Comparison of the procedure results of ectopic papillae encountered during ERCP procedure with the procedure results of papillae with normal localization

Abstract

Background/Aim: In Endoscopic retrograde cholangiopancreatography (ERCP), Ampulla of Vater is found on the posteromedial wall of the second part of the duodenum. However, ectopic expansion of the common bile duct to the 3rd or 4th part of the duodenum or the proximal stomach, pylorus, or bulb was reported in the literature. This study primarily aims to investigate the risk of complications in patients with ectopic papillae and evaluate the applicability of endoscopic sphincterotomy in these patients.

Methods: In this a case-control study, the data of 3,048 patients who underwent ERCP procedure in the ERCP unit of our clinic between January 2013 and December 2018 were retrospectively analyzed, and 30 patients with ectopic bulbar papillae and 30 randomly selected patients with normally localized papillae were compared in terms of age, gender, duration of the procedure, post-procedural biochemical tests, cannulation success, precision rate, post-procedural pancreatitis complications and the need for analgesics. Power analysis was performed with the G*power 3.1.9.7 package program (1-B = 0.95, alpha = 0.05). With a power of 0.954, the sample size to be reached was thirty-three for each group.

Results: The rate of pancreatitis complications was higher in patients with ectopic bulb papillae (50%) compared to those without (16.7%) (P=0.006). Even though the rate of pre-cut was higher in patients with ectopic bulb papillae (33.3%) compared to patients with normally localized papillae (13.3%), this difference was not statistically significant (P=0.063). Cannulation success in patients with ectopic bulb papillae (83.3%) was insignificantly lower than in patients with normally localized papillae (90.0%) (P=0.353). The need for both narcotic and non-steroidal anti-inflammatory analgesics was higher in patients with ectopic bulb papillae (P<0.001, P=0.005, respectively).

Conclusions: It should be kept in mind that ectopic biliary drainage may be found in an alternative location when no papillae are observed in the expected anatomical region. The complication risks, including pancreatitis, are increased in the intervention of ectopic papillae. Novel studies showing that endoscopic sphincterotomy and pre-cut are successfully used in patients with ectopic papillae are needed.

Keywords: Endoscopy, Endoscopic Retrograde Cholangiopancreatography (ERCP), Ectopic papilla, Pancreatitis
Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a method of imaging the canals that drain the gallbladder, liver, and pancreas with the help of a duodenoscope, contrast agent, and X-rays. Ampulla of Vater is endoscopically visualized; bile ducts and pancreatic ducts are cannulated. Thus, liver, gallbladder, pancreas, bile, and pancreatic duct pathologies can be diagnosed, and problems within the ducts can be intervene with therapeutic approaches [1,2].

Ampulla of Vater is found on the posteromedial wall of the second part of the duodenum. The common bile duct, on the other hand, extends down the medial wall of the descending part and opens into this part. However, ectopic expansion of the common bile duct to the 3rd or 4th part of the duodenum or the proximal stomach, pylorus, or bulb was reported in the literature [3-5].

Cannulation of the ectopic papillae is difficult during ERCP as it is quite far away from the duodenoscope. In this case, operating in a long position would be the most appropriate solution. ERCP is difficult in these patients and requires high endoscopic skills, experience, and familiarity with these cases. There are studies showing that sphincterotomy is risky in these cases because it causes complications such as perforation and bleeding. Therefore, it can be intervened using a choledochal balloon after dilatation [6].

The ERCP procedure results of thirty patients with ectopic bulbar papillae who were diagnosed with choledocholithiasis in our clinic were compared with those performed in patients with normally located papillae. Endoscopic sphincterotomy was performed to patients with ectopic bulbar papillae using pre-cut when necessary, not balloon dilatation, and the results of the procedure were compared.

This study primarily aims to investigate the risk of complications, which are reportedly increased in patients with ectopic papillae and evaluate the applicability of endoscopic sphincterotomy in patients with ectopic papillae.

Materials and methods

The results of 3,048 patients who underwent ERCP in the ERCP Unit of the General Surgery Department of the Medical Faculty Hospital between January 2013 and December 2018 were retrospectively analyzed. Thirty patients with ectopic bulbar and thirty with normally localized papillae were randomly selected among them.

