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Association of duodenal papillary morphology with underlying periampullary ductal structures in adult post-MRCP/ERCP patients

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Abstract^

Background: Various duodenal papilla morphologies {large/small protrusions, unstructured/gyrus/annular/longitudinal patterns) were shown to predict difficult cannulation, and different periampullary ductal variants (acute distal common bile duct (CBD) angle ≤30°, non-draining Santorini duct, ansa pancreatitis, V type and B-P type CBD-PD junctions) were correlated to pancreatitis. **Aim:** To explore the association of papilla morphology with periampullary ductal vatiations. **Methods:** We performed a retrospective analysis of 61 patients with naïve papilla who underwent magnetic resonance cholangiopancreatography (MRCP) and endoscopic retrograde cholangiopancreatography (ERCP). From MRCP images, the periampullary ducts were classified according to cystic duct (CD) insertion, CD course, distal CBD angle, PD variation, and CBD-PD junction. From duodenoscopy videos, the papilla was classified according to the oral protrusion and papilla pattern. **Results:** Fisher's exact tests for independence showed a significant result between papilla protrusion and distal CBD angle (p = 0.002) with 87% of large protrusions having acute distal CBD angle ≤30°. Though not statistically significant, (a) large protrusion had more parallel CD course (52.2%); and (b) gyrus papilla had more PD dominant CBD-PD junction (66.7%). **Conclusion:** Large protrusions predict acute distal CBD angle of ≤30°, which is related to difficult cannulation. Though not statistically significant, large protrusions have a more parallel CD course which could theoretically contribute to difficult cannulation if there is distal CD insertion; and gyrus papilla has more PD dominant junction which, as shown in earlier studies, is associated with difficult cannulation for inexperienced endoscopists.

Keywords: duodenal papilla morphology, CBD angulation, pancreatic duct types, cystic duct insertion, cystic duct course

Duodenal morphology was shown to be associated with cannulation difficulty.[1-4] Watanabe et al. revealed that a large protrusion is a risk factor for difficult biliary cannulation (OR 3.772; 95% CI 1.359-10.464).[1] Haraldsson et al. demonstrated that small Type 2 (52%; 95% CI 45-59%) and large Type 3 (48%; 95% CI 42-53%) papillae were susceptible to failed biliary cannulation.[2] Chen et al. also showed that Haraldsson small Type 2 papilla (OR 7.18, p = 0.045) and large Type 3 papilla (OR 7.44, p = 0.016) were associated with greater risk of cannulation failure.[3] They further showed that post ERCP pancreatitis (PEP) was significantly higher with Haraldsson small Type 2 papilla (20% as compared to the other types <7%).[2] Onilla et al. also showed both small (OR 2.331, p = 0.215) and large protrusions (OR 2.3415, p = 0.335) had the highest risk for difficult cannulation. In

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addition, they showed that unstructured papilla pattern was significantly associated with difficult cannulation (OR 2.2741, $p = 0.020$).[4]

The pancreaticobiliary system has various anatomic morphologies: from its formation within the liver and pancreatic parenchyma up to its union at the duodenum. Classifications have been derived to describe every level of connection in the pancreaticobiliary tree. Type 1 CD insertion (distal CBD) was associated with intrapancreatic insertion of CD and high risk for CBD stones.[5] Forty percent of parallel CD course had gallbladder stones.[6] An acute distal CBD angle ≤30° is high risk for PEP among beginners but not experts.[7] Type 3 PD (non-draining Santorini) was associated with pancreatitis in the pediatric population which was attributed to the Santorini duct being important in relief of obstruction and prevention of pancreatitis.[8] Type 5 PD (ansa pancreatica) was associated with recurrent acute pancreatitis due to the tortuous outflow.[9,10] V type CBD-PD junction (without common channel) and B-P type (CBD drains into PD) had a higher prevalence of acute pancreatitis than P-B type (PD drains into CBD).[11]

Since different duodenal papilla and periampullary morphologies were associated with difficult biliary cannulation and, together with various underlying periampullary ducts associated with PEP, could different duodenal papilla morphology be associated with different underlying periampullary ducts? If the periampullary ducts can be predicted from the papilla morphology, this could help tailor the technique to make ERCP safer and more successful. There are no previous studies on the possible correlation between duodenal papilla morphology and periampullary ducts. This study aimed to explore this association.

Methodology

This was a retrospective cross-sectional study with purposive sampling of all eligible patients ≥18 years old who underwent MRCP and ERCP between October 2015 to December 2021. Earlier records were not available.

The following were excluded: (a) patients who had previous ERCP and surgical intestinal reconstruction; (b) periampullary masses; (c) intradiverticular papillae; (d) presence of anatomical alterations (duodenal fistula); and (e) difficulty in identifying or reconstructing the periampullary ducts and duodenal papilla from MRCP images and ERCP videos.

The study originally planned to get data from two tertiary hospitals. However, one arm did not materialize as their MRCP files were corrupted before we could collect the data.

