

Original Article

Influence of juxtampullary duodenal diverticula on endoscopic retrograde cholangiopancreatography for pancreaticobiliary disease

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Abstract: The influence of the presence and localization of a juxta-ampullary duodenal diverticulum (JPDD) on endoscopic retrograde cholangiopancreatography (ERCP) for pancreaticobiliary disease is controversial. From January 2011 to June 2017, 486 patients enrolled at Department of Hepatobiliary Surgery, Dongyang People's Hospital underwent ERCP. These patients' characteristics and the details of their ERCP procedures were retrospectively evaluated. The primary outcome was the overall occurrence of successful cannulation, post-ERCP complications, and mortality. Two different types of JPDDs were identified according to the localization of the duodenal papilla: those with a peridiverticular papilla (PDP) (n=38, 56.72%), which was located near or in the margin of the diverticulum, and those with an interdiverticular papilla (IDP) (n=29, 43.28%), which was located inside the diverticulum. The success rate of the first cannulation was significantly lower in patients with JPDD than those without (72.73% vs. 87.25%, respectively). There was not significant difference in the success rate of total cannulation (84.41% vs. 96.81%). The incidence of post-ERCP complications (post-ERCP pancreatitis, hyperamylasemia, and bleeding) was higher in patients with JPDD than those without. The success rates of the first cannulation (88.64% vs. 51.72%) and total cannulation (93.18% vs. 72.73%) were higher in the PDP group than that in the IDP group. There was no significant difference in ERCP-related complications between the PDP group and IDP groups. ERCP in patients with a JPDD requires a higher skill level and may be associated with an increased complication rate after the procedure. A PDP is associated with higher success rates of the first and total cannulation.

Keywords: Juxtampullary duodenal diverticula, endoscopic retrograde cholangiopancreatography, complication

Introduction

With technological advances and better operating experience, endoscopic retrograde cholangiopancreatography (ERCP) has become an alternative procedure in patients with pancreaticobiliary disease, including elderly patients [1]. However, complications including pancreatitis, hemorrhage, and perforation may occur after ERCP. A juxta-ampullary duodenal diverticulum (JPDD) located in the second part of the duodenum is an extraluminal mucosal out-pouching of the duodenum arising within a radius of 2 to 3 cm from the ampulla of Vater. The prevalence of JPDD ranges from 9.0% to 32.8% in several studies involving various diagnostic methods and study populations [2-4]. JPDD is associated with an increased risk of cholangio-pancreatic diseases such as obstructive jaundice, acute cholangitis, and acute pancreatitis [5, 6]. Studies have suggested that the pres-

ence of a JPDD makes ERCP technically difficult while increasing the risk of post-ERCP complications; however, findings have been inconclusive. Several studies have also suggested that the presence of a JPDD affects the fluoroscopy time [7-11], and that the presence of a JPDD and the location of the papilla affect the success of cannulation. However, post-ERCP complications remain unknown. The present retrospective analysis was performed to investigate the impact of the presence and location of a JPDD on the success of cannulation and the occurrence of post-ERCP complications.

Materials and methods

Study design

We retrospectively analyzed 486 patients who underwent ERCP from January 2011 to December 2016, during which time the patients

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Table 1. The baseline characteristic, the underlying disease and the indications of patients

	JPDD (n=77)	Non-JPDD (n=409)	P value
Age (yr)	72.24±13.29	68.46±11.19	0.004*
Sex (male/female)	41 (53.25)	214 (52.32)	0.881
Indication			
Common bile duct stones	45 (58.44)	257 (62.84)	0.466
Malignant biliary obstructive	18 (23.38)	80 (19.56)	0.443
Acute pancreatitis	14 (18.18)	72 (17.6)	0.903
Cholecystectomy	15 (19.48)	105 (25.67)	0.248
History of pancreatitis	8 (10.39)	56 (13.69)	0.431
Coexisting disorders			
Diabetes	13 (16.88)	82 (20.05)	0.521
Hypertension	25 (32.47)	154 (37.65)	0.387
Coronary heart disease	11 (14.29)	78 (19.07)	0.319
Chronic pulmonary disease	7 (9.09)	40 (9.78)	0.851

Continuous variables are expressed as median (interquartile range; IQR), categorical variables are expressed as n (%). JPDD: Juxtampullary Duodenal Diverticula. *students' test.