Only patients with choledocholithiasis were included in the study and those younger than 18 years of age, who could not tolerate general anesthesia, patients with acute pancreatitis, cholecystitis, empyema, portal hypertension, malignancy, bleeding disorders, and those who underwent upper gastrointestinal surgery (such as subtotal gastrectomy) were excluded from the study.

Examination of patient files revealed that similar anesthesia protocols were used during the procedures. All procedures were performed by the same general surgeon.

Thirty patients with ectopic bulbar papillae and thirty randomly selected patients with normally localized papillae were compared in terms of age, gender, duration of the procedure, post-procedural biochemical tests (Alanine transaminase-ALT, Aspartate aminotransferase-AST, Amylase, Gamma-glutamyl transferase-GGT), cannulation success, postprocedural pancreatitis complications, and the need for analgesics. Amylase value being three times higher than normal and typical abdominal pain were considered sufficient criteria for pancreatitis.

Ethics committee approval

The Ethics Committee of Afyonkarahisar Health Sciences University Medical Faculty approved this study with the decision of the General Surgery Department Board dated 05.07.2019 and numbered 244, and a signed informed consent form was obtained from all patients.

Statistical analysis

The power analysis of the study was performed with the G*power 3.1.9.7 package program. (1-B = 0.95, alpha = 0.05). With a power of 0.954, and the sample size to be reached was thirty-three for each group.

The data were registered into an Excel document, transferred to the IBM SPSS 23 program, and evaluated with proper statistical methods. Data checks were performed to prevent data entry errors before continuing to analysis. The normality assumption of continuous variables was examined, and analyses were performed according to whether the normality assumption was met.

Categorical variables were given as frequency and percentage while continuous variables were presented as mean, standard deviation, and minimum-maximum. Independent samples and Mann-Whitney U tests were used to compare normally and non-normally distributed continuous two-level variables, respectively. The relationships between categorical variables were examined by the Chi-square analysis/Fisher's exact test. The significance level was accepted as $P < 0.05$ in all analyses.

Results

A total of sixty patients, thirty with ectopic bulbar papillae and thirty with normally localized papillae were included in the study. Of all patients, thirty-one were female (51.7%) and twenty-nine (48.3%) were male. Among those with ectopic and normally localized papillae, fourteen (46.6%) and seventeen (56.6%), respectively, were females.

The mean and standard deviation values of the treatment duration, age, and biochemical parameters of the patients included in the study were presented in Table 1. The age range of all patients varied between 32 and 93 years, the mean age was 66.08 (15.96) years. The duration of the procedure varied between 21 and 76 minutes, with a mean of 47.62 (12.85) minutes.

The mean GGT, ALT, AST and amylase levels of all patients were 153.47 (85.89) U/L, 70.68 (59.70) U/L, 79.18 (66.21) U/L, and 315.33 (444.34) U/L, respectively.

Frequencies and percentages of patients in terms of cannulation success, pre-cut rate, postprocedural pancreatitis complications, and the need for analgesics were presented in Table 2. Twenty (33.3%) patients had pancreatitis complications, 14 (23.3%) patients underwent pre-cut, cannulation was successful in 52 (86.7%), 26 (46.3%) patients needed narcotic...
The papilla of Vater typically enters through a 1 cm to 2 cm-long intramura l tunnel inclined posteromedial to the second part of the duodenum. It sometimes may open abnormally, including the stomach [7-9], the pyloric canal, the duodenal bulb [10-13], and the third or fourth part of the duodenum [14]. We conducted a retrospective cohort study comparing patients with ectopic papillae opening to the duodenal bulb, which is the most common ectopic site in our clinic, with patients with normally localized papillae.

The rate of abnormal opening of the common bile duct is reported as 5.6%-23% due to a limited number of cases in rare studies on the extrahepatic biliary tree [4,5,11].