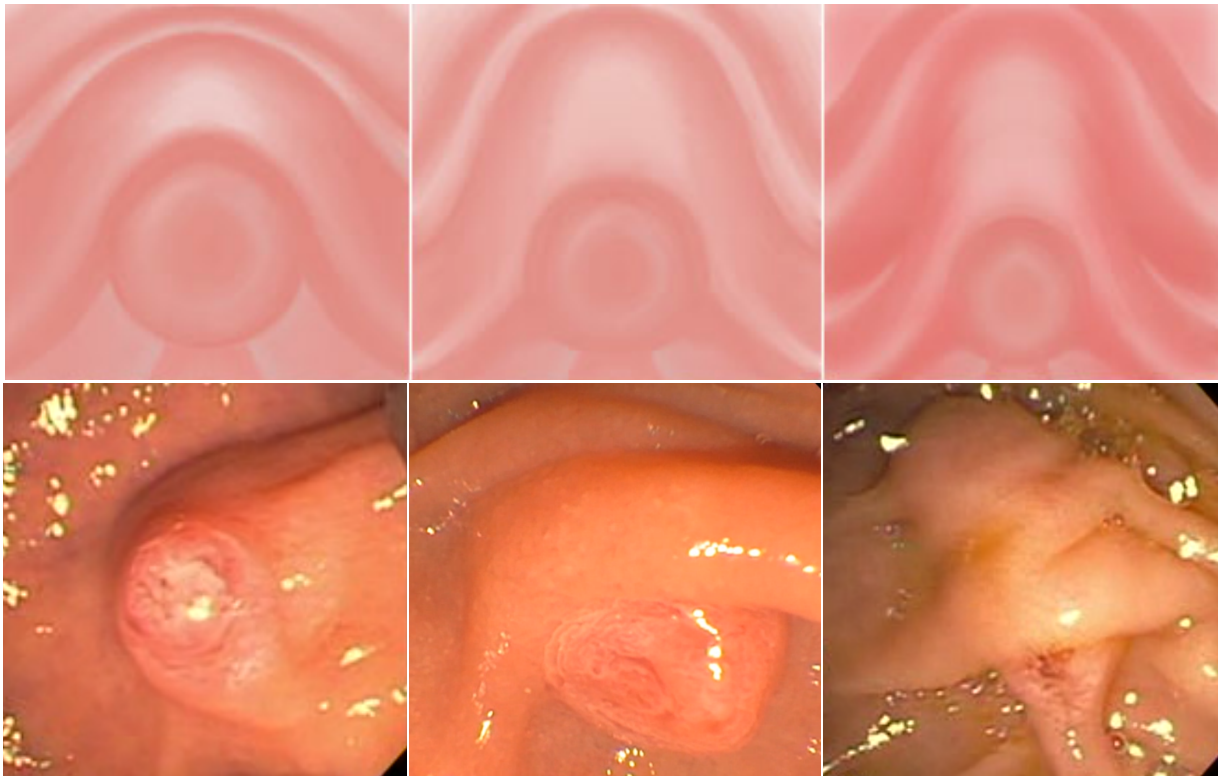
All the ERCP procedures were performed using Olympus TJF-Q180V therapeutic video duodenoscope. Two consultant endoscopists categorized each papilla, with disagreements settled by a third consultant endoscopist. They did not have knowledge of the MRCP results. Classification of the duodenal papilla was based on Watanabe, which is composed of two sub-classifications: oral protrusion and papilla pattern (Supplemental **Figures 1 and 2**).[1]

A. CD insertion according to Renzulli[5] (Supplemental **Figure 3**):
   CD insertion was classified as Type 1 (cystic duct-duodenal papilla/extrahepatic bile duct ratio ≤50%); Type 2 (CDDP/EHBD ratio >50% and ≤75%); and Type 3 (CDDP/EHBD ratio >75%).
B. CD course according to Sarawagi (Supplemental **Figure 4**):[6]
   The course was parallel when ≥2 cm of CD run parallel to the CHD.
C. Distal CBD angle according to Han[7] (Supplemental **Figure 5**):
   The distal CBD angle was measured relative to a vertical line drawn on the lower wall of the CBD on coronal images. Based on the mean angle value, the cases were classified as acute angle ≤30° and angle >30°.
D. PD anatomy according to Adibelli[9] (Supplemental **Figure 6**):
   Types 1 and 2 had bifid configurations with a dominant Wirsung (Type 1), and a dominant Santorini (Type 2). Type 3 had a rudimentary non-draining Santorini, Type 4 had a rudimentary non-draining Wirsung (pancreatic divisum), and Type 5 had the Santorini forming an inferior loop and connecting with a side branch of the Wirsung at the uncinate process (ansa pancreatica).
E. Pancreaticobiliary union (Supplemental **Figure 7**).
   This was patterned after the description of the union of the PD and the CBD as classically defined in relation to anomalous pancreaticobiliary ductal junction (APBDJ), but to avoid confusion with those

pertaining to APBDJ we decided not to use the terminologies of V, B-P, and P-B.[13] The union was divided into two major categories: separate (absent common channel) and present common channel. The latter category is further subdivided into: (a) no dominant duct (similar to the V type), (b) dominant CBD (similar to the P-B type), and (c) dominant PD (similar to the B-P type). The length of the common channel was also measured.

One or more pictures (as needed) of the duodenal papilla and periampullary ducts were incorporated into the data collection form.

Image source: Watanabe et al., 2019[1]



Protrusion-S
Ratio of length of oral protrusion to transverse diameter is <0.5

Protrusion-R
Ratio of length of oral protrusion to transverse diameter is 0.5 to <2

Protrusion-L
Ratio of length of oral protrusion to transverse diameter is ≥2

Figure 1 (Supplemental images)**.** Oral protrusion pattern. L, length of the oral protrusion; D, diameter of the papilla. Small (Protrusion-S), L/D <0.5; regular (Protrusion-R), 0.5 ≤ L/D < 2; and large (Protrusion-L), L/D ≥ 2.

