学位論文

「Transpapillary Biliary Cannulation is Difficult in Cases with Large Oral Protrusion of the Duodenal Papilla」（十二指腸乳頭形態の新分類と胆管挿管困難との関連性の検討― 口側隆起の大きな十二指腸乳頭は胆管挿管困難である ― ）

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著者の宣言

本学位論文は、著者の責任において実験を遂行し、得られた真実の結果に基づいて正確に作成したものに相違ないことをここに宣言する。

論文要旨

論文題目：「Transpapillary Biliary Cannulation is Difficult in Cases with Large Oral Protrusion of the Duodenal Papilla」

（十二指腸乳頭形態の新分類と胆管挿管困難との関連性の検証

— 口側隆起の大きな十二指腸乳頭は胆管挿管困難である —）

【背景】

Endoscopic retrograde cholangiopancreatography（ERCP）では，胆管挿管を得るための様々な手法がこれまでに考案されてきたが，未だに一定数の胆管挿管困難例が存在する．胆管挿管困難は重篤な偶発症であるERCP後膵炎のリスク因子の1つとして知られており，胆管挿管困難例を理解することはERCPの経験の浅い内視鏡医への教育において重要であり，胆管挿管成功率の向上にも寄与する可能性がある．胆管挿管を困難にする要因の一つとして，十二指腸乳頭の形態の違いによる影響が経験的に知られているが，十二指腸乳頭の形態と胆管挿管率との関連性の検証は不十分であった．そこで我々は，十二指腸乳頭を口側隆起の大きさと開口部の形態の2つの観点に着目した新たな分類法を考案し，分類と胆管挿管困難との関連性を検証した．

【対象】

2013年9月1日から2017年6月30日の間に，当教室でERCPを施行した3052例から未処置の十二指腸乳頭を有した589例を抽出し，解析対象とした．

【方法】

我々が考案した十二指腸乳頭形態の分類では，口側隆起の大きさを規定するoral protrusion pattern：small，S；regular，R；large，Lと，開口部の形態を規定するpapilla pattern：annular，A；unstructured，U；longitudinal，LO；isolated，I；gyrus，Gに細分類した．分類は予め指定された3名の評価者（日本消化器内視鏡学会指導医）が各々独立して行い，2名以上の一致をもって決定した．分類の一致率と，全体および各型における胆管挿管成功率，胆管挿管困難例の割合を検証した．さらに修練医（ERCP経験年数5年以内）と指導医（ERCP経験年数6年以上，経験例数300例以上）の，内視鏡経験の異なる2群に分け，サブ解析を行った．胆管挿管の成功に至るまでに5回以上胆管挿管を試みた症例を胆管挿管困難例と定義した．修練医が10分以内に胆管挿管に成功しない場合，もしくは5-10回の胆管挿管を試みても胆管挿管に成功しない場合は，指導医に術者を変更してその後の胆管挿管を行い，修練医の成績として解析した．分類の一致率にはkappa statistic，2群間の比較にはFisher's exact test，胆管挿管困難のリスク因子の抽出にはロジスティック回帰分析を用いた．$p<0.05$の場合，統計学的有意と定義した．

【結果】

細分類における型の割合は，Protrusion-S 11.7%，R 77.9%，L 10.4%，Papilla-A 67.1%，U 7.0%，LO 7.5%，I 1.2%，G 15.6%，分類不能1.7%であった．3名の評価者に

よる分類の一致係数（Fleiss kappa）は，oral protrusion pattern：0.788（95% confidence interval [CI]：0.753-0.824，p<0.001），papilla pattern：0.750（95% CI：0.719-0.781，p<0.001）であった．

主実施医の割合は，61.0%が修練医であった．全例における胆管挿管成功率は97.6%で，修練医開始群（97.5%）と指導医開始群（97.8%）に差は認めなかった．胆管挿管困難例