The clinical importance of different localizations of the papilla associated with juxtapapillary duodenal diverticula

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Background: Previous studies have evaluated the presence of juxtapapillary duodenal diverticula (JPDD) and the association with pancreatobiliary disease, but not the association of the papilla with an existing JPDD. We investigated the association of different localizations of the papilla with JPDD.

Methods: We studied patients in whom JPDD was detected during endoscopic retrograde cholangiopancreatography. Patients were classified into 3 groups: 1) papilla located inside the diverticulum, 2) papilla located at the edge of the diverticulum and 3) papilla located closer than 3 cm to the diverticulum. The patients were examined with respect to localization of papilla–diverticula and to the association of the localization with pancreaticobiliary disease.

Results: We enrolled 274 patients in our study. Biliary stone disease more frequently existed in group 3. The number of patients presenting with obstructive jaundice was higher in groups 2 (83.6%) and 3 (83.3%) than group 1 (66%). Cholangitis was more common in group 1 (21.3%) than in groups 2 (6.7%) and 3 (2.3%). The presence of biliary stone disease among patients presenting with pancreatitis was significantly different between groups 1 and 3 (p = 0.013) and between groups 2 and 3 (p = 0.017). The common bile duct more frequently contained stones or sludge in group 3 than in groups 1 and 2.

Conclusion: When the papilla is located close to the JPDD, the incidence of biliary stone disease decreases, and pancreatobiliary diseases are caused mostly in the absence of biliary stone disease.

Contexte : Des études antérieures ont évalué la présence de diverticules duodénaux juxtapapillaires (DDJP) et leur lien avec la maladie pancréatobiliaire, mais n'ont pas analysé le lien entre la papille et les DDJP existants. Nous avons analysé le lien entre diverses localisations de la papille et les DDJP.

Méthodes : Nous avons étudié des patients chez qui des DDJP ont été détectés lors d'une cholangiopancréatographie endoscopique rétrograde. Les patients ont été classés en 3 groupes : 1) papille à l'intérieur du diverticule, 2) papille à l'extrémité du diverticule et 3) papille à moins de 3 cm du diverticule. L'examen a donc porté sur la localisation de la papille par rapport aux diverticules et sur le lien entre sa localisation et la maladie pancréatobiliaire.

Résultats : Nous avons inscrit 274 patients à notre étude. La cholélithiase s'observait davantage dans le groupe 3. Le nombre de patients souffrant d'ictère obstructif était plus élevé dans les groupes 2 (83,6 %) et 3 (83,3 %) que dans le groupe 1 (66 %). La cholangite était plus fréquente dans le groupe 1 (21,3 %) que dans les groupes 2 (6,7 %) et 3 (2,3 %). Le taux de cholélithiase chez les patients souffrant de pancréatite était significativement différent entre les groupes 1 et 3 (p = 0,013) et entre les groupes 2 et 3 (p = 0,017). Il y avait plus de calculs ou de boue biliaires dans le canal cholédoque des patients du groupe 3 que dans ceux des groupes 1 et 2.

Conclusion : Lorsque la papille est située près des DDJP, l'incidence de la cholélithiase diminue, et les maladies pancréatobiliaires sont pour la plupart causées en l'absence de cholélithiase.

Duodenal diverticula (DD) are classified as primary (true) or secondary (false) diverticula. Primary diverticula are mostly solitary and can be observed in the second part of the duodenum, in the ampulla vateri region (periampullary diverticula).[1,2] They are also called juxtapapillary duodenal diverticula (JPDD). The clinical importance of JPDD originates from its association with the papilla and pancreaticobiliary disease. Several studies have suggested that JPDD are the reason for biliary stone disease.[2,3] However, the association of the papilla with the diverticula and the effect of different positions of the papilla on biliary stone disease have not been investigated. To our knowledge, this association was first investigated in an earlier study conducted in our clinic.[4] The present paper presents further results of this investigation.