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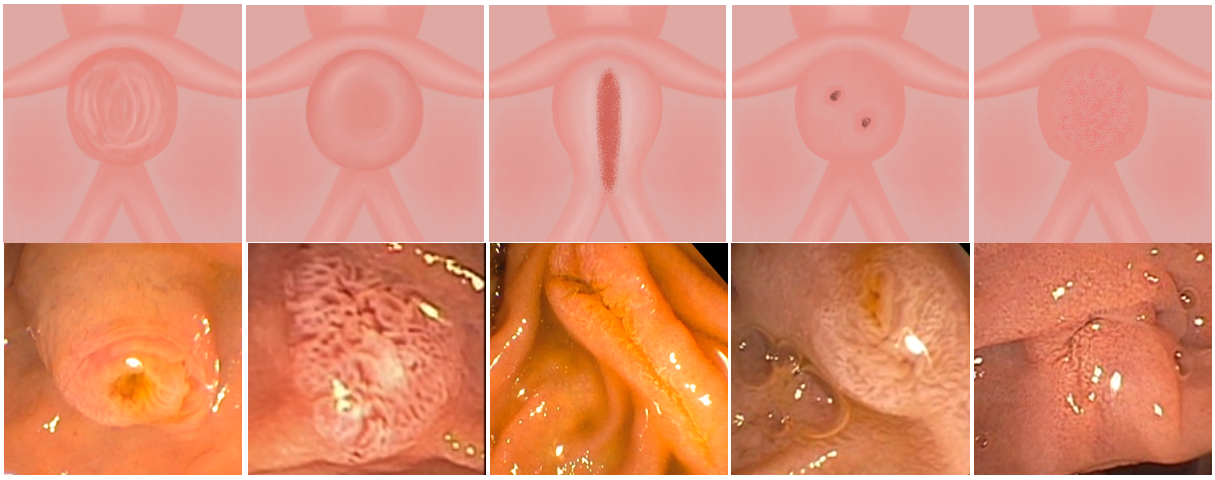
Image source: Watanabe et al., 2019[1]



Papilla-A	Papilla-U	Papilla-LO	Papilla-I	Papilla-G
Typical papilla with annular shape with some having nodular changes on the oral side of the center (10-11 o'clock) and others, for which these were difficult to discern	Without a clear orifice	Longitudinal grooves with their length continuous with the orifice, and length longer than the transverse diameter of the biliary duct axis of the papilla	Two separate isolated orifices of the biliary and pancreatic ducts (the orifice on the oral or left side is that of the biliary tract, and that on the anal or right side is that of the pancreatic duct)	Gyrate structure

Figure 2 (Supplemental images)**.** Papilla pattern: Papilla-A, annular shape, Papilla-U, unstructured without a clear orifice; Papilla-LO, comprising longitudinal grooves continuous with the orifice; Papilla-I, comprising two separate, isolated orifices of the biliary and pancreatic ducts; Papilla-G, with a gyrate structure

Image source: Renzulli et al., 2020[5]

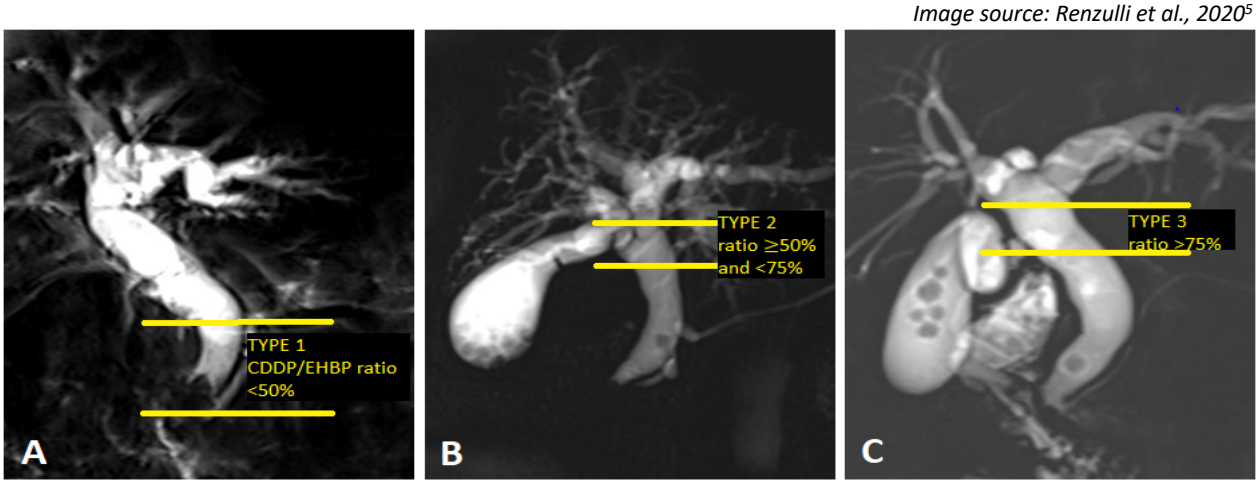


Figure 3 (Supplemental images)**.** Cystic duct insertion. **A.** Type 1, **B.** Type 2, **C.** Type 3.
EHBD: extrahepatic bile duct. *CD:* cystic duct. *DP:* duodenal papilla. *CDDP:* cystic duct-duodenal papilla.

