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ORIGINAL ARTICLE

# Relationship of difficult endoscopic retrograde cholangiopancreatography cannulation and visual characteristics of papilla

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bile visibility, cannulation, endoscopic retrograde cholangiopancreatography, papilla orifice.

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## Abstract

**Background and Aim:** Endoscopic retrograde cholangiopancreatography (ERCP) is commonly used to diagnose and treat bile duct and pancreatic disorders. Successful cannulation of the papilla is crucial for the effectiveness of ERCP; however, sometimes, it can be challenging to achieve. This study explores the relationship between net difficult ERCP cannulation with bile visibility, papilla orifice visibility, and papilla position and compares it with successful cannulation.

**Methods:** These data were collected from the ERCP database at the Center for Liver Disease, Holy Family Hospital, Rawalpindi, between November 2019 and November 2022. IBM SPSS version 26.0 software was used for statistical analysis.

**Results:** The study included 329 patients, with 186 (56.6%) female and 143 (43.5%) male participants. Most patients were in the 39–48 age group (28.3%), with a mean age of 51 ± 1. Bile visibility was noted in 268 (81.5%) cases, papilla orifice visibility in 296 (90%) participants, atypical papilla in 20 (6.1%), and typical papilla in 309 (93.9%) participants. Bile visibility ($P = 0.004$) and papilla orifice visibility ($P = 0.006$) were significantly associated with successful cannulation, while papilla position ($P = 0.116$) was not. Significant associations were also found between difficult cannulation and bile visibility ($P = 0.000$), papilla orifice visibility ($P = 0.000$), and papilla position ($P = 0.000$).

**Conclusion:** Understanding this relationship can improve success rates and reduce complications associated with difficult cannulation during ERCP procedures. Further research is needed to establish clear correlations and guidelines for endoscopists to plan appropriate strategies for challenging cases.

## Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is a prevalent procedure used to manage pancreaticobiliary conditions. The success rate and post-procedure complications are related to cannulation time and duration in the bile duct, increasing the number of scope contacts with major duodenal papillae or unintentionally entering the pancreatic duct.[1–3] While offering high technical and clinical success, ERCP is associated with measurable rates of adverse events, including post-ERCP pancreatitis (PEP) and bleeding, both of which carry the potential for serious patient morbidity and substantial healthcare utilization.[4]

The characteristics of the papilla considered are the position of the papilla (typically on the posteromedial wall of the second part of the duodenum) being typical or atypical, visibility of the bile stream flowing from the major duodenal papilla, and visibility of the orifice of the major duodenal papilla. The gross appearance of the major duodenal papilla plays an essential role in cannulation, whereas the small papilla is significantly more challenging to cannulate.[5] According to recent ESGE guidelines, difficult cannulation is defined as one that takes more than 5 min or >5 attempts, that is, contacts of the scope with papilla. For this study, we have considered any unintentional pancreatic duct cannulation as an unsuccessful cannulation.[6,7] So, this study aimed to determine a relationship between some visual characteristics of the papilla and difficulty in selective bile duct cannulation.

## Methods

This study was conducted at the Center for Liver Disease, Holy Family Hospital, Rawalpindi (a tertiary care hospital) between Nov 2019 and Nov 2022. The data were collected from the ERCP database, including diagnostic ERCP with or without therapeutic intervention (biopsy, sampling, stenting, sphincterotomy, stone extraction).

A total of 329 patients were included in this study. Exclusion criteria were age under 18 years; pancreatic management (e.g. initial duct of interest was pancreatic duct); type 1 periampullary diverticulum (PAD), which often makes classification of papilla type and cannulation difficult; tumor involvement of the papilla; papilla could not be classified due to other reasons (e.g. duodenal mucosa swelling, deformity, ulcer on the surface of papilla); surgically altered anatomy or anomalous pancreaticobiliary ductal union, which makes cannulation difficult. With a previous history of sphincterotomy or ERCP, cannulation was also excluded.

The total time for ERCP cannulation and the number of attempts were observed and recorded. The ERCP cannulation difficulty index was used to define whether cannulation was easy or difficult. Any cannulation requiring more than five attempts or needle cut sphincterotomy or that which took more than 5 min was considered difficult, while cannulation achieved in <5 attempts with <5 min was considered easy.

Successful cannulation was achieved by gaining deep access to the bile duct, aided by cholangiography. Visual characteristics of the papilla, such as position (typical or atypical), orifice visibility of the bile stream, and relationship with ERCP cannulation difficulty, were analyzed. For statistical analysis, IBM SPSS version 26.0 software was used.