Lurje reported that the papilla opened to the third part of the duodenum in 16 (8.26%) of 194 autopsy cases [15]. Lindner et al. found that in 17.9% of 1,000 patients who underwent intraoperative cholangiography, the papilla of Vater opened to the distal second part of the duodenum, the third part of the duodenum, or the fourth part of the duodenum [14]. Dowdy et al. found that the distance between the papilla of Vater and pyloric sphincter was less than 5 cm in 4 of 100 autopsy cases [16].

The etiology of this abnormal opening is unknown, but there are opinions that developmental errors during embryogenesis may be a causal factor. The liver originates from the hepatic diverticulum, and it forms the cranial part (pars hepatica), the intrahepatic and common hepatic ducts as well as the caudal part (pars cystica), gallbladder, and cystic ducts [17]. The most accepted hypothesis about the ectopic opening of the common bile duct was explained by Boyden. According to this hypothesis, if the lower cleft occurs too early in the first weeks of embryogenesis, pars hepatica develops into a duct draining into the pyloric region by leaving the stomach above the growth region which separates it from the duodenum [18].

In the literature, more than 80% of the cases with ectopic biliary drainage were male. In the study conducted by Saritas et al. [19], 90% of the patients were male. Similar findings were reported in the studies of Guerra et al. [20], Sung et al. [21], and Ersöz et al. [22], which suggests an etiological relationship with embryonic abnormality caused by the Y chromosome. However, this can also be observed in female patients, like the female patient with ectopic papilla opening to the pyloric part of the stomach in the study by Nasserimoghadam et al. [23]. Also, in the study of Sezgin et al. [24], 5 of 11 patients with ectopic papillae were females. Of the patients with ectopic bulbar papillae in our study, fourteen were female (46.6%). Contrary to earlier studies, there was no difference in terms of gender between patients with ectopic and normally localized papillae.

In the studies of Sezgin et al. [24], Disibeyaz et al. [6], and Saritas et al. [19], the age ranges of the patients were 42-87 years, 36-78 years, and 38-74 years, respectively, with median ages of 59.2 years, 55 years, and 54 years, respectively. In our study, patients with ectopic bulbar papillae were between 33 and 90 years of age, and their mean age was 62.33 years.

Earlier studies focused on the indications for the procedure of patients with ectopic papillae, the largest series of ectopic opening were reported by Lee et al. [10], and most patients in this series had choledocholithiasis or cholangitis. The

Table 3: Comparison of biochemical parameters of patients with ectopic bulbar papillae and patients with normally localized papillae

<table>
<thead>
<tr>
<th>Clinical Conditions</th>
<th>Patients with ectopic bulbar papillae</th>
<th>Patients with normally localized papillae</th>
<th>χ²</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreatitis</td>
<td>No (25.8%)</td>
<td>15 (50)</td>
<td>7.50</td>
<td>0.006</td>
</tr>
<tr>
<td></td>
<td>Yes (5.16%)</td>
<td>15 (50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Precut rate</td>
<td>No (26.86%)</td>
<td>20 (66.7)</td>
<td>3.35</td>
<td>0.063</td>
</tr>
<tr>
<td></td>
<td>Yes (4.13%)</td>
<td>10 (33.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cannulation success</td>
<td>No (3.10)</td>
<td>5 (16.7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Yes (27.90)</td>
<td>25 (83.3)</td>
<td>0.57</td>
<td>0.353</td>
</tr>
<tr>
<td>The need for narcotic analgesics</td>
<td>No (25.83)</td>
<td>9 (30)</td>
<td>17.38</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Yes (5.167)</td>
<td>21 (70)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Need for nonsteroidal analgesics</td>
<td>No (11.36)</td>
<td>2 (6.7)</td>
<td>7.95</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Yes (19.63)</td>
<td>28 (93.3)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

χ²: Chi-square analysis, P<0.05.
most common indication for ERCP in patients with ectopic papilla was choledocholithiasis in the study conducted by Sezgin et al. [24]. Other indications included acute pancreatitis, common bile duct dilatation, extrahepatic cholestasis, cholangitis, and complications of bile fistula and laparoscopic cholecystectomy. Cholangitis was detected in 59% of the patients in the study conducted by Disibeyaz et al. [6]. The patients included in our study had choledocholithiasis, the most common indication in the literature.