Table 2. Patients characteristics of patients with JPDD n (%)

	PDP (n=44)	IDP (n=33)	P value
Age (mean ± SD) (years)	72.57±11.45	67.91±15.18	0.064
Sex (male/female)	23 (52.27)	18 (54.55)	0.843
Indication [n (%)]			
Common bile duct stones	25 (56.82)	20 (60.61)	0.739
Malignant biliary obstructive	10 (22.73)	7 (21.21)	0.874
Acute pancreatitis	8 (18.18)	6 (18.18)	0.614*
Cholecystectomy [n (%)]	7 (15.91)	8 (24.24)	0.361
History of pancreatitis [n (%)]	5 (11.36)	3 (9.09)	0.746
Coexisting disorders [n (%)]			
Diabetes	8 (18.18)	5 (15.15)	0.725
Hypertension	15 (34.09)	10 (30.3)	0.725
Coronary heart disease	7 (15.91)	6 (18.18)	0.792
Chronic pulmonary disease	4 (9.09)	3 (9.09)	0.649*

Continuous variables are expressed as median (interquartile range; IQR), categorical variables are expressed as n (%). PDP: Peridiverticular Papilla. IDP: Intradiverticular Papilla. *fisher exact.

were continuously enrolled in Department of Hepatobiliary Surgery, Dongyang People's Hospital. We also analyzed the patients' clinical data, laboratory data, and ERCP procedure. Data analysis included the patients' characteristics, details of ERCP, cannulation success rate, and complications. This study was approved by the Institutional Review Board of the Research and Ethics Committee of our hospital.

Patients

Each patient or his/her relatives provided written informed consent after receiving verbal and written explanations of ERCP and possible post-procedure complications. The inclusion criteria: patients with age over 18 years old; underwent elective ERCP, the conditions of patients were informed. The exclusion criteria were an age of <18 years, pregnancy or breastfeeding, upper gastrointestinal obstruction, Billroth II operation, severe hypoxemia with ventilation/perfusion imbalance, acute myocardial infarction within 3 months before the procedure, coagulopathy, and refusal to participate in the study. All patients' medical history was recorded, including the indications for ERCP, the presence of concomitant diseases, and current medications.

Endoscopic procedure

All ERCP procedures were performed by experienced endoscopists using standard therapeutic duodenoscopy with a side-viewing duodenoscope (JF-260V; Olympus Co. Ltd., Tokyo, Japan). The patients fasted for 8 hours preoperatively, and moderate sedation was administered by intramuscular injections of atropine, diazepam, and phenytoin. Continuous monitoring by an electrocardiogram and 2 L/min of oxygen through a nasal cannula was performed during the procedure.

After selective cannulation, cholangiography was performed with a standard iodinated contrast medium (30% iohexol injection). The presence of a JPDD and the location of the papilla in relation to the JPDD were recorded.

Definitions

The JPDDs were classified into two groups according to the location of the papilla and

Table 3. Comparison of laboratory postoperatively data between patients with and without juxtampillary duodenal diverticula

	JPDD (n=77)	Non-JPDD (n=409)	P value
TB (mmol/L)	110±26.73	89.27±27.73	<0.001
DB (mmol/L)	70.12±28.10	62.19±21.22	0.002
ALT (U/L)	219±13.97	205±15.42	<0.001
AST (U/L)	183±26.19	101±25.18	<0.001
ALP (U/L)	713±99.53	580±102.67	<0.001
γ-GTP (U/L)	408±78.34	370±67.36	<0.001

Continuous variables are expressed as median (interquartile range; IQR), categorical variables are expressed as n (%). TB: Total Bilirubin; DB: Direct Bilirubin; ALT: Alanine Transaminase; AST: Aspartate Transaminase; ALP: Alkaline Phosphatase; γ-GTP: γ-Glutamyl Transpeptidase. JPDD: Juxtampillary Duodenal Diverticula.