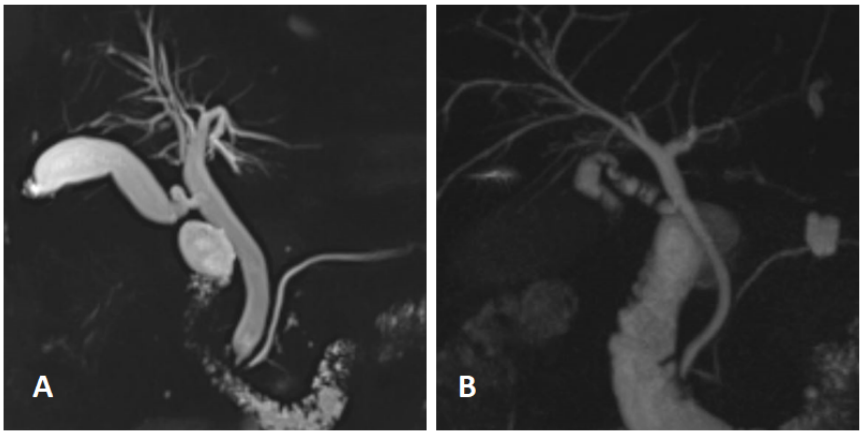


Figure 4 (Supplemental images)**.** Course of the cystic duct. **A.** Non-parallel course. **B.** Parallel course.

Image source: Han et al., 2020[7]

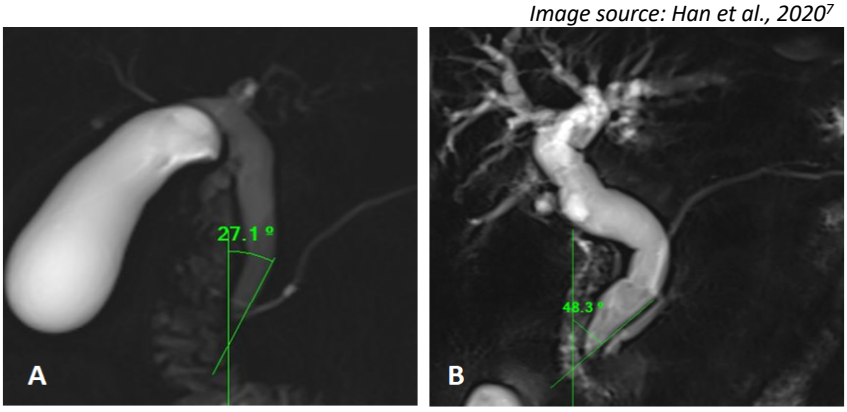


Figure 5 (Supplemental images)**.** Measurement of distal CBD angle. **A.** acute angle. **B.** Obtuse angle.

Image source: Abidelli et al., 2020[9]

