Duodenal Papilla Morphology and ERCP Cannulation Difficulties, Failure and Complications in Manila Doctors Hospital, A Tertiary Private Hospital: A Cross-Sectional Study

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Abstract

BACKGROUND/OBJECTIVES: Different major duodenal papilla morphology pose various challenges of cannulation and development of ERCP complications. These morphologies may guide the endoscopist in his cannulation approach and complication prevention. The aim of this study is to determine the major duodenal papilla morphologies of ERCP patients in Manila Doctors Hospital and their associated cannulation difficulties, failure, and complications.

METHODS: This is a retrospective cross-sectional study of 246 ERCPs at the Manila Doctors Hospital from January 2017 to December 2018 with naïve duodenal papillae classified according to Watanabe (2019) as follows: oral protrusion (small, regular, large) and papilla pattern (annular, unstructured, longitudinal, isolated, gyrate). Association of papilla morphology with cannulation difficulties, failure, and complications were analyzed using logistic regression.

RESULTS: Among protrusions, small oral protrusions were more difficult to cannulate compared to regular (OR 0.493, p=0.017) and large protrusions (OR 0.702, p=0.426). Large protrusions had the highest risk for failed cannulation (OR 2.04, p=0.445). Among papilla patterns, unstructured papilla patterns had the highest risk for difficult (OR 3, p=0.008) and failed cannulation (OR 7.08, p=0.020). Complications developed in 7 in-patients with 3 (1.73%) post-ERCP pancreatitis, 1 (0.58%) post- sphincterotomy bleeding, and 1 (0.58%) cholangitis and 2 (1.16%) mortalities. One had myocardial infarction 2 days post-ERCP and another had septic shock after 2 days despite endoscopic biliary drainage and antibiotics.

CONCLUSION: Among protrusions, small oral protrusions had the highest risk for difficult cannulation while large protrusions had the highest risk for failed cannulation. Among papilla patterns, unstructured papilla patterns had the highest risk for difficult and failed cannulation.

KEYWORDS: ERCP, papilla morphology, cannulation success

INTRODUCTION and OBJECTIVES

Endoscopic retrograde cholangiopancrea-tography (ERCP) is a procedure requiring expertise with risks of life-threatening complications. Endoscopists who perform ERCP recognize the obvious differences in the macroscopic appearance of the major duodenal papilla or ampulla of Vater. This has led to a widespread conception among endoscopists that certain specified appearances of the papilla are more difficult to cannulate and therefore more prone to adverse events [1]. Difficult cannulation has previously been shown to correlate with increased complication rates, foremost being post-ERCP pancreatitis. Other complications include hemorrhage, cholangitis and perforation of the common bile duct or duodenum [2]. The quality indicators of ERCP practice include adequate indications and success rate of cannulation as well as low complication [3,4]. In 2019, Watanabe et, al. proposed a classification system of the duodenal papilla according to oral protrusion pattern and papillary patterns. They noted a significant difficulty in cannulating the protrusion-L type of papilla [5]. This study aims to investigate the morphologic differences of the major duodenal papilla of the ERCPs done in

Manila Doctors Hospital from January 2017 to December 2018 and determine the cannulation success rates, and associated difficulties of cannulation and post-procedural complications encountered, hypogeusia, abdominal discomfort and gastrointestinal bleeding have as well been documented; these varies significantly among different study populations, presenting frequently with early and mild onset followed by the typical respiratory symptoms.[4]

METHODOLOGY

PATIENTS. This is a retrospective cross-sectional study of a total of 411 patients who underwent ERCP at the Manila Doctors Hospital, a tertiary hospital, between January 2017 to December 2018 by going through the report database (ImageArk Endosoft) and CD recordings in the endoscopy unit. Patients included were those who underwent ERCP for the first time either as outpatient or inpatient by experienced endoscopists (>300 career ERCPs). Patients excluded were those who have previous history of ERCP and sphincterotomy or stenting, surgically altered intestinal anatomy, and those with duodenal papilla appearing to be difficult to classify on video documentation (unclassifiable due to distortion from tumor invasion, hidden within diverticulum, incomplete/unclear/missing video documentation). Patient's demographic data, indication for ERCP, endoscopic diagnosis, procedural findings were likewise recorded. Inpatient records were reviewed to document complications arising post-procedure.

