (Figure 3).

Figure 1: Image of papillae within the diverticulum (Type I)

Figure 2: Papillae at the edge of the diverticulum (Type II)

Figure 3: Papillae located around the diverticulum (Type III)

Panteris et al. [3] have classified PAD according to whether the papillae are within the diverticulum. According to their study, the Type II and Type III groups, stated by Boix et al. [4], constitute Type A, and Type I constitutes Type B. ERCP is an invasive procedure for the treatment of biliary and pancreatic disorders rather than diagnosis. This procedure is known to carry many complication risks, such as pancreatitis, bleeding, and perforation, all of which may lead to serious mortality, especially in elderly patients [5]. However, given the benefits of ERCP, which removes the need for surgery and reduces the burden of various interventions on the patient, it is an indispensable procedure, especially in cases requiring CBD intervention [6].

The aim of this study is to investigate demographic findings, indications, successful cannulation rates and post-ERCP complications according to diverticulum types.

Materials and methods

A total of 864 patients who were referred to the ERCP endoscopy unit between January 2010 and November 2019 were retrospectively analyzed. Among them, 273 patients (31.5%) had a periampullary diverticulum in the duodenum, 31 of which were Type I, 86 were Type II, and 156 were Type III. Demographic findings, indications, successful cannulation rates and complications were investigated among these groups. All patients included in the study signed a consent form prior to the ERCP procedure.

Prophylactic antibiotics were routinely administered to all patients prior to ERCP procedures. ERCP was performed under sedation with topical 10% Xylocain® (lidocaine, AstraZeneca, Cambridge, Britain) followed by intravenous Aldolan® (pethidine HCl, G.L. Pharma GmbH, Lannach, Austria) and Dormicum® (midazolam, Roche, Basel, Switzerland). Buscopan® (Hyposin-N-butyl bromide, Boehringer Ingelheim, Ingelheim, Germany) was used to reduce intestinal peristalsis. After papillary cannulation, contrast material was injected. Endoscopic sphincterotomy was performed in both groups.

Bleeding was defined as at least a two-point decrease in hemoglobin, with no other source of bleeding in endoscopy. Acute pancreatitis was defined as a three-fold increase in lipase value in the patient's biochemical tests after ERCP. Cholangitis was defined as the occurrence of Charcot triad (pain, fever, jaundice).

This study was approved on 3/11/2020 by the Ministry of Health Istanbul Medeniyet University Göztepe Training and Research Hospital Clinical Research Ethics Committee with the decision numbered 2013-KAEK-64.

Statistical analysis

Chi-square test or Fisher's exact test were used for statistical analysis of categorical data. Ratios were calculated in 95% confidence. All data analyses were performed using SPSS statistical software program, version 19.0 Windows (SPSS Inc., Chicago, IL, USA). $P<0.05$ was considered statistically significant.

Results

Among the included 864 patients over 65 years of age who underwent ERCP, 487 (56.4%) were female and 377 (43.6%) were male. The mean age of all patients was 77.39 (65-90) years, 77.35 years among patients without a diverticulum, 76.71 years in the type I group, 77.63 years in the type II group and 77.56 years in the type III group.

CBD stones (92.1%) were the most common indication in all patient groups included in the study. These patients presented with a low rate (1.4%) of cholangitis. Other indications included sphincter Oddi dysfunction (1.6%), pancreatitis (2.1%), biliary compression due to acute cholecystitis (Mirizzi syndrome) (2.7%), postoperative gallbladder fistula (0.7%),

periampullary tumoral formations (0.57%) and biliary tract stenosis (0.23%).

Cannulation was performed with sphincterotome in 563 (95.2%) of 591 patients without a diverticulum, 28 (90.3%) of 31 type I patients, 76 (88.3%) of 86 type II patients and 144 (92.3%) of 156 type III patients. In a total of 53 (6.1%) patients, cannulation was tried with pre-cut. In the first pre-cut trial, 31 of these patients were successfully cannulated. After 3 days of rest (the regression of the edema in the papillae was expected), 16 of the non-cannulated patients were cannulated so that a total of 49 (5.6%) patients were cannulated. In 26 patients without a diverticulum, 2 patients in type I group, 10 patients in type II group, and 11 patients in type III group were cannulated with pre-cut (Table 1).