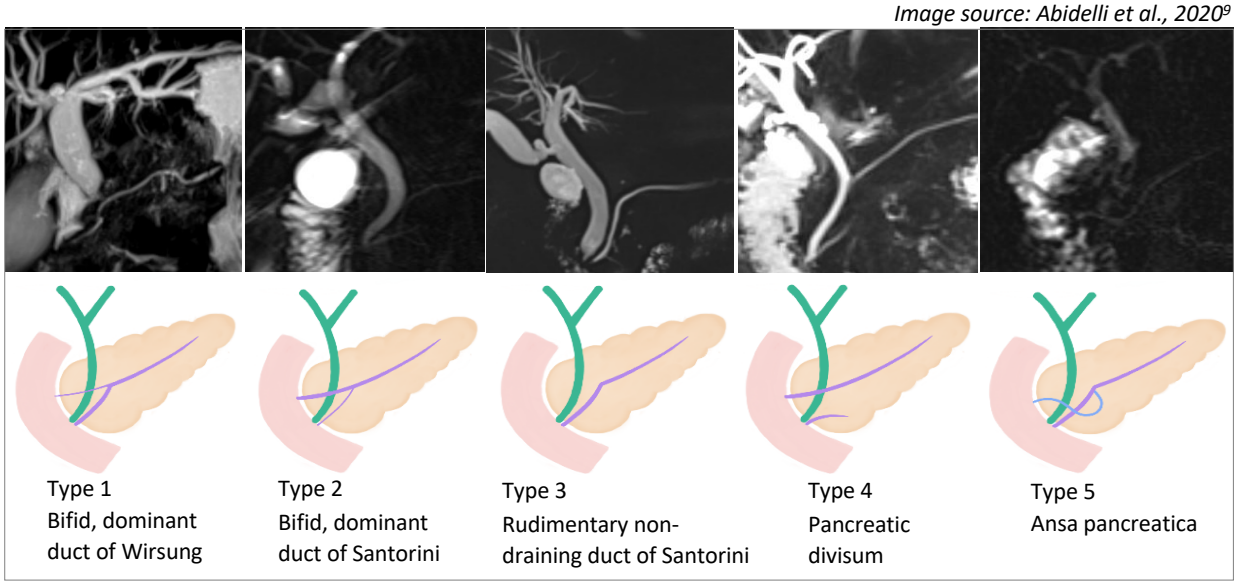


Figure 6 (Supplemental images)**.** Classification of pancreatic duct anatomy

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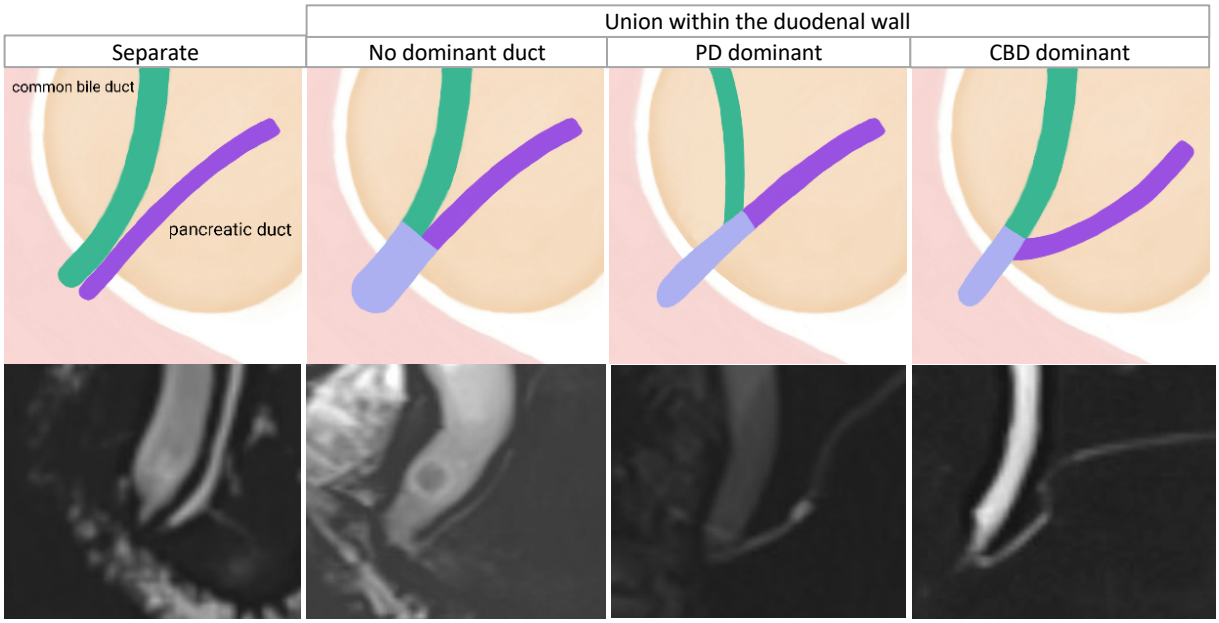

Figure 7 (Supplemental images)**.** Classification of pancreaticobiliary anatomy

Data Privacy Statement and Ethical Consideration

The identities of the patients and doctors involved were not identified in the study. Vulnerable and special population groups were excluded. The recruitment of the participants was based on purposeful sampling based on previous records. The cases were identified using control numbers, whose list is only accessible to the researcher. The data files were then encrypted. The study conformed with the Data Privacy Act of 2012 (Republic Act No. 10173) and the principles of the Declaration of Helsinski. The patients included in the study did not receive any form of compensation for their participation.

The collected raw data (also those with the names of the patients) were shredded and cross-shredded after the completion of the data analysis. The research presented with no more than minimal risk of harm to the subjects and involved no procedure for which written consent is normally required outside of the research context. In light of these reasons, the study did not attempt to secure written informed consent from the participants.

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This study was reviewed and approved by the Manila Doctors Hospital Institutional Review Board (MDH IRB 2021-046_II-F).

Data Analysis and Sample Size Computation

The sample size computation was done using the software StatCalc from EpiInfo 7.1.4.0. Estimation was based on the following assumptions: (1) large number of patients who underwent ERCP for the first time; (2) percentage of patients with annular pattern occurs in 72% of the patients (based on the most common papilla pattern from the study of Onilla et al.[4]). In a computation of the rate of patients with papilla morphology and those patients who underwent ERCP for the first time carried out at 95% confidence level and a 5% margin of error, a sample size of 309 patients will have 80% power of rejecting the null hypothesis if the alternative holds.

The demographic profile was summarized as descriptive statistics. Continuous data scales (age and common channel length) were summarized as means and standard deviations. Categorical data (sex, presenting symptoms, final diagnosis, papilla morphology and periampullary ductal morphology) were summarized as frequencies and percentages. Inter-observer agreement was calculated and interpreted using Cohen's kappa (κ) statistics. To avoid allowing very little agreement among raters to be described as "substantial", the Cohen's kappa statistic was interpreted as suggested by McHugh[12]: none for 0-0.20, minimal for 0.21-0.39, weak for 0.4-0.59, moderate for 0.6-0.79, strong 0.8-0.9, and almost perfect for above 0.9. Correlational analysis used Fisher's exact test for independence with a 5% level of significance and a corresponding level of confidence of 95%.

Results

There was a total of 1,120 MRCPs and 1,204 ERCPs performed between October 2015 to December 2021 with 224 patients having both. After exclusion of 163 cases due to various reasons, only 61 subjects were included **(Figure 8**).

Our study population had 52.5% males and 44.3% aged 18-40 years old. The most common complaint was abdominal pain (85.2%). The most common diagnosis was choledocholithiasis (57.4%) (**Table 1**).

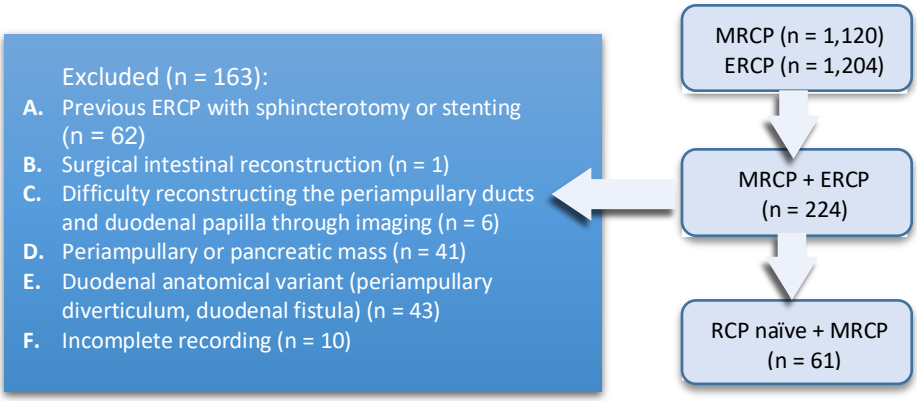

Figure 8. Flow diagram of patient enrolment and exclusion

Table 1. Demographic profile of study population (N = 61)

Profile		n (%)
Sex	Male	32 (52.5)
	Female	29 (48.5)
Age	18-40	27 (44.3)
	41-60	18 (29.5)
	> 60	16 (26.2)
	mean	46.295 ± 18.949
Chief Complaint	Abdominal pain	52 (85.2)
	Jaundice	33 (54.1)
	Fever	6 (9.8)
Final Diagnosis	Choledocholithiasis	35 (57.4)
	Malignancy	1 (1.6)
	Normal	2 (3.3)
	Bile leak	1 (1.6)

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Based on the first two endoscopists, endoscopic classification of papilla morphology had weak agreement for oral protrusion (κ 0.481, 95%CI 0.297-0.665) and minimal agreement for papillary pattern (κ 0.240, 95%CI 0.084-0.396) **(Table 2)**.