CLASSIFICATION OF DUODENAL PAPILLA. The classification used to identify the different papilla morphology was the proposed classification by Watanabe et. al. in 2019 [5]. They described the papilla according to the oral protrusion (OP) pattern or the ratio of length of oral protrusion to the transverse diameter of the papilla and the papilla pattern (PP) or the surface pattern of the orifice. The OP is classified into three types: small (S) for which the ratio of the length of the oral protrusion to the transverse diameter of the papilla was less than one-half; regular (R) for which the ratio was one-half or more but less than two; and large (L) for which the ratio is two or more (Figure 1A). The PP is classified into five types: annular (A) comprised of the typical papilla with an annular shape; unstructured (U), comprised those with no clear orifice; longitudinal (LO) comprised of longitudinal grooves continuous with the orifice with the length of the groove being longer than the transverse diameter of the biliary duct axis of the papilla; isolated (I) comprised of two separate isolated orifices of the biliary and pancreatic ducts; and gyrus (G) comprised of gyrate pattern of the papilla (Figure 1B) [5]. Other endoscopic finding that was noted and related to the papilla was the presence of a periampullary diverticulum. Two endoscopist classified the images of the papilla morphology independently, and a third endoscopist was consulted to decide the classification if there was disagreement.
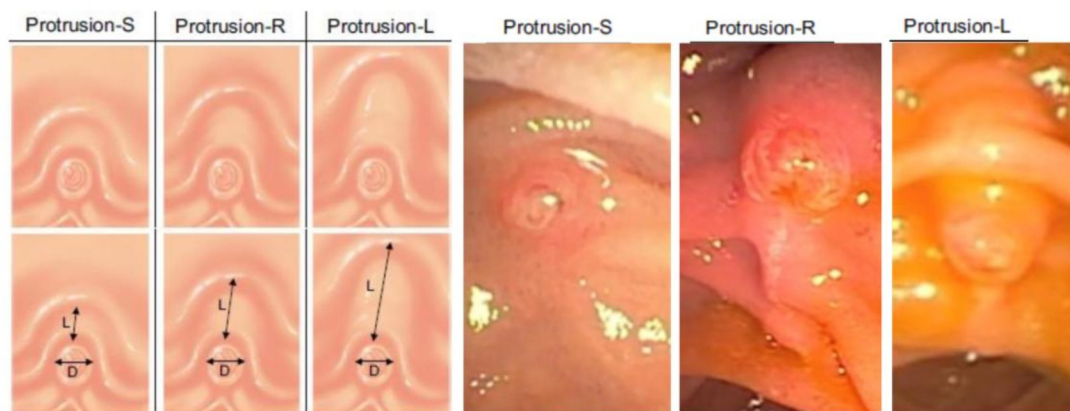