Methods

This study was designed in a retrospective manner. We reviewed the cases of patients admitted to the Endoscopy Unit of the Department of General Surgery, Ataturk University School of Medicine, between May 1999 and December 2007 for endoscopic retrograde cholangiopancreatography (ERCP), and we enrolled those in whom JPDD were detected during ERCP. We noted the age and sex of the patients, indications for ERCP and endoscopic sphincterotomy (ES), the association of the JPDD with the papilla, laboratory values, cannulation success of the biliary tract and the diameter and contents of the common bile duct (CBD). We examined the localization of the papilla–diverticula and the association of the localization with pancreaticobiliary disease. The indications for ERCP were obstructive jaundice, cholangitis and pancreatitis. Patients who had gallbladder stones (including patients who previously underwent cholecystectomy for known gallbladder stones and patients who had a gallbladder stone and were not operated on at the time when the study was conducted), CBD stones, or both were considered to have biliary stone disease. Obstructive jaundice was defined as hyperbilirubinemia caused by mechanical obstruction of the biliary tract; cholangitis was defined as hyperbilirubinemia accompanied by fever and leucocytosis; and pancreatitis was defined as strongly suggestive evidence for pancreatitis of biliary origin (radiological and laboratory findings). Patients with known hepatocellular diseases, such as viral or toxic hepatitis, cirrhosis, hepatic or biliary malignancies, or hepatic or biliary benign masses, patients using medication influencing the hepatocellular functions, and patients who were operated on previously for a biliary tract disease (not cholecystectomy) were excluded from the study. Patients were classified according to the location of the papilla and diverticula into 3 groups, as done by Yildirgan and colleagues:[4] 1) papilla located inside the diverticulum, 2) papilla located at the edge of the diverticulum and 3) papilla located closer than 3 cm to the diverticulum. Patients with a papilla far away from the diverticulum were excluded. The patients were followed for at least 18 (range 18–24) months.

Statistical analysis

We conducted our analyses using SPSS software version 12.0 for Windows. Data were compared among the 3 groups. In addition, the association between indications for ERCP and biliary stone disease were investigated within groups. We conducted Student t tests for continuous variables and the χ^2 test or Fisher exact test for categorical variables. We considered results to be significant at $p < 0.05$.

Results

A total of 2327 patients underwent ERCP in our endoscopy unit during our study period. Of these, 274 (11.7%) had JPDD. Twenty-five patients did not meet the inclusion criteria and were excluded. From the remaining 249 patients with JPDD, 103 (41.3%) were in group 1, 104 (41.7%) were in group 2, and 42 (17%) were in group 3.

The mean age; sex; indications; mean levels and activities of serum total blirubin, conjugated bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ-glutamyl transferase (GGT) and alkaline phosphatase (ALP); deep cannulation success of the CBD; and mean diameter of the CBD are shown in Tables 1–4.

In group 1 (n = 103), 38 (36.9%) patients had biliary stones. Twelve (31.6%) of them had only gallbladder stones, 17 (44.7%) had both CBD and gallbladder stones, and 9 (23.7%) had only CBD stones.

In group 2 (n = 104), 35 (33.6%) patients had biliary stones. Six (17.1%) of them had only gallbladder stones, 19 (54.3%) had both CBD and gallbladder stones, and 10 (28.6%) had only CBD stones.

In group 3 (n = 42), 33 (78.6%) patients had biliary stones. Eight (24.2%) of them had only gallbladder stones, 19 (57.6%) had both CBD and gallbladder stones, and 6 (18.2%) had only CBD stones.

The number of patients presenting with obstructive jaundice was higher in groups 2 (83.6%) and 3 (83.3%) than in group 1 (66%; both p = 0.016). When the presence of biliary stone disease was compared among patients presenting with obstructive jaundice, patients in group 3 had a higher incidence of biliary stone disease than patients in the other 2 groups (both p = 0.001), and there was no difference between groups 1 and 2.

The number of patients who presented with cholangitis was significantly higher in group 1 (21.3%) than in groups 2 (6.7%, p = 0.011) and 3 (2.3%, p = 0.001). Among patients with cholangitis, 22.7% in group 1, 57.1% in group 2 and 100% in group 3 had biliary stone disease. There was a significant difference between groups 1 and 2 (p = 0.013), 1 and 3 (p = 0.001), and 2 and 3 (p = 0.014).

There was no difference among the groups in the presence of pancreatitis. The presence of biliary stone disease among patients presenting with pancreatitis was significantly different between groups 1 (38.4%) and 3 (83.3%, $p = 0.013$) and between groups 2 (50%) and 3 (83.3%, $p = 0.017$; Table 1).

The CBD more frequently contained stones or sludge in group 3 than in the other groups (both $p = 0.016$).

Table 1. Shows age, sex, cannulation success and CBD diameter

Characteristic	Group 1, *n* = 103	Group 2, *n* = 104	Group 3, *n* = 42	Total, *n* = 249
Age, mean (IQR), yr	63.1 (31–80)	66.8 (34–85)	64.1 (29–76)	64.7 (29–85)
Sex, male:female	36:67	41:63	16:24	93:154
Cannulation success on first attempt, no. (%)	88 (85.4)	92 (88.4)	38 (90.4)	218 (87.5)
CBD diameter, mean, mm	14.6	14.3	15.2	14.7

CBD = common bile duct; IQR = interquartile range.