Table 4. Comparison of laboratory postoperatively data between patients of PDP and IDP

	PDP (n=44)	IDP (n=33)	P value
TB (mmol/L)	112±25.78	108±23.53	0.243
DB (mmol/L)	74±25.26	66±25.72	0.088
ALT (U/L)	221±15.67	217±15.42	0.134
AST (U/L)	186±23.49	180±27.25	0.152
ALP (U/L)	790±75.38	776±105.65	0.249
γ-GTP (U/L)	425±82.15	403±94.13	0.139

Continuous variables are expressed as median (interquartile range; IQR), categorical variables are expressed as n (%). TB: total Bilirubin; DB: Direct Bilirubin; ALT: Alanine Transaminase; AST: Aspartate Transaminase; ALP: Alkaline Phosphatase; γ-GTP: γ-Glutamyl Transpeptidase. PDP: Peridiverticular Papilla; IDP: Intradiverticular Papilla.

diverticula: the peridiverticular papilla (PDP) group, in which the papilla was located at the edge of the diverticula or <3 cm from the diverticula, and the interdiverticular papilla (IDP) group, in which the papilla was located inside the diverticula.

The fluoroscopy time was recorded based on the screen recording time, starting from endoscope insertion and ending at endoscope withdrawal. Successful cannulation was defined as free and deep instrumentation of the biliary tree. A cannulation attempt was defined as sustained contact with the cannulating device and the papilla keeping for at least 5 seconds.

Previously established consensus criteria were used for the definition of post-ERCP complica-

tions and the grading of their severity [12]. Post-ERCP pancreatitis was defined as new or worsened abdominal pain persisting for more than 24 hours, with a serum amylase level more than three times the upper normal limit [13, 14]. Hyperamylasemia was defined as a serum amylase level exceeding three times the upper normal limit without simultaneous abdominal pain, nausea, or vomiting 2 to 24 hours after ERCP. Post-ERCP bleeding was considered to be present when patients required transfusion or endoscopic hemostasis [15].

Data collection

The retrospectively collected data included the presence of a JPDD, the location of the papilla in relation to the JPDD, the success of cannulation, and post-ERCP complications. The patient-related data (demographic characteristics, medical history, and clinical presentations) were recorded through an interview on the day of admission to the hospital if required. Laboratory parameters (liver function test results) were also measured on the day of admission. After ERCP, all patients were monitored in the ward. Venous blood was drawn from each patient to measure the amylase level using an automated analyzer at baseline and at 4 and 24 hours after the procedure. Detailed written information regarding potential post-ERCP complications (post-ERCP pancreatitis, bleeding, and perforation) was provided to the patients and their escorts.

Statistical analysis

Statistical analysis was performed using SPSS software (SPSS Inc., Chicago, IL). All values are expressed as mean ± standard deviation. The statistical analysis was conducted using Student's t test for continuous outcomes and the χ² test or Fisher's exact test for categorical outcomes. In all cases, a P value of <0.05 was considered statistically significant.