Figure 1A. Oral Protrusion Pattern Classification According to Watanabe 2019 with sample photos on the right from this study.
(Image from Watanabe M, Okuwaki K, Kida M, et al. Transpapillary Biliary Cannulation is Difficult in Cases with Large Oral Protrusion of the Duodenal Papilla. Dig Dis Sci. 2019;64(8):2291-2299. doi:10.1007/s10620-019-05510-z)
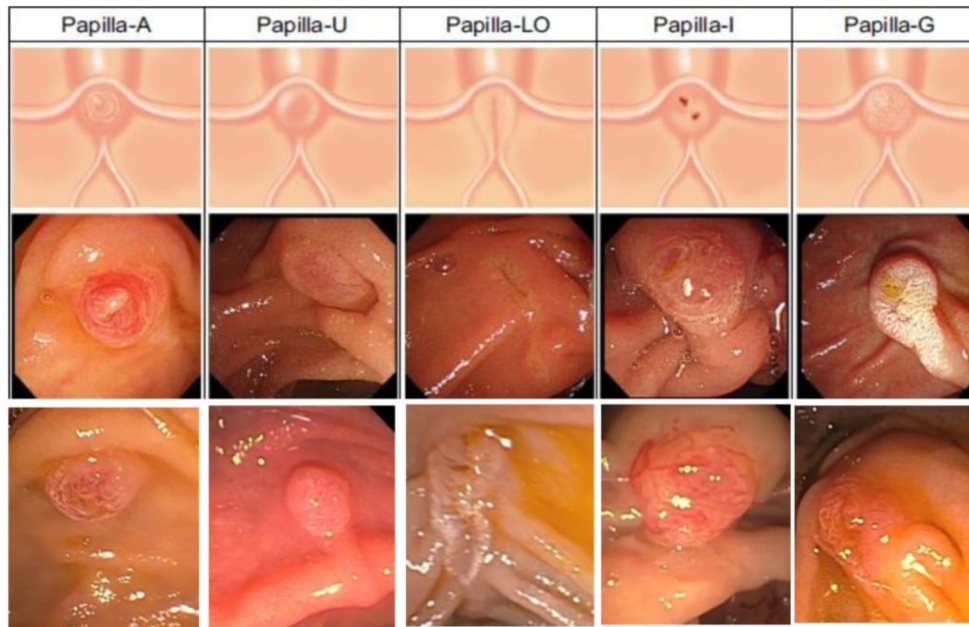
Figure 1B. Papilla Pattern Classification According to Watanabe 2019 and sample photos from this study.

(Image from Watanabe M, Okuwaki K, Kida M, et al. Transpapillary Biliary Cannulation is Difficult in Cases with Large Oral Protrusion of the Duodenal Papilla. Dig Dis Sci. 2019;64(8):2291-2299. doi:107/s10620-019-05510-z)

Difficulty of cannulation was defined by European Society for Gastrointestinal Endoscopy (ESGE) in 2016 by the presence of any of the following criteria: (1) more than five minutes, (2) five attempts at touching the orifice, or (3) two pancreatic guidewire passages [6].

Complications related to the ERCP procedure were reported for the inpatients only because outpatients do not have charts available for review. Complications included post-ERCP pancreatitis, bleeding, perforation, cholangitis, and death directly arising from the aforementioned events occurring within 30 days of ERCP. These were reported as percentage frequency

STATISTICAL ANALYSIS AND ETHICS

Quantitative variables are summarized as mean and standard deviation, while qualitative variables are tabulated as frequency and percentage. Inter-observer agreement with the oral protrusion and papilla pattern classifications were determined by using kappa statistics and interpreted as poor ($k \leq 0.2$), fair ($0.21 \leq k \leq 0.40$), moderate ($0.41 \leq k \leq 0.60$), good ($0.61 \leq k \leq 0.80$)

to very good ($0.81 \leq k \leq 1.00$) [7]. The association of papilla morphology and cannulation success and difficulty was analyzed using univariate analysis thru Epi Info Version 7, with p value <0.05 considered as significant. Minimum sample size of at least 144 patients was calculated based on the cannulation success rate of 97.6% on the study of Watanabe (2019) with margin of error of 2.5% and confidence level of 95%.

The study protocol was reviewed and approved by the Manila Doctors Hospital Institutional Review Board (Ref MDH IRB 2021-004 R).