Table 2. Distribution of Kappa inter-observer agreement of the different classifications of papilla morphology

Papilla Morphology		n (%)	Kappa (κ)	CI (95%)	Level of Agreement
Oral protrusion pattern	Regular (Protrusion-R)	16 (26.2)	0.481	0.297 to 0.66	Weak agreement
	Small (Protrusion-S)	22 (36.1)			
	Large (Protrusion-L)	23 (37.7)			
Papilla Pattern	Annular (Papilla-A)	25 (41.1)	0.240	0.084 to 0.39	Minimal agreement
	Unstructured (Papilla-U)	16 (26.2)			
	Longitudinal (Papilla-L)	11 (18)			
	Isolated (Papilla-I)	6 (9.8)			
	Gyrus (Papilla-G)	3 (4.9)			

Based on the consensus of at least two of three endoscopists, Protrusion-L and Protrusion-S comprised 37.7% and 36.1%, respectively, of oral protrusions; while Papilla-A comprised 41.1% of papilla patterns.

Based on the first two radiologists, MRCP classification of periampullary ducts had strong agreement for CD insertion (κ 0.852, 95% CI 0.729-0.977), CD course (κ 0.834, 95% CI 0.697-0.972), distal CBD angle (κ 0.868, 95% CI 0.743-0.992), and CBD-PD junction (κ 0.886, 95% CI 0.791-0.980). There was moderate agreement for pancreatic duct type (κ 0.759, 95% CI 0.576-0.942) **(Table 3).**

Table 3. Distribution and kappa inter-observer agreement of different classifications of periampullary ductal morphology

Periampullary Ductal Morphology		n (%)	Kappa (κ)	CI (95%)	Level of Agreement
CD insertion	Type 1 (CDDP/EHBD), ratio of ≤50%	4 (6.6)	0.852	0.729 to 0.977	Strong agreement
	Type 2 (CDDP/EHBD), ratio of >50% and ≤75%	34 (55.7)			
	Type 3 (CDDP/EHBD), ratio of >75	23 (37.7)			
CD course	Not parallel to CHD	26 (42.6)	0.834	0.697 to 0.972	Strong agreement
	Parallel to CHD	35 (57.4)			
Distal CBD angulation	Acute angle ≤30^0	17 (27.9)	0.868	0.743 to 0.992	Strong agreement
	Acute angle >30^0	44 (72.1)			
Pancreatic duct type	Type 1 (bifid, dominant Wirsung)	8 (13.1)	0.759	0.576 to 0.942	Moderate agreement
	Type 2 (bifid, dominant Santorini)	3 (4.9)			
	Type 3 (rudimentary non-draining duct of Santorini	47 (77)			
	Type 4 (pancreatic divisum)	1 (1.6)			
	Type 5 (ansa pancreatica)	2 (3.3)			
CBD-PD junction	Separate	24 (39)	0.886	0.791 to 0.980	Strong agreement
	No dominant duct	14 (23.7)			
	PD dominant	8 (13.6)			
	CBD dominant	15 (23.7)			

Based on the consensus of at least two of three radiologists, Type 2 (mid-CBD) comprised 55.7% of CD insertion; parallel course comprised 57.4% of CD course; angle >30^{o} comprised 72.1% of distal CBD angle; Type 3 (non-draining Santorini) comprised 77% of pancreatic duct type; and absent common channel comprised 39% of CBD-PD junction.

Between papilla protrusions and periampullary ducts, Fisher's exact test for independence was statistically significant only for distal CBD angle (p = 0.002) with large protrusions having more acute distal CBD angle ≤30^{o} (87%); while small and regular protrusions had more CBD angle >30^{o} (63.6% and 62.5%, respectively). Though not statistically significant, (a) small and large protrusions had more Type 2 CD insertion (mid-CBD) at 54.5% and 69.6%, respectively, while regular protrusion had more Type 3 (proximal CBD) at 50%; (b) small and regular protrusions had more non-parallel CD course at 68.2% and 68.8%, respectively, while large protrusions had more parallel CD course at 52.2%; and (c) regular protrusions had more absent common channel at 56.3%. There seemed to be no correlation between protrusions and pancreatic duct types with all three protrusions having more Type 3 (non-draining Santorini) followed by Type 1 pancreatic duct type (Wirsung dominant bifid) **(Table 4).**

Table 4. Periampullary ductal morphology in relation to duodenal papillary protrusion morphology