Results

Comparison of general conditions between two groups

In total, 486 consecutive patients who had undergone ERCP from January 2011 to June 2017 were included in the present analysis. These patients were divided into two groups

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Table 5. Comparison of ERCP result data between patients with and without JPDD n (%)

	JPDD (n=77)	Non-JPDD (n=409)	P value
Success of first cannulation	56 (72.73)	340 (87.25)	0.031
Success of total cannulation	65 (84.41)	350 (96.81)	0.792
Post-ERCP pancreatitis	10 (12.99)	20 (4.89)	0.007
Mild	7 (9.09)	16 (3.91)	0.049
Moderate to severe	3 (3.90)	4 (0.98)	0.986*
Hyperamylasemia	20 (25.97)	57 (13.94)	0.008
Bleed	10 (12.99)	21 (5.13)	0.009
Mild	7 (9.09)	15 (3.67)	0.036
Moderate	2 (2.60)	3 (0.73)	0.969*
Severe	1 (1.30)	2 (0.49)	0.933*
Perforation	0 (0)	1 (0.2)	0.664
Death	0 (0)	0 (0)	-

Categorical variables are expressed as n (%). JPDD: Juxtampullary Duodenal Diverticula. *fisher exact.

according to the presence (77 patients) or absence (409 patients) of a JPDD. Additionally, the patients with a JPDD were divided into two groups: the PDP group (44 patients) and the IDP group (33 patients). The patients' baseline characteristic, underlying diseases, and indications for treatment are shown in **Table 1**. The patients with a JPDD were older than those without a JPDD (72.24±13.29 vs. 68.46±11.19 years, $p=0.004$). No significant differences in age, sex, or treatment indications were present between the PDP and IDP groups ($p=0.064$) (**Table 2**).

Comparison of laboratory preoperatively data between two groups

The serum levels of total bilirubin (TB), direct bilirubin (DB), alanine aminotransferase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), and gamma glutamyltransferase (γ -GTP) were significantly higher in patients with than without a JPDD ($p<0.05$) (**Table 3**). Nevertheless, there was no distinct difference between the PDP and IDP groups ($p>0.05$) (**Table 4**).

Comparison of ERCP result data between patients between two groups

The success rate of the first-attempt cannulation was obviously lower in patients with JPDD than those without (87.25% vs. 72.73%,

$p=0.031$) (**Table 5**). The rate of post-ERCP pancreatitis, hyperamylasemia and bleed of ERCP was higher in patients with JPDD than those without (12.99% vs. 4.89, 25.97% vs. 13.94%, 12.99% vs. 5.13%) (**Table 5**). There was no significant difference in the success of total cannulation between these two groups (84.41% vs. 96.81%, $p=0.792$) (**Table 5**). The success rates of the first and total cannulations were apparently higher in the PDP than IDP group (88.64% vs. 51.72%, 93.18% vs. 72.73%) (**Table 6**). There was no significant difference in post-ERCP pancreatitis, hyperamylasemia and bleed between the PDP and IDP groups ($p=0.202$, $p=0.453$, $p=0.240$) (**Table 6**).

Discussion

In our retrospective study, 77 patients (44 with a PDP and 33 with an IDP) were confirmed to have JPDD by endoscopists during the ERCP procedure. JPDDs are more commonly found in elderly patients, and the incidence accordingly increased with age in our study. In this study, the success rate of the first-attempt cannulation was lower in patients with JPDD than those without. Nevertheless, there was no difference in the success rate of total cannulation. The success rates of the first cannulation (88.64% vs. 51.72%) and total cannulation (93.18% vs. 72.73%) were relatively higher in the PDP than IDP group. However, there was no significant difference in ERCP-related complications between the PDP and IDP groups. In our analysis, the rates of post-ERCP pancreatitis, hyperamylasemia, and bleeding were higher in the JPDD than non-JPDD group; however, no difference was found between the PDP and IDP groups.

The prevalence of a JPDD largely depends on the chosen imaging method, patient sex, and patient age. The prevalence ranged from 9.0% to 32.8% in recent studies [2-5]. In the present study, the prevalence of JPDD was 15.84%, and the mean age of patients with a JPDD was 72.24 years, which was older than that of patients without a JPDD. This is similar to some previous studies [7, 16].