RESULTS

A total of 411 ERCPs were reviewed. A total of 165 patients were excluded from the study due to the following reasons: 61 patients had previous ERCP, 14 had ampullary tumors precluding classification of the papilla, and 20 had unclear video images; 80 patients had missing video documentations (Figure 2). A total of 246 subjects were included in the study. Table 1 describes the demographics of our patient population.
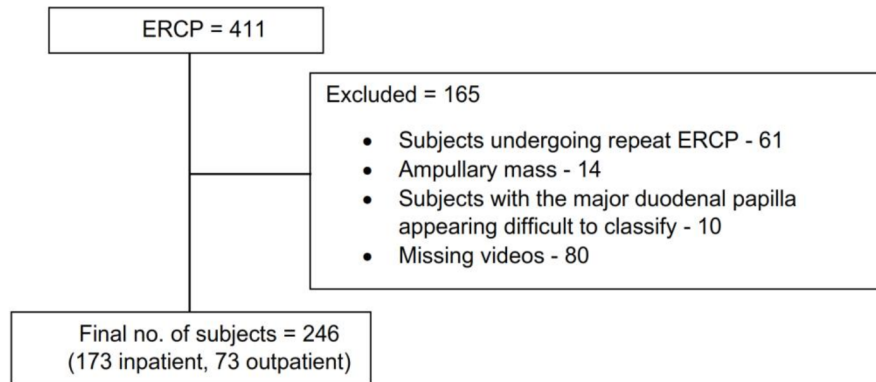
FIGURE 2. Flow diagram of patient enrolment and exclusion of ERCP naïve patients who underwent ERCP from 2017 to 2018 at MDH.

The most common indication was presence of choledocholithiasis (80.89%), followed by malignant obstruction (cholangiocarcinoma, pancreatic new growth) (8.94%), biliary stricture (4.87%), and cholangitis (3.66%). Other indications included evaluation and management of post-cholecystectomy biliary leak and consideration of sump syndrome (1.62%).

The most common endoscopic diagnosis post procedure was the presence of choledocholithiasis (59.35%) followed by recent passage of stone (37%), malignant obstruction (cholangiocarcinoma, pancreatic new growth) (7.32%), biliary stricture (6.91%) and normal pancreatic duct (3.25%). Other diagnosis included biliary ectasia, biliary leak post cholecystectomy, and sump syndrome (8.54%).

TABLE 1. Demographic data of patients who underwent ERCP for the first time in MDH Endoscopy Unit from 2017 to 2018

CHARACTERISTIC	N = 246	%
Age (years)	52 +/- 17	-
Female	148	60.16%
Male	98	39.84%
Inpatient	173	70.33%
Outpatient	73	29.67%
Indications		
• Choledocholithiasis	199	80.89%
• Malignancy	22	8.94%
• Stricture	12	4.87%
• Cholangitis	9	3.66%
• Others	4	1.62%
Diagnosis		
• Choledocholithiasis	146	59.35%
• Recent passage of stone	36	14.63%
• Malignancy	18	7.32%
• Stricture	17	6.91%
• Normal	8	3.25%
• Others	21	8.54%
Failed Cannulation	9	3.65%
Difficult cannulation*	80	32.5%
• > 5 min duration to cannulate	77	31.3%
• Pre-Cut sphincterotomy	25	10.16%
• Pancreatic duct cannulation	18	7.31%
Periampullary Diverticulum (PAD)	57	23.27%

The inter-observer agreement between the two endoscopists who classified the papillae according to oral protrusion and papilla patterns was calculated using kappa statistics with good and moderate agreement (OP k 0.619, CI 0.523 – 0.716; PP k 0.607, CI 0.459 – 0.754) for the oral protrusion and papillary pattern classifications, respectively (Table 2).

TABLE 2. Distribution and Kappa Inter-observer Agreement of the Different Classifications of Papilla Morphology

Papillary Morphology	n (%)	Kappa (k)	CI (95%)	Agreement
Oral protrusion pattern				
Small (Protrusion-S)	89 (36.18%)			
Regular (Protrusion-R)	127 (51.63%)	0.619	0.523 – 0.716	Good
Large (Protrusion-L)	30 (12.2%)			
Papilla pattern				
Annular (Papilla-A)	180 (73.17%)			
Unstructured (Papilla-U)	28 (11.38%)			
Longitudinal (Papilla-LO)	23 (9.35%)	0.607	0.459 – 0.754	Moderate
Isolated (Papilla-I)	2 (0.81%)			
Gyrus (Papilla-G)	13 (5.28%)			

Difficult cannulation was noted in 80 (32.5%) patients (Table 3). Among oral protrusion patterns, protrusion-S has the highest risk for difficult cannulation (Protrusion-R - OR 0.493, p=0.017; Protrusion-L -OR 0.702, p=0.426). Among the papilla patterns, papilla-U has the highest risk for difficult cannulation (OR 3, p=0.008).