Periampullary Ductal Structures		Oral Protrusion Pattern			*p* value
		n = 22 **Small Protrusion** n (%)	n = 16 **Regular Protrusion** n (%)	n = 23 **Large Protrusion** n (%)	
CD insertion	Type 1 (CDDP/EHBD), ratio of ≤50% Type 2 (CDDP/EHBD), ratio of >50% and ≤75% Type 3 (CDDP/EHBD), ratio of >75	1 (4.5) 12 (54.5) 9 (40.9)	2 (12.5) 6 (37.5) 8 (50.0)	1 (4.3) 16 (69.6) 6 (26.1)	0.311
CD course	Not parallel to CHD Parallel to CHD	15 (68.8) 7 (31.8)	11 (68.8) 5 (31.3)	11 (47.8) 12 (52.2)	0.306
Distal CBD angulation	Acute angle ≤30^{0} Acute angle >30^{0}	8 (36.4) 14 (63.6)	6 (37.5) 10 (62.5)	20 (87.0) 3 (13.0)	**0.002**
Pancreatic duct type	Type 1 (bifid, dominant Wirsung) Type 2 (bifid, dominant Santorini) Type 3 (rudimentary non-draining duct of Santorini) Type 4 (pancreatic divisum) Type 5 (ansa pancreatica)	2 (9.1) 1 (4.55) 18 (81.8) 0 (0) 1 4.55)	3 (18.8) 0 (0) 11 (68.6) 1 (6.3) 1 (6.3)	3 (13.0) 2 (8.7) 18 (78.3) 18 (78.3) 0 (0)	0.590
Length of common channel	0.38 ± 0.35	0.38 ± 0.35	0.37 ± 0.47	0.52 ± 0.41	0.431
CBD-PD junction	Separate No dominant duct PD dominant CBD dominant	8 (36.4) 4 (18.2) 3 (13.6) 7 (31.8)	9(56.3) 1 (6.3) 4 (25.0) 2 (12.5)	7 (30.4) 9 (39.1) 1 (4.3) 6 (26.1)	0.481

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Between papilla pattern and periampullary ducts, though Fisher's exact test for independence did not yield any statistically significant results, (a) gyrus papilla had more type 3 CD insertion (proximal CBD) at 66.7%, while the rest had more type 2 CD insertion (mid-CBD) at 56.3-83.3%; (b) isolated papilla had more parallel CD course at 66.7%, while the rest had more non-parallel CD course at 54.5-100%; and (c) isolated papilla had more absent common channel at 66.7%, while gyrus papilla had more PD dominant CBD-PD junction at 66.7%. There seemed to be no correlation between papilla pattern and distal CBD angle (all papilla patterns had more distal CBD angle >30^o) and pancreatic duct type (all papilla patterns had more Type 3 non-draining Santorini followed by Type 1 Wirsung dominant bifid) **(Table 5)**.

Table 5. Periampullary ductal morphology in relation to duodenal papillary pattern morphology

	Periampullary Ductal Structures	n = 25 **Annular (Papilla-A)** n (%)	n = 16 **Unstructured (Papilla-U)** n (%)	n = 11 **Longitudinal (Papilla-LO)** n (%)	n = 6 **Isolated (Papilla-I)** n (%)	n = 3 **Gyrus (Papilla-G)** n (%)	*p*-value
CD insertion	Type 1 (CDDP/EHBD) ratio of ≤50%	4 (16)	0 (0)	0 (0)	0 (0)	0 (0)	0.284
	Type 1 (CDDP/EHBD) ratio of >50% & ≤75%	11 (68.8)	9 (56.3)	8 (72.7)	5 (83.3)	1 (33.3)	
	Type 1 (CDDP/EHBD) ratio of >75%	10 (40)	7 (43.8)	3 (27.3)	1 (16.7)	2 (66.7)	
CD course	Not parallel to CHD	15 (60)	9 (56.3)	6 (54.5)	2 (33.3)	3 (100)	0.580
	Parallel to CHD	10 (40)	7 (43.8)	5 (45.5)	4 (66.7)	0 (0)	
Distal CBD angulation	Acute angle ≤30^0	6 (24)	4 (25.0)	5 (45.5)	1 (16.7)	1 (33.3)	0.594
	Angle >30^0	19 (76)	12 (75.0)	6 (54.5)	5 (83.3)	2 (66.7)	
Pancreatic duct type	Type 1 (bifid, dominant duct of Wirsung)	2 (8)	3 (18.8)	2 (18.2)	0 (0)	1 (33.3)	0.142
	Type 2 (bifid, dominant duct of Sartorini)	1 (4)	2 (12.5)	0 (0)	0 (0)	0 (0)	
	Type 3 (rudimentary non-draining duct of Sartorini)	21 (84)	9 (56.3)	9 (81.8)	6 (100)	2 (66.7)	
	Type 4 (pancreatic divisum)	0 (0)	1 (6.3)	0 (0)	0 (0)	0 (0)	
	Type 5 (ansa pancreatica	1 (4)	1 (6.3)	0 (0)	0 (0)	0 (0)	
Length of common channel		0.382 ± 0.367	0.693 ± 0.358	0.217 ± 0.386	0.534 ± 0.413	0.472 ± 0.473	0.398
CBD-PD junction	Separate	10 (40)	7 (43.8)	3 (27.3)	4 (66.7)	0 (0)	0.416
	No dominant duct	5 (20)	4 (25.0)	4 (36.4)	1 (16.7)	0 (0)	
	PD dominant	3 (12)	0 (0)	2 (18.2)	1(16.7)	2 (66.7)	
	CBD dominant	7 (28)	5 (31.3)	2 (18.2)	0 (0)	1 (33.3)	

Discussion

Our study showed moderate-strong agreement for the MRCP classification of the periampullary ducts, but only weak to minimal agreement for the endoscopic classification of the duodenal papilla. This is in contrast to the original data by Watanabe which showed good agreement at 0.788 for oral protrusion and 0.750 for papilla pattern.[1] However, our results were based on the agreement between two observers as computed by Cohen's kappa, while their results were based on the agreement between three observers as computed by Fleiss kappa. Unfortunately, we did not have the third endoscopist look at all the videos, only those with disagreements between the first two endoscopists.