Table 2. Indications for intervention

	Group; no. (%)			
Indication	Group 1, *n* = 103	Group 2, *n* = 104	Group 3, *n* = 42	Total, *n* = 249
Obstructive jaundice				
Total	68 (66)	87 (83.6)	35 (83.3)	190 (76.3)
BSD	28 (41.1)	26 (29.8)	27 (77.1)	81 (42.6)
Cholangitis				
Total	22 (21.3)	7 (6.7)	1 (2.3)	30 (12)
BSD	5 (22.7)	4 (57.1)	1 (100)	10 (33.3)
Biliary pancreatitis				
Total	13 (12.6)	10 (9.6)	6 (14.2)	29 (11.6)
BSD	5 (38.4)	5 (50)	5 (83.3)	15 (51.7)

BSD = biliary stone disease.

Table 3. Patient laboratory data

	Group; mean			
Laboratory data	Group 1, *n* = 103	Group 2, *n* = 104	Group 3, *n* = 42	Total, *n* = 249
Bilirubin, μmol/L				
Total	75.60	71.49	68.07	68.59
Conjugated	28.56	33.35	28.05	30.44
AST, μkat/L	1.15	1.29	0.94	1.09
ALT, μkat/L	1.30	1.45	1.19	1.29
GGT, μkat/L	5.68	5.32	4.03	4.65
ALP, μkat/L	5.88	6.20	5.69	5.60

ALT = alanine amino transferase; ALP = alkaline phosphatase; AST = aspartate amino transferase; GGT = γ-glutamyl transferase.

Table 4. Common bile duct content and biliary stone presence

	Group; no. (%)			
Presence	Group 1, *n* = 103	Group 2, *n* = 104	Group 3, *n* = 42	Total, *n* = 249
CBD content				
None	77 (74.7)	75 (72.1)	17 (40.4)	169 (67.8)
Stone or sludge	26 (25.3)	29 (27.9)	25 (59.6)	80 (32.7)
Biliary stone				
Gallbladder stone only	12 (11.6)	6 (5.7)	8 (19)	26 (10.4)
CBD stone only	9 (8.7)	10 (9.6)	6 (14.2)	25 (10)
Gallbladder and CBD stone	17 (16.5)	19 (18.2)	19 (45.2)	55 (22)
Total BSD	38 (36.8)	35 (33.6)	33 (78.5)	106 (42.5)

BSD = biliary stone disease; CBD = common bile duct.

Biliary stone disease (including gallbladder stone, CBD stone, or both) more frequently existed in group 3 than in the other 2 groups (both $p = 0.014$). The biochemical values of bilirubin (total and conjugated), AST, ALT, GGT and ALP did not differ significantly among the groups. The CBD diameters and cannulation success of the CBD were also similar among the groups.

The median follow-up period was 61 (range 6–71) months. A total of 19 patients (7 in group 1, 9 patients in group 2, and 3 patients in group 3) were readmitted to the clinic because of different reports of pancreatobiliary origin. Only 6 patients underwent re-evaluation with ERCP (2 in group 1, 3 in group 2, and 1 in group 3). There was no recurrent stone disease in readmitted patients.

Discussion

Several studies on the association between JPDD and biliary stone disease have been performed. Most of these studies state that biliary stone disease is associated with JPDD. The pathological mechanism of this association is explained by several hypotheses. The mechanical pressure of the diveticulum to the distal end of the biliary tract is commonly discussed. Another simple explanation is the dysfunction of the sphincter of Oddi (SO), which is believed to be caused by the accumulation of food in the diverticulum, putting pressure on the end of the bile duct and SO and leading to stricture of the sphincter. The dysfunction of the SO causes obstruction and stasis of bile juice. Additional reflux caused by contractional malfunction of the sphincter leads to the reflux of gastrointestinal juice into the bile duct, bacterial infection of the bile duct and formation of pigment bile duct stones.[2,5–8] The dysfunction of the SO (decrease of the pressure) has been demonstrated in manometric studies.[9,10] The clinical result of the dysfunction of SO is the formation of CBD stones, infection (cholangitis) or pancreatic disease.

We sought to investigate the clinical effect of different localizations of the papilla associated with JPDD and management. We investigated whether the localization of the papilla was associated with JPDD, if this was important in the clinical presentation of JPDD, and what the therapeutic approach should be.

The reported incidence of biliary stone formation in patients with JPDD varies between 10% and 32%.[3,11–15] In our series the incidence was 11.7%. Our patients had a median of age of 64.7 (range 29–85) years. It has been reported that DD is a disease of advanced age; the mean age of patients is reported to be 70–79 years in some series. It has been reported that the association with advanced age suggests a degenerative process involving local supporting structures as an additional factor in the pathogenesis of JPDD.[3,11,13] We found no age difference among the groups.