## Results

***Gender-based distribution.*** A total of 329 ERCPs were performed over the 12-month study period. They comprised 186 (56.6%) females and 143 (43.5%) males. The age range was 17–95 years, and the mean was 51 ± 1. Based on age groups, 20 (6.1%) were in the 18–28 years age group, 49 (14.9%) were in the 29–38 years age group, 54 (16.4%) were in the 39–48 years age group, 93 (28.3%) were in 49–58 years age group, 64 (19.5%) were in 59–68 years age group, 36 (10.9%) were in 69–78 year age group, 9 (2.7%) were in 79–88 years age group, while 4 (1.2%) were in 89–98 years age group, as shown in Figure 1. The overall success rate was 316 (96%), whereas 13 (4%) were unsuccessful.

***Bile visibility role, papilla orifice visibility, and papilla position association with successful cannulation and net difficulty.*** Among 329 subjects, bile was visible in 268 (81.5%), while in 61 (18.5%), participants' bile was invisible. The association of bile visibility ($P = 0.004$) was significant with successful canulation. The Papilla orifice visibility was noted in 296 (90%) participants, while the papilla was invisible in 33 (10%) participants. We divided the position of the duodenum papilla into two types: The atypical type was noted in 20 (6.1%), while the typical type was seen in 309 (93.9%) participants. Papilla orifice visibility ($P = 0.006$) with successful cannulation was significant, while the position of the papilla ($P = 0.116$) has no association with successful cannulation. The association of bile visibility ($P = 0.000$), Papilla orifice visibility ($P = 0.000$), and position of pallia ($P = 0.000$) were significant with the net difficulty of canulation shown in Figure 2 and Table 1.

Figure 3 represents endoscopic images illustrating the visibility of bile flow from the papilla orifice (Fig. 3a), indicating normal ductal function and an open pathway for successful cannulation. In contrast, Figure 3b presents the papilla as visible, but no bile flow is observed, which could suggest an obstruction, spasm, or other underlying condition, potentially complicating the cannulation process. Figure 3c shows a papilla with a visible orifice aiding in smooth and successful cannulation, whereas, in Figure 3d, the papilla exhibits standard anatomical features, including a distinct frenulum, orifice, and infundibulum, indicative of a typical and easily recognizable morphology.

## Discussion

ERCP is a procedure used for diagnosing and treating conditions of the bile ducts and pancreas. During ERCP, the successful cannulation of the papilla (also known as the major duodenal papilla or ampulla of Vater) is crucial for accessing the bile and