TABLE 3. Logistic Regression Analysis of Papilla Morphology with Difficult Cannulation among ERCP-naïve patients who underwent ERCP at MDH from 2017 to 2018

Papillary Morphology	Difficult cannulation	Non-Difficult cannulation	OR	CI (95%)	P-value
Oral protrusion pattern					
Small (Protrusion-S) (n=89)	37	52	REF*	-	-
Regular (Protrusion-R) (n=127)	33	94	0.493	0.277 – 0.880	0.017
Large (Protrusion-L) (n=30)	10	20	0.702	0.294 – 1.674	0.426
TOTAL	80	166			
Papilla pattern					
Annular (Papilla-A) (n=180)	50	130	REF	-	-
Unstructured (Papilla-U) (n=28)	15	13	3	1.333 – 6.751	0.008
Longitudinal (Papilla-LO) (n=23)	8	15	1.387	0.554 – 3.472	0.485
Isolated (Papilla-I) (n=2)	1	1	2.6	0.160 – 42.37	0.502
Gyrus (Papilla-G).(n=13)	6	7	2.229	0.714 – 6.955	0.168
TOTAL	80	166			

*REF – Reference Category to which each other category is compared

Overall cannulation success rate was 96% (237/246) (Table 4). Nine patients had failed ERCP due to inability to cannulate the CBD. Of these 9 patients, 4 had protrusion-R (2 papilla_A, 1 papilla-U, and 1 papilla-LO), 3 protrusion-S (1 papilla-A, 2 papilla-U) and 2 had protrusion-L (1 papilla-LO, 1 papilla-G). Six of these patients also underwent pre-cut sphincterotomy of the papilla, however, still failed at CBD cannulation. Among oral protrusion patterns, protrusion-L has the highest risk for failed cannulation, however, did not reach statistical significance (OR 2.04, p=0.445). Among papilla patterns, Papilla-U pattern has the highest risk for failed cannulation (OR 7.08, p=0.020).

TABLE 4. Logistic Regression Analysis of Papilla Morphology with Failure to cannulate among ERCP-naïve patients who underwent ERCP at MDH from 2017 to 2018

Papillary Morphology	Failed cannulation	Successful cannulation	OR	CI (95%)	P-value
Oral protrusion pattern					
Small (Protrusion-S) (n=89)	3	86	*REF	-	-
Regular (Protrusion-R) (n=127)	4	123	0.932	0.203 – 4.271	0.928
Large (Protrusion-L) (n=30)	2	28	2.04	0.325 – 12.884	0.445
TOTAL	9	237			
Papilla pattern					
Annular (Papilla-A) (n=180)	3	177	REF	-	-
Unstructured (Papilla-U) (n=28)	3	25	7.08	1.354 – 37.020	0.020
Longitudinal (Papilla-LO) (n=23)	2	21	5.619	0.887 – 35.575	0.067
Isolated (Papilla-I) (n=2)	0	2	-	-	-
Gyrus (Papilla-G).(n=13)	1	12	4.917	0.474 – 50.912	0.182
TOTAL	9	237			

*REF – Reference Category to which each other category is compared

ERCP-related complications occurred in 7 inpatients (4.05%) (Table 5). Three patients (2 patients with protrusion-R, papilla-A, and 1 patient with protrusion R, papilla-U) had post-ERCP pancreatitis (1.73%) resolved within 4-7 days hospital observation, one patient with protrusion-R, papilla-G had post-sphincterotomy site bleeding requiring endoscopic hemostasis (0.58%), and one patient protrusion R, papilla A had cholangitis developing after the procedure (0.58%) resolved with antibiotic therapy. There were 2 mortalities noted; one patient with protrusion R, papilla A was a 73 year-old female developing myocardial infarction 2 days post ERCP and another was a 43 year-old male with protrusion-R, papilla-U admitted for severe cholangitis prior to ERCP with sphincterotomy and balloon stone extraction with findings of purulent bile and three CBD stones, unfortunately, patient succumbed to the infection 2 days post procedure; both mortalities occurring within 30 days post procedure and was still considered an ERCP-related mortality. No perforation related to the endoscopic procedure was noted among the patients.