Table 1: Selective and pre-cut cannulation success between the non-duodenal diverticulum and the type I, type II and type III groups with duodenal diverticulum

Cannulation success	Non diverticulum n (%)	Type I n (%)	Type II n (%)	Type III n (%)	Total n (%)
Selective cannulation	563 (95.2%)	28 (90.3%)	76 (88.3%)	144 (92.3%)	811 (93.8%)
Unsuccessful	2 (0.33%)	1 (3.22%)	0	1 (0.64%)	4 (0.46%)
Pre-cut success	26 (4.39%)	2 (6.45%)	10 (11.7%)	11 (7.05%)	49 (5.6%)
Total	591	31	86	156	864

In two patients in the non-duodenal diverticulum group, pre-cut cannulation could not be performed. One of these patients had cholangitis. The patient underwent choledochal exploration under antibiotherapy as an open surgical procedure. The patient was mortal in the postoperative period due sepsis. The other patient had facet stones up to 2 cm in size. Since the stones of this patient could not be broken with a stone crushing device, the patient underwent open surgery. Choledochal exploration and T tube placement was performed and the patient was discharged with surgical recovery.

Pre-cut cannulation was unsuccessful in one patient in type I group. This patient developed bleeding during the procedure and underwent emergency exploration because the bleeding could not be controlled by saline with adrenaline, balloon compression and coagulation with electrocautery. Duodenotomy was performed to control the bleeding and the pathology of the common bile duct was intervened. Postoperative period was uneventful, and the patient was discharged.

Pre-cut cannulation failed in one patient in the type III group. This patient had a periampullary tumor, developed perforation during ampullectomy and was immediately operated. Hepaticopancreaticojejunostomy was performed. In the postoperative period, the patient died due to pulmonary embolism despite anticoagulant therapy.

No complications were encountered in 587 (99.3%) of 591 patients (patients without a duodenal diverticulum). Two (0.34%) had pancreatitis, 1 (0.17%) had cholangitis and 1 (0.17%) had bleeding. One of the patients who developed pancreatitis had edematous pancreatitis, which regressed with medical treatment. Necrotizing pancreatitis progressed in the follow-up of the other patient with pancreatitis. The patient remained under long-term follow-up, and percutaneous catheter drainage was applied when abscess developed. Since the patient who developed cholangitis could not be cannulated, she was operated immediately but died in the postoperative period due to sepsis. Balloon compression was applied to the bleeding patient during the procedure and bleeding was controlled.

Of the 31 patients in the type I group, 24 (77.4%) had no complications. In this group, 4 (12.9%) patients had pancreatitis and 3 (9.6%) had bleeding. A patient who developed bleeding was urgently operated. Bleeding of the other two patients was controlled by saline irrigation with adrenaline and balloon compression. Contrast injection was not applied to the pancreatic duct of the other three patients except one. Pancreatic cannulation was performed with a standard sphincterotome in these patients. Edematous pancreatitis developed in these patients and regressed with medical treatment.

In the type II group, 83 (96.5%) of 86 patients had no complications. 1 (1.16%) had pancreatitis, 1 (1.16%) had cholangitis and 2 (2.33%) had bleeding. Among these patients, edematous pancreatitis developed in the patient with pancreatitis and his clinical condition regressed with medical treatment. Adrenaline saline irrigation and balloon compression were applied to the patients with bleeding complications. In one of these patients, blood pressure increased due to usage of excessive adrenaline solution during the procedure, the procedure was postponed, and cannulation was achieved 3 days later. Another patient developed cholangitis after pre-cut and underwent ERCP. However, Sump Syndrome occurred, and food residues were cleaned from the CBD and a stent was placed. The patient was discharged uneventfully 1 month after stent withdrawal.

Among 156 patients in type III group, only two patients developed complications. Pancreatitis and perforation developed in 1 (0.64%) patient each. Pancreatitis regressed with medical treatment. Perforation occurred during the ampullectomy procedure in a patient with ampullary tumoral mass and the patient was taken to operation immediately.