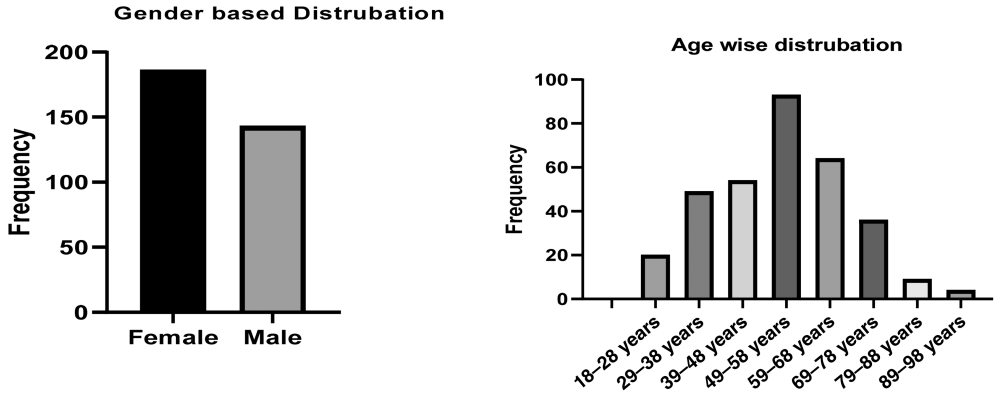


**Figure 1** Gender-based distribution and age-wise distribution. (■), Female; (▭), male.

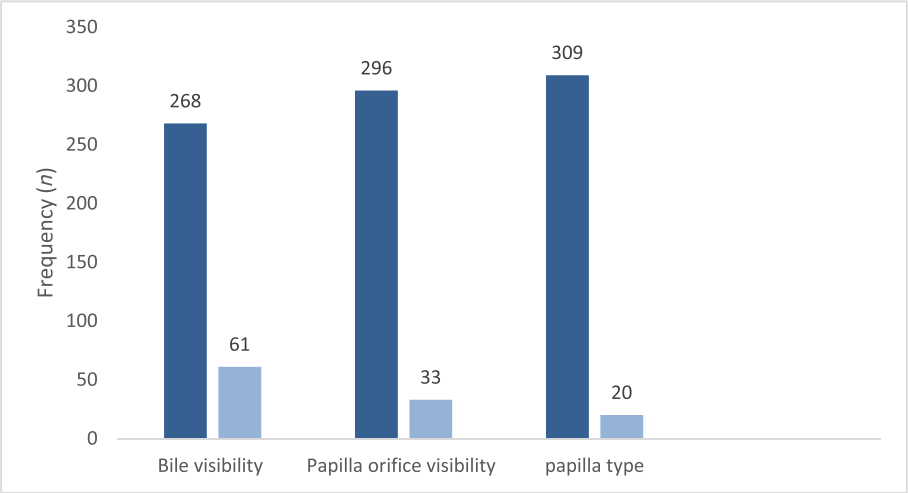


**Figure 2** Different variables in 329 participants such as bile visibility in 268 participants and bile invisibility in 61 participants; papilla orifice visibility in 296 participants, while Papilla orifice invisibility in 33 participants; atypical type was noted in 20 participants, while the typical type was noted in 309 participants.

**Table 1** Different variables associated with successful canulation and net difficulty

| Variables | Frequency (%) | Successful cannulation variables (*P*-value) | Net difficulty |
|---|---|---|---|
| Bile visibility (visibility/invisibility) | 268 (81.5%)/61 (18.5%) | 0.004* | 0.000* |
| Papilla orifice visibility (visibility/invisibility) | 296 (90%)/33 (10%) | 0.006* | 0.000* |
| Position of papilla (typical/atypical type) | 309 (93.9%)/20 (6.1%) | 0.116 | 0.000* |

*$P < 0.05$ is significant.

pancreatic ducts. However, in some cases, papilla cannulation can be challenging to achieve.

Several factors can contribute to difficult cannulation, including anatomical variations, previous surgeries or interventions, and inflammatory conditions. However, recent studies have also focused on the visual characteristics of the papilla as potential predictors of difficult cannulation. Visual characteristics such as the papilla's size, shape, orientation, and certain features like periampullary diverticula or intra diverticular papilla have been investigated to determine their association with difficult cannulation. Some studies have suggested that specific visual characteristics, such as a large or nondilated papilla, a horizontally oriented papilla, or the presence of periampullary diverticula, may increase the likelihood of difficult cannulation. However, the evidence regarding these associations needs to be more consistent, and further research is required to establish clear correlations.

Understanding the relationship between difficult cannulation and the visual characteristics of the papilla can help endoscopists anticipate challenges and plan appropriate strategies during ERCP procedures. It may also guide the development of techniques or technologies to improve success rates and reduce complications associated with difficult cannulation.

We concluded that bile duct cannulation could be deemed complex in cases of nonvisibility of the orifice of MDP, in those cases that have an atypical position of the major duodenal papilla, that is, other than the posteromedial wall of second part of the duodenum and in cases with nonvisibility of bile stream flow from the papilla in the duodenum. Difficult cannulation is a single major factor leading to an increase in the frequency of post-procedure complications like post-ERCP pancreatitis.[8]

Factors like age, female gender, and dysfunction of the sphincter of Oddi have also been defined as causative factors of post-ERCP complications.[3] In our study, a total of 329 patients were included. The female participants accounted for 56.6% of the sample, while males accounted for 43.5%. The age distribution of the participants was as follows: 6.1% in the 18–28 years age group, 14.9% in the 29–38 years age group, 16.4% in the 39–48 years age group, 28.3% in the 49–58 years age group, 19.5% in the 59–68 years age group, 10.9% in the 69–78 years age group, 2.7% in the 79–88 years age group, and 1.2% in the 89–98 years age group. The mean age of the participants was $51 \pm 1$. Among all age groups, the highest number of participants was in the 59–68 (19.5%) age group, while the lowest was in the 89–98 (1.2%) age group.