One of the parameters we evaluated, unlike the other studies, is the duration of the procedure, which was significantly longer in patients with ectopic papillae. This may be due to technical reasons such as the examination of the area of the duodenum up to the bulb region, a long-axis approach to the ectopic papilla, and difficult cannulation during deciding the localization of the papilla.

Another important parameter in the study is the biochemical tests in the follow-up of patients after the ERCP procedure. AST, ALT, GGT values were significantly, and amylase values were insignificantly higher compared to those of patients with normally localized papillae. These biochemical parameters are directly proportional to pancreatitis. Elevated levels of ALT and GGT were present in fifty-two patients (97%) before the procedure [6]. However, there are no studies in the literature comparing biochemical parameters after the procedure, and our study can be presented as a pioneering study in this field.

Patients with ectopic papillae are difficult to cannulate [25-28]. Disibeyaz et al. [6] successfully removed stones in 59% of the patients with stones in the common bile duct when compared with another study involving ectopic bulb papilla series. In our study, no statistically significant difference was found in terms of choledochal cannulation. Our study also shows that choledochal cannulation can be performed successfully in patients with ectopic papillae.

Pancreatitis developed in five patients with normally localized papillae, and in fifteen patients with ectopic bulb papillae. This parameter is directly proportional to the high amylase test result after the procedure in patients with ectopic bulb papillae. The higher incidence of the need for NSAIDs and narcotic analgesics in patients with ectopic bulb papillae after the ERCP procedure is also related. Cannulation was tried in four patients with normally localized papillae via pre-cut while the common bile duct was cannulated with the help of a pre-cut procedure in ten patients with ectopic bulb papillae. Our study shows the usability of the pre-cut procedure in ectopic papillae cases. Besides, duodenal biliary reflux and stasis are significantly seen in patients with ectopic papillae due to the loss of the inclined course of the pancreatic duct and common bile duct in the duodenal wall. Not only gastric juice, but also pancreatic juice and bile juice can contribute to recurrent peptic ulcers [21]. There is a need for studies on peptic complaints in these patients.

It has been suggested that there is a slit-like opening that does not have a sphincteric structure at the entrance of the choledochal duodenum in patients with ectopic papillae, and sphincterotomy carries a significant risk of difficulty and retro duodenal perforation in these cases [29,30]. However, perforation was not encountered in patients undergoing choledochal cannulation and pre-cut in this study. Retropertitoneal perforation occurred in the intrapancreatic segment of the common bile duct after dilatation of the common bile duct with a 12 mm balloon in the study by Ersoz et al. [22], and perforation and bleeding occurred during sphincterotomy in one patient in the study by Disibeyaz et al. [6]. Dacha et al. [31] suggest that a regular, a forward viewing gastroscope should be used to visualize the stomach better, and no major sphincterotomy should be performed due to the substantial risk of perforation.

**Strengths and limitations**

Since ectopic papillae is a rare entity, the study could not be conducted with more patients, despite power analysis calculations showing that thirty-three patients were needed in each group.

Strengths of the study were the referral of multiple ERCP procedures from various hospitals to our tertiary hospital, so we had the opportunity to examine ectopic papillae, and evaluate the procedures and complications that should be considered in the intervention of these patients. On the other hand, we think that further, larger scale studies are needed on ectopic papillae.

**Conclusion**

ERCP has a particularly prominent place in the diagnosis and treatment of biliary, liver, and pancreatic diseases. Frequent use of ERCP increases the number of cases diagnosed with ectopic papilla although ectopic papilla is a rare finding. It should be kept in mind that ectopic biliary drainage may be found in an alternative location when no papilla are observed in the expected anatomical region, and bile-stained slit like biliary orifice should be investigated in the first, third, or fourth parts of the duodenum, stomach, and pylorus.

It is necessary to support with our results with other studies. The treatment does not only consist of the operation. Other endoscopic treatments, such as endoscopic sphincterotomy and pre-cut procedure, can be successfully performed. More caution should be exercised for pancreatitis complications that may occur after the procedure in patients with ectopic papillae.

**References**