Of the 864 patients, 848 (98.1%) had no complications, 8 (0.93%) had pancreatitis, 6 (0.69%) had bleeding, 2 (0.23%) had cholangitis and 1 (0.12%) had perforation. The frequency of complications in the group with duodenal diverticula (Type 1, type 2, and type 3) was significantly higher compared to the group without ($p<0.001$). Mortality was seen in 2 (0.23%) patients for reasons explained above (Table 2).

Table 2: Prevalence of complications between the group without duodenal diverticulum and type I, type II and type III groups with duodenal diverticulum

Complication	Non diverticulum n (%)	Type I n (%)	Type II n (%)	Type III n (%)	Total n (%)
Pancreatitis	2 (0.34%)	4 (12.90%)	1 (1.16%)	1 (0.64%)	8 (0.93%)
Bleeding	1 (0.17%)	3 (9.68%)	2 (2.33%)	0 (0.00%)	6 (0.69%)
Cholangitis	1 (0.17%)	0 (0.00%)	1 (1.16%)	0 (0.00%)	2 (0.23%)
Perforation	0 (0.00%)	0 (0.00%)	0 (0.00%)	1 (0.64%)	1 (0.12%)
No complications	587 (99.32%)	24 (77.42%)	83 (96.51%)	154 (98.72%)	848 (98.15%)
Total	591(100.00%)	31(100.00%)	86(100.00%)	156(100.00%)	864(100.00%)

Pearson Chi Square, $P<0.001$

We observed that the incidence of complications increased significantly in patients with a duodenal diverticulum. When we asked the question of whether the likelihood of complications would be different according to the types, we found that pancreatitis and bleeding complications were higher in the Type I group than the other groups and the population without diverticula. However, the number of patients was insufficient for statistical evaluation.

A total of 5 (0.57%) periampullary tumors were detected in the study, 3 patients (0.5%) of which belonged to the non-duodenal diverticulum group and 2 (1.2%), to the type III group.

Discussion

In the previously published studies, the results were affected by the significant heterogeneity. Therefore, in this study, homogeneity was aimed for, comparing patients over 65 years of age with diverticula [7].

In their study, Tham and Kelly [8] reported that the rates of mortality, morbidity and successful cannulation following ERCP between patients with and without PAD were highly similar, which contradicted with our results. They also confirmed that localization of the Vater ampulla near only one diverticulum significantly increased the incidence of stone in the bile duct. Choledocholithiasis was found in 64% of patients with diverticula and 33% of patients without. Zoepf et al. [9] reached similar results. In their studies, 46% CBD stones were found in the diverticulum group and 33% in the diverticulum-free group. In our study, CBD stones were the most common indication with a rate of 92.1%. Other indication rates were similar to those of other studies [10].

The selective cannulation of the bile duct is main step for a successful ERCP and the prerequisite to get maximum benefit. Despite advances and new developments in endoscopic accessories such as endoscopic instruments, selective biliary cannulation fails in %5-15 of cases, even in expert, high-volume centers [11]. Repeating ERCP within a few days of the first failed pre-incision reduces the risk of complications by reducing the edema of the papilla and increases the chance of cannulation [12-15]. In our study, cannulation was performed with a sphincterotome in 563 (95.2%) of 591 patients without diverticula, 28 (90.3%) of 31 type I patients, 76 (88.3%) of 86 type II patients and 144 (92.3%) of 156 type III patients. In a total of 53 (6.1%) patients, cannulation was tried with pre-cut. In the first pre-cut trial, 31 of these patients were successfully cannulated. After 3 days of rest (regression of the edema in the papillae was expected), 16 of the non-cannulated patients were cannulated so that a total of 49 (5.6%) patients were cannulated.

In the study of Ketwaroo et al. [16] on 1325 patients, it was concluded that the formation of a diverticulum does not make a difference in cannulation success during ERCP. However, in many studies, it was concluded that the presence of a diverticulum is one of the difficult cannulation criteria which reduces cannulation success rates. In these studies, the success rates for ERCP in the presence of diverticulum were between 61-97.2% [17]. The European Gastrointestinal Endoscopy Society has suggested that selective cannulation may not be sufficient in patients with a duodenal diverticulum and advanced procedures such as pre-cut can be limited [18].