In his study,[9] Martin concluded that managing bile duct stones using ERCP and altered anatomy can pose significant challenges to the endoscopist and team regarding selective biliary cannulation. Morphology of the major duodenal papilla

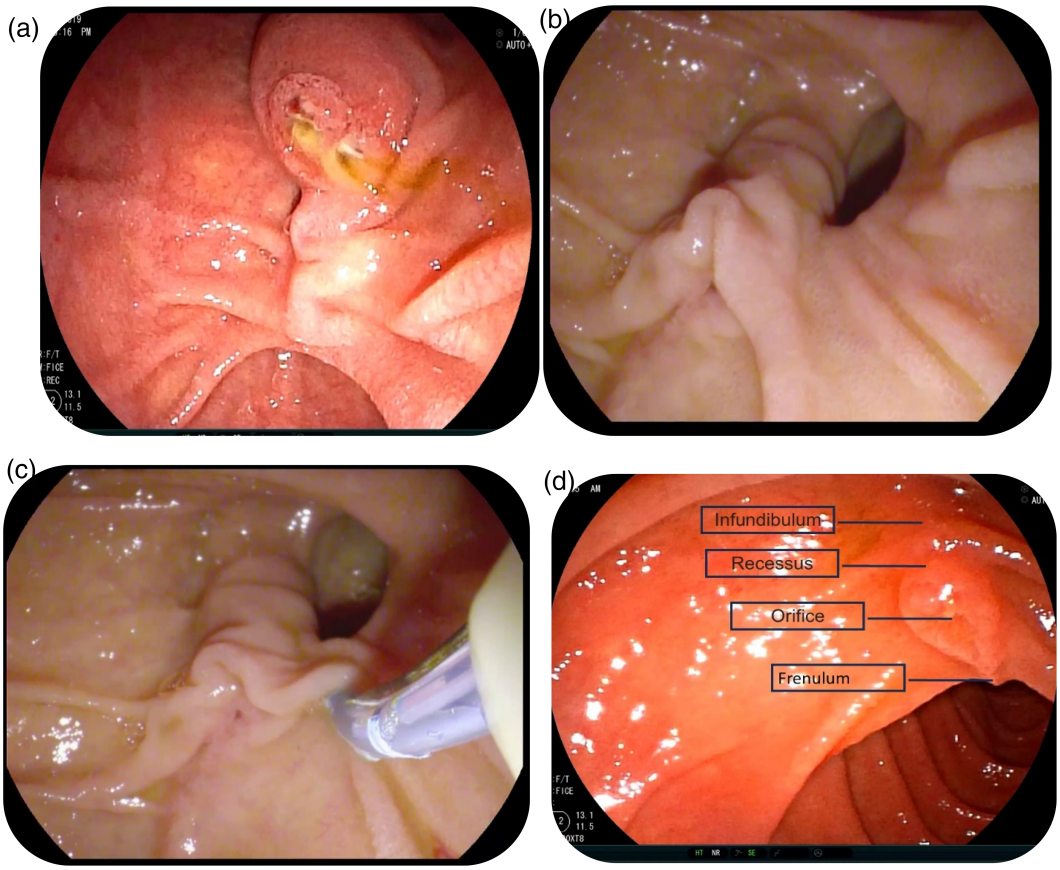


**Figure 3** (a) Orifice with visible bile flow; (b) orifice without visible bile flow; (c) papilla with visible orifice; (d) typical Papilla.

influences cannulation rates irrespective of the technique used.[10] In our study, bile visibility was 81.5%, while 18.5% was invisible.

In a study by Haraldsson *et al*., cannulation difficulty was determined based on four different types of papillae, which a similar group of researchers classified in 2016.[11,12] It was concluded that small and protruding papillae were significantly more challenging to cannulate than regular papillae, with percentages of difficult cannulation being 52% and 48%, respectively, compared with 36% in regular papillae. Watanabe *et al*. classified oral protrusion of papillae into small, regular, and large types, and categorized papillae pattern into annular, unstructured, longitudinal, isolated, and gyrus types, and concluded that large protrusion papillae were an independent risk factor for difficult biliary cannulation (95% CI).[13]

We noted papilla orifice visibility was in 90% of participants, while in 10% of participants, papilla was invisible; we divided the position of duodenum papilla into two types: the atypical type was 6.1% while the typical type was 93.9%. Based on pancreatic cannulation, 14% were done successfully, while 86% failed. The association of bile visibility ($P = 0.004$) and papilla orifice visibility ($P = 0.006$) with successful cannulation was significant.

The position of the papilla's orifice varies. In a study by Lindner *et al*., carried out on 1000 patients, it was concluded that in 86.9% of patients, the orifice was present in the descending part of the duodenum. In 13.1% of patients, the position of the orifice varied between the junction of the descending and transverse parts and the transverse part of the duodenum.[14] In a pilot study to characterize the papillae as described by endoscopists, Zuber-Jerger *et al*. concluded that the combined presence of a visible orifice and the typical position of the duodenoscope had a positive predictive value of 96% of successful biliary cannulation.[15]