Table 5. Frequency of ERCP-related complications among patients undergoing ERCP at MDH from 2017 to 2018

Papillary Morphology	PEP	Bleeding	Perforation	Cholangitis	Mortality
Oral protrusion pattern					
Small (Protrusion-S) (n=89)	0	0	0	0	0
Regular (Protrusion-R) (n=127)	3	1	0	1	2
Large (Protrusion-L) (n=30)	0	0	0	0	0
TOTAL	3	1	0	1	2
Papilla Pattern					
Annular (Papilla-A) (n=180)	2	0	0	1	1
Unstructured (Papilla-U) (n=28)	1	0	0	0	1
Longitudinal (Papilla-LO) (n=23)	0	0	0	0	0
Isolated (Papilla-I) (n=2)	0	0	0	0	0
Gyrus (Papilla-G).(n=13)	0	1	0	0	0
TOTAL	3	1	0	1	2

There was noted significant occurrence of periampullary diverticulum among the studied subjects (57, 23.17%) and a Fishers exact test was conducted to determine if the presence of a diverticulum posed a significant risk of difficulty in papilla cannulation. However, the test failed to show a significant association (p=0.747) (Table 6).

Table 6. Fishers exact test for association of periampullary diverticulum with difficulty cannulation.

	Non-difficult Cannulation (n=166)	Difficult cannulation (n=80)	P=value
Without Diverticulum	126 (75.9)	63 (78.75)	0.747
With Diverticulum	40 (24.10)	17 (21.25)	

DISCUSSION

Several studies have acknowledged that the morphology of the major duodenal papilla posed a challenge to cannulating the CBD [8]. In 2017, Harraldson et. al. proposed a classification scheme of the duodenal papilla which predicted cannulation difficulty. The 4 types of papilla (regular, small, protruding/pendulous, ridged) provided a reliable classification and in 2018, a follow-up study provided correlation with regards to cannulation difficulty with the small type being the most difficult to cannulate and highest risk for post-ERCP pancreatitis [9,10]. In 2019, Watanabe et. al. proposed a new classification scheme incorporating elements of Harraldson's, with their classification of Protrusion S corresponding to Type 2 small papilla, Protrusion R to Type 1 regular papilla and Protrusion L to Type 3 protruding papilla. They found protrusion L to be more difficult with higher risk of cannulation failure probably due to misalignment between the ERCP catheter and the biliary duct axis during cannulation leading to difficult cannulation and failure [5]. Our study showed that both small and large oral protrusions were more difficult to cannulate than regular protrusions, however, only large protrusion pattern was noted to have a greater risk for failed cannulation, though, not statistically significant probably due to sample size limitation and small event rate for failed cannulation. After we started our study, Balan et al published another classification in 2020. Their classification appears to be an expanded Harraldson classification of the major papilla morphology [11]. Balan regular type corresponds to the Harraldson's Type 1 Regular papilla, Balan Types 1 and 2 corresponds to Harraldon's Type 2 Small papilla, and Balan Types 3 and 4 corresponds to Harraldson's Type 3 Protruding papilla. Similarly, their study found that their Balan Type 1 papillae (small and/or retracted papilla, without a recessus and infundibulum) were significantly linked to difficult cannulation and the Balan type 4 papillae (large papilla with multiple overlying folds over the orifice (commonly referred to as a hooded papilla or a Shar-Pei dog papilla) were noted to be independent risk factors for post-ERCP pancreatitis [11].

Haraldsson's classification included only 1 papilla pattern – the ridge pattern. Watanabe's classification included 5 patterns with the longitudinal pattern corresponding to the ridge pattern of Haraldsson's. In Watanabe's study, papilla pattern A and G proved more difficult to cannulate requiring more attempts. In contrast, our study found that papilla pattern A to have the lowest risk for difficult and failed cannulation. In our study, the unstructured papilla (papilla-U) was the most difficult and at risk for failed cannulation. This might be due to difficulty in directing the catheter tip in a papilla without a discernible orifice. Balan's classification did not include papilla patterns.