Duodenal diverticula are incidental unless they become symptomatic. If they affect the biliary tract, they can cause many complications such as biliary obstruction, cholangitis, pancreatitis, bleeding, and perforation. It was thought that the mechanical stress of the Oddi sphincter diverticulum and bacterial growth were effective in the formation of these complications [19]. In our study, complication rates were significantly increased in patients with duodenal diverticula.

Among the general population, the most common complication associated with ERCP is pancreatitis with an incidence of 1.3-30%. Although multiple risk factors for pancreatitis have been reported after ERCP, predisposing factors include the vast usage of contrast agent, multiple cannulation attempts and manipulations in the pancreatic duct [20].

There are different views on the association of PAD with pancreatitis. Some investigators have suggested that pancreatitis is not associated with PAD. Others have reported a higher rate of acute pancreatitis in patients with PAD [21]. In our study, we found significantly higher complication rates in PAD patients compared to non-PAD patients. In addition, patients with type I PAD have higher complication rates than patients with type 2 or type 3 PAD. In their study, Sun et al. suggested that the papillae residing within the diverticulum may compress the pancreatic duct to cause pancreatitis [22]. In our study, 848 (98.1%) of 864 patients had no complications, 8 (0.93%) had pancreatitis, 6 (0.69%) had bleeding, 2 (0.23%) had cholangitis and 1 (0.12%) had perforation.

Gastrointestinal bleeding most commonly occurs after endoscopic sphincterotomy and its incidence is estimated to be between 5% and 30% [23]. In some studies, the incidence of bleeding in elderly patients undergoing ERCP was not high [24]. In our study, especially in patients with type I PAD, the bleeding complication was high. Two of these were intervened endoscopically, and the other patient was taken into surgery emergently.

Digestive system perforation is a rare but serious complication of ERCP. Its occurrence depends on the anatomy of the distal segment of the common bile duct and the length of the major duodenal papillotomy. Procedures susceptible to this complication include Billroth II gastrectomy, endoscopic sphincterotomy, intraluminal injection of contrast material, and dilation of the bile duct stenosis [25]. Conservative treatment is sufficient in most studies [26]. In our study, perforation occurred during an ampullectomy procedure in a patient with a periampullary tumor and a stent was placed because of the tumor component and it was thought that conservative follow-up would not be appropriate.

In their study, Sun et al. [27] presented a negative correlation between the presence of a PAD and periampullary carcinoma prevalence, a finding which had not been reported previously in the literature. In another study from Korea, it was found that the risk of cancer increased in the region affected by the diverticulum. However, in our study, a similar number of periampullary tumors were detected in patients with and without diverticula. Therefore, it is not possible to mention a statistically verifiable relationship between a diverticulum and cancer. However, we believe that the presence of a periampullary tumor in the group farthest from the diverticulum will support the opinion of Sun et al.

Death from ERCP is rare (less than 0.5%) and is mostly associated with cardiopulmonary complications. Although advanced age is thought to be one of the common factors increasing risk, multivariate analyses do not support this idea [28]. Two (0.23%) patients also died in our study; the mortality of both were due to ERCP-independent factors.

Strengths and limitations

The strengths of the study are that the use of pre-cut sphincterotomy according to routine ERCP procedures is routinely performed in patients who cannot undergo standard sphincterotomy, and the expectation for reduction of the

papillary edema increases the chances of a sphincterotomy and reflects on the results.

Considering the limitations of the study, percutaneous transhepatic cholangiography (PTC) can be performed in the presence of interventional radiology in patients whose bile ducts cannot be intervened, to regress and treat the patient's disease. However, it is not applied in our hospital. Also, we think that further, larger studies are needed to investigate complication rates between duodenal diverticulum types.

Conclusions

Our study revealed that patients with a duodenal diverticulum experience more complications than the normal population. The rate is insignificantly increased in those with a type I duodenal diverticulum. Further studies are needed on this subject.

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