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Table 6. Comparison of ERCP results between patients of PDP and IDP n (%)

	PDP (n=44)	IDP (n=33)	P value
Success of first cannulation	39 (88.64)	17 (51.72)	<0.001
Success of total cannulation	41 (93.18)	24 (72.73)	0.014
Post-ERCP pancreatitis	4 (9.09)	6 (18.18)	0.202*
Mild	3 (6.82)	4 (12.12)	0.341*
Moderate to severe	1 (2.27)	2 (6.06)	0.392*
Hyperamylasemia	10 (22.73)	10 (30.30)	0.453
Bleed	4 (9.09)	6 (18.18)	0.240
Mild	3 (6.82)	4 (12.12)	0.423
Moderate	1 (9.09)	2 (6.06)	0.395
Severe	0 (9.09)	0 (9.09)	-
Perforation	0 (0)	0 (0)	-
Death	0 (0)	0 (0)	-

Categorical variables are expressed as n (%). PDP: Peridiverticular Papilla. IDP: Intradiverticular Papilla. *fisher exact.

In earlier studies, the success rate of cannulation in patients with a JPDD reportedly ranged from 61.0% to 95.4%, which is significantly lower than that in patients without a JPDD [1, 17]. However, these results remain controversial [18]. Four studies revealed no significant difference in the success rate between patients with and without a JPDD [6, 7, 11, 14], while another study revealed a significantly lower success rate in patients without a JPDD [12]. One study indicated that a JPDD should not be considered a barrier to successful cannulation. In contrast, endoscopic sphincterotomy was found to be less effective than endoscopic papillary balloon dilation in patients with JPDD, whereas endoscopic sphincterotomy and endoscopic papillary balloon dilation were equally safe in patients with a JPDD [15]. In the present study, the presence of a JPDD was associated with a lower success rate of the first cannulation, but no significant difference was found in the success rate of total cannulation. A lower success rate of first cannulation can be attributed to inability of the endoscopist to detect the papilla. However, the various techniques for cannulation can be responsible for explaining no significant difference in the success rate of total cannulation. In recent years, the techniques and devices used for cannulation in ERCP have undergone remarkable development. The relationship between the presence of a JPDD and the success rate of cannulation remains unclear.

In this study, we investigated the JDPP classifications and their relationships to the cannulation success rate and development of complications. The success rates of the first cannulation and total cannulation were relatively higher in the PDP group. Previous studies have shown that a PDP is relatively easier to cannulate and is associated with lower complication rates [18]. However, an IDP often lies at the bottom of the diverticulum so that it is difficult to cannulate. Cannulation of an IDP can be challenging, and the higher time requirement often necessitates the higher skill level of more experienced endoscopists [13, 17]. The results of a study by Kanelos [11] showed a trend toward a higher complication rate with PDP, which remains to

be confirmed in future studies with larger samples. The results of previous studies are controversial. Interestingly, we found no difference in complications between the PDP and IDP groups. The different indications of previous studies can be responsible for the differences.

The relationship between the presence of a JPDD and laboratory data is controversial and unclear. Some authors have reported that the bile flow might be disturbed in patients with a JPDD because the ALP level was higher in patients with than without a JPDD [19]. In the present study, the TB, DB, ALP, ALT, AST, and γ -GTP levels were higher in patients with than without a JPDD, suggesting that bile flow might be disturbed in patients with a JPDD. However, the difference between the PDP and IDP groups was not statistically significant. The specific mechanism remains to be elucidated in prospective studies with larger samples.

Importantly, this study has several limitations. First, it was a retrospective study. Second, the success rates were comparable between the operative techniques, with the choice of technique depending on the endoscopist's preference and experience. Finally, the study population was relatively small.

In conclusion, more experienced endoscopists should perform ERCP in patients with a JPDD because of the longer time, higher skill level, and more complicated technique required in

such patients. Our findings indicate that a PDP has a higher success rate of cannulation than an IDP with no difference in complications.

Disclosure of conflict of interest

None.

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