The strength of our study is that we have limited inter-observer variation by allocating only two personnel to the task of data observation and recording and restricted the variation of ERCP expertise by defining two well-experienced endoscopists; endoscopist expertise is another major factor in determining the rates of cannulation success, as specified in various studies on the subject, like the one carried out by Aabakken and Bhat.[16] Advancements in imaging technologies, such as Texture and Color Enhancement Imaging (TXI), have been reported to enhance the visualization of the papilla orifice and improve procedural outcomes. By enhancing the contrast and texture of the papilla, TXI has shown promising results in improving the identification of the orifice, particularly in cases where it is difficult to visualize with standard techniques.[17] However, its application in our setting, particularly in Pakistan, currently needs to be improved due to the unavailability of this technology, making it

impractical for us to apply this technique. That said, we acknowledge its value and look forward to the possibility of adopting such advanced technologies in the future as healthcare infrastructure evolves.

In conclusion, this study aims to explore the relationship between difficult ERCP cannulation and the visual characteristics of the papilla. Understanding this relationship can improve success rates and reduce complications associated with difficult cannulation during ERCP procedures. Further research is needed to establish clear correlations and guide endoscopists in planning appropriate strategies for challenging cases.

Conducting the study at a single medical center means the findings may not represent the broader population or different practice settings. The lack of a control group makes assessing the proper relationship between difficult cannulation and the papilla's visual characteristics challenging.

## References


1 Hawes RH, Devière J. How I cannulate the bile duct. *Endoscopy*. 2018; **50**: 75–7.
2 Berry R, Han JY, Tabibian JH. Difficult biliary cannulation: historical perspective, practical updates, and guide for the endoscopist. *World J. Gastrointest. Endosc.* 2019; **11**: 5–21.
3 Han SY, Kim DU, Lee MW *et al*. Acute distal common bile duct angle is risk factor for post-endoscopic retrograde cholangiopancreatography pancreatitis in beginner endoscopist. *World J. Clin. Cases*. 2020; **8**: 20–8.
4 Mohamed R, Lethebe BC, Gonzalez-Moreno E *et al*. Morphology of the major papilla predicts ERCP procedural outcomes and adverse events. *Surg. Endosc.* 2021; **35**: 6455–65.
5 Kayhan B, Akdoğan M, Sahin B. ERCP subsequent to retroperitoneal perforation caused by endoscopic sphincterotomy. *Gastrointest. Endosc.* 2004; **60**: 833–5.
6 Balan GG, Arya M, Catinean A *et al*. Anatomy of major duodenal papilla influences ERCP outcomes and complication rates: a single center prospective study. *J. Clin. Med.* 2020; **9**: 1637.
7 Sayeed S, Ara S, Hoque M, Ferdous Z, Kashem K. Location of major duodenal papilla in human duodenum. *Bangladesh J. Anat.* 2015; **12**: 22–4.
8 Reddy DN, Nabi Z, Lakhtakia S. How to improve cannulation rates during endoscopic retrograde cholangiopancreatography. *Gastroenterology*. 2017; **152**: 1275–9.
9 Martin JA. Endoscopic retrograde cholangiopancreatography in the management of bile duct stones. *Tech. Gastrointest. Endosc.* 2012; **14**: 156–63.
10 Hew S, Bechara R, Hookey L. Papillary morphology influences biliary cannulation: beware the small papilla! *Gastrointest. Endosc.* 2020; **91**: 959.
11 Haraldsson E, Kylänpää L, Grönroos J *et al*. The macroscopic appearance of the major duodenal papilla influences bile duct cannulation: a prospective multicenter study by the Scandinavian Association for Digestive Endoscopy Study Group for ERCP. *Gastrointest. Endosc.* 2019; **90**: 957–63.
12 Haraldsson E, Lundell L, Swahn F *et al*. Endoscopic classification of the papilla of Vater: results of an inter- and intraobserver agreement study. *United European Gastroenterol. J.* 2017; **5**: 504–10.
13 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**: 2291–9.
14 Lindner HH, Peña VA, Ruggeri RA. A clinical and anatomical study of anomalous terminations of the common bile duct into the duodenum. *Ann. Surg.* 1976; **184**: 626–32.
15 Zuber-Jerger I, Gelbmann MC, Kullmann F. Visual characteristics of the papilla to estimate cannulation of the common bile duct – a pilot study. *N. Am. J. Med. Sci.* 2009; **1**: 66–73.
16 Aabakken L, Bhat P. How to access the common bile duct. *Minimally invasive Surg.* 2021; **5**: 25.
17 Miyaguchi K, Mizuide M, Tanisaka Y *et al*. Distinguishing the papilla of Vater during biliary cannulation using texture and color enhancement imaging: A pilot study. *DEN Open*. 2022; **3**: e125.