Our study showed that large protrusions predicted an acute distal CBD angle of ≤30^o. Progressively larger protrusions were associated with increasing step angle and intramural CBD length.[13] We also demonstrated that the larger the protrusion, the higher the proportion of

acute distal CBD angle ≤30^{o} (87% of large, 37.5% of regular, and 36.4% of small protrusions). However, we did not measure the intramural CBD length. We did measure the length of the common channel but did not find a correlation between this and protrusion. Studies consistently found that large protrusions had more difficult cannulation.[1-4] This could be due to the above-mentioned acute distal CBD angle ≤30^{0}. Among CBD angles, acute CBD angle had been shown to lead to less ERCP success, longer cannulation time, higher PD cannulation, and higher PEP among beginners.[7] Recently, large protrusions with pleats were associated with longer intraduodenal portion of the CBD and prolonged cannulation time using needle knife fistulotomy.[14]

Though not significant, our study also showed that large protrusions have high proportion of Type 3 PD (non-draining Santorini). Studies had consistently found large protrusions to have higher PEP.[14-16] Recently, Wang found papilla with long axis length/short axis length (L/S ratio) ≥1.5 have higher PEP.[17] This could be due the Type 3 PD, especially in the presence of difficult cannulation from the acute distal CBD angle ≤ 30^{o}. Type 3 PD (non-draining Santorini) had been shown to increase risk for pancreatitis,[18] and could conceivably predispose to higher rates of PEP due to lack of secondary drainage path. Type 4 PD (pancreas divisum) had also been associated with pancreatitis, but the studies have been contradictory.[19] Types 4 and 5 PD (ansa pancreatica) do not allow for double guidewire technique when there is difficult cannulation.

Though not significant, we also showed that regular protrusions had more non-parallel CD, Type 3 (proximal CBD) CD insertion, distal CBD angle >30^{o}, and absent common channel. This could also be the reason why none of the studies associated regular protrusions with difficult cannulation.[1-4] We did not find any trend that could explain why small protrusions were associated with difficult cannulation.[1-4,16]

Though also not significant, our study showed that isolated papilla had more parallel CD, Type 2 CD insertion (mid-CBD), distal CBD angle >30^{0}, Type 3 PD (non-draining Santorini), and absent common channel. These could explain why isolated papilla was never associated with difficult cannulation.[1-4] Parallel CD course could theoretically cause difficult cannulation only with Type 1 CD insertion (distal CBD) through unrecognized repeated cannulation and manipulation of the CD instead of the CBD which could sometimes lead to complications.[20] All these could offset the higher theoretical risk of PEP from the Type 3 PD (non-draining Santorini).

Though not significant, our study also showed that gyrus papilla had more PD dominant junction. In their study, Watanabe demonstrated that gyrus papillae were more difficult to cannulate for inexperienced endoscopists.[1] Two studies showed that the P-B type (similar to our CBD dominant junction) was equal to an acute angle and the B-P type (similar to our PD dominant junction) was equal to a right angle.[21,22] It is conceivable that a gyrus papilla with a PD dominant type of PB union would be more difficult to cannulate by virtue of the PD being in line with the common channel and the CBD joining it at a right angle. We did not find any trend that could explain why unstructured, annular, and longitudinal papilla were previously associated with difficult cannulation.[1,4]

Strengths, Limitations, and Recommendations

The strength of our study is that we excluded anatomical factors that could confound the association of duodenal papilla morphology and periampullary ducts. We also used the consensus of at least two out of three blinded observers to classify our papilla and periampullary ductal morphology. In the process, we found some correlations of the papilla morphology to the periampullary ducts that could explain previously published associations between duodenal papilla morphology and cannulation difficulty and PEP. These may help guide endoscopists in their cannulation attempts.

However, our study had limitations. We did not reach our intended sample size. We were also not able to correlate these anatomies with biliary cannulation and PEP as we had to include ERCPs done by endoscopists of different skill level in our failed attempt to reach our target sample size.

We recommend that a prospective multicenter study be conducted to include more patients. Such study could also explore number of pleats over the protrusions, L/S ratio, biliary cannulation, and PEP.

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Conclusion

Large protrusions predicted acute distal CBD angle ≤30^0 which is related to difficult cannulation. Knowing that with an acutely angled distal CBD, the endoscopist is conscious that the CBD angle is likely directed upwards relative to the bile duct, which should affect the angle of approach of the sphincterotome, this can be facilitated by a curved tip sphincterotome to navigate the bend. Furthermore, it is prudent to have a lower threshold in implementing maneuvers to facilitate cannulation (such as precut papillotomy, double guidewire technique and the use of a sphincterotome); likewise, the attempts made by a trainee endoscopist are ideally minimized.

Though not statistically significant, large protrusions seem to have more Type 3 PD (non-draining Santorini) (previously associated with pancreatitis), and regular protrusions seem to have more non-parallel CD course, proximal CBD CD insertion, distal CBD angle >30^o, and absent common channel (all not associated with difficult cannulation and PEP).

Though also not significant, isolated papilla had more parallel CD course and Type 3 PD (that could theoretically lead to more difficult cannulation and PEP, respectively), but these were possibly negated by more mid CBD CD insertion, distal CBD angle >30^o, and absent common channel (all not associated with difficult cannulation). Though also not significant, gyrus papilla had more PD dominant junction (previously associated with more difficult cannulation), and we recommend avoiding multiple attempts that end with PD entry, but rather proceeding with a double guidewire cannulation after the first PD entry.

Conflicts of Interest

The authors declare no conflicts of interest.

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