The clinical presentation of JPDD is associated with biliary symptoms, including cholangitis, obstructive jaundice and pancreatitis.[3,16–22]

The clinical presentation of our patients was mostly associated with elevated bilirubin and other liver enzymes, including AST, ALT, GGT and ALP, with or without abdominal pain, fever and leucocytosis (obstructive jaundice or cholangitis). It has been reported that patients with JPDD had less abdominal pain and more symptoms of biliary obstruction than patients without JPDD.[3,16–22] The values of bilirubin (total and conjugated), AST, ALT, GGT and ALP did not differ among the groups. Patients in groups 2 and 3 were more likely to be admitted with symptoms of obstructive jaundice. But, the existence of biliary stone disease among patients with obstructive jaundice was different among the groups. Patients in group 3 had biliary stones more frequently than those in other groups.

Cholangitis was commonly seen in group 1. Zoepf and colleagues[3] reported that suppurative cholangitis was more frequent in patients with JPDD than in control patients, but that this difference was not significant.[3] They also claimed that the higher cholangitis rate associated with JPDD in their series was based only on the bile duct obstruction resulting from bile duct stones rather than on specific mechanisms associated with JPDD (e.g., ascending bacteria).[2] In our series, however, cholangitis was more frequent in group 1, and these patients had biliary stone disease less frequently than those in the other groups. In contrast to Zoepf and colleagues,[3] we thought that the high cholangitis rate in group 1 should be associated with specific mechanisms associated with JPDD rather than bile duct obstruction resulting from bile duct stones. Furthermore, obstructive jaundice was more commonly associated with biliary stone disease in group 3 patients. These 2 findings lead us to speculate that cholangitis and obstructive jaundice resulting from biliary obstruction were more commonly associated with stones in group 3 patients. Moreover, when the papilla is located closer to the JPDD, and even when the papilla is located inside it, cholangitis and obstructive jaundice become less frequently associated with the biliary stones.

There are some different reports about the development of pancreatitis in JPDD. Some investigators have suggested that pancreatitis is not associated with JPDD.[3,23] Others reported that patients with DD have a higher rate of acute pancreatitis.[24–26] The mechanism of pancreatitis in these patients is believed to be mainly of biliary origin. However, other investigators have suggested that JPDD is associated with acute idiopathic pancreatitis and have postulated that DD is a risk factor for acute idiopathic pancreatitis, especially in elderly patients.[26] In our series, pancreatitis existed in 29 (11.6%) patients. We are not able to discuss the association with pancreatitis because we did not include control patients in the study. However, when the existing patients were evaluated, the distribution was homogeneous among

groups and there was no significant difference among the groups. We determined that the presence of biliary stone disease among patients presenting with pancreatitis differed significantly between groups 1 and 3 ($p = 0.013$) and groups 2 and 3 ($p = 0.017$). We think that this finding suggests that JPDD is associated with acute idiopathic pancreatitis and that DD is a risk factor for acute idiopathic pancreatitis, especially when the papilla is located close to the JPDD. We also think that pan-creatitis is caused by specific mechanisms, as mentioned previously.

Boix and colleagues[11] have proposed a classification of the localization of the papilla according to the JPDD. They reported that JPDD do not significantly increase the difficulty of deep cannulation. We had an overall cannulation success rate of 87.5% at the first occurrence of ERCP. All patients were cannulated during the study for the first or second time. There was no statistical difference in cannulation success among the groups. We found that cannulation success did not depend on the localization of the papilla.

All of our patients underwent sphincterotomy. In our earlier paper, we stated that ES should be performed in the presence of biliary stone disease in group 3 patients.[4] The present findings lead us to the same conclusion. Our findings showed that the biliopancreatic presentation of the JPDD depends on the existence of biliary stone disease in group 3 patients, and is partially independent from biliary stone disease in groups 1 and 2. Thus, we suggest ES in groups 1 and 2 even if there is no existing biliary stone disease. In group 3, ES should be performed according to the guidelines for biliary stone disease independently from JPDD.

Conclusion

When the papilla is located close to the JPDD, the incidence of biliary stone disease decreases, and pancreatobiliary diseases are caused mostly in the absence of biliary stone disease.

Competing interests: None declared.

Contributors: B. Ozogul, G. Ozturk, B. Aydinli and S.S. Atamanalp designed the study. B. Ozogul, A. Kisaoglu and M. Yildirgan acquired the data, which B. Ozogul, G. Ozturk and A. Kisaoglu analyzed. B. Ozogul, G. Ozturk, A. Kisaoglu, B. Aydinli and S.S. Atamanalp wrote the article, which B. Ozogul and M. Yildirgan reviewed. All authors approved the final version for publication.

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