Several studies have investigated the influence of periampullary diverticulum (PAD) in the success and difficulty of duodenal papilla cannulation. Failures in cannulation may be partially attributable to difficulties in detecting the papilla, especially in cases where the papilla is found deep within, often at the very bottom of, the diverticulum. But in some other studies,

the presence of PAD had no influence on cannulation of CBD [12]. Our study noted the presence of PAD in 23.17% of the cases and analysis thru Fisher's exact test did not find a significant difference towards difficulty cannulating the duodenal papilla among subjects with clearly visible and classifiable papilla with PAD.

In the literature, complications directly attributed to ERCP are as high as 6.8%. Mortality rates are about 0.3%. The incidence of post-ERCP pancreatitis (PEP) is 3.5%, making it the most frequent complication following the procedure. In 90% of cases, pancreatitis is mild-to-moderate in severity. Gastrointestinal bleeding happens 1.3% of the time. Infections, as cholangitis and cholecystitis, occur at a rate of 1.4% [4]. Haraldsson's study showed that small papillae were found to be associated with higher frequency of PEP, which increased in parallel with the frequency of difficult cannulation, probably due to the biliary or papillary manipulation, but they were not able to support this statistically. Watanabe's study was not able to analyze the association of the different papilla morphology with the incidence of PEP because their population included patients who had undergone preventive procedures and those who have not, rendering evaluation impossible [5]. On the other hand, Balan's recent study have found out that their type 4 papilla have proven to be an independent risk factor for post-ERCP pancreatitis (OR = 12.176, 95%CI, p = 0.005), attributed indirectly to difficult cannulation and contributive factors of increased frequency of rescue needle-knife papillotomy and prophylactic pancreatic stenting for patients with type 4 papillae [11]. Our study results showed complication rates with the same figures seen in literature. However, due to the small occurrence of the specific post-ERCP complications, we were not able to statistically correlate the papilla morphology with the risk of their development. In our study, post ERCP pancreatitis occurred in 3 patients with regular oral protrusion pattern and unstructured papilla probably because of prolonged and multiple attempts at cannulating the papilla predisposing to edema and inflammation as these cases have not reported any incident of pancreatic duct cannulation or contrast injection. The other complications noted in the study were a case of post-sphincterotomy bleeding (case of cholangitis, with no coagulation derangement with a 1.5 cm sphincterotomy done at 11 -12 o'clock position) and two cases of severe cholangitis and a

case of myocardial infarction post-procedure were probably isolated cases that cannot be associated with difficult cannulation of the duodenal papilla. There were no noted complications on the patients who had failed cannulation.

LIMITATION

Being a retrospective study, data gathering relied on the accuracy of data recorded in the endoscopy reports, ERCP video documentations, and inpatient charts. Pancreatic duct cannulation, particularly, was considered only on review of the endoscopic reports which some may have not reported the inadvertent pancreatic duct cannulation therefore, underestimating the number of patients with difficult cannulation. The influence of a fellow-in-training doing the cannulation process may also affect classifying the procedure as difficult cannulation if the process takes more than 5 minutes and more than 5 attempts to successfully cannulate the papilla. This influence is not documented in the reports, though most of the procedures are fully performed by the expert endoscopists in our institution.

CONCLUSION

Among oral protrusion pattern, a small oral protrusion pattern has the highest risk for difficult cannulation while a large protrusion pattern has the highest risk for failed cannulation; among papilla pattern, an unstructured papilla pattern was a risk factor for cannulation failure. Though the rate of complication is found to be small in our institution, these morphologic differences of the papilla and risk for difficult cannulation and post-ERCP complications should be considered.

RECOMMENDATIONS

We recommend prospective multicenter studies to include more patients to observe cannulation difficulties performed by experienced endoscopists related to the differences in papilla protrusion and orifice pattern and observe for post-ERCP complications. This can also be used to develop cannulation techniques for each specific papilla morphology minimizing risk for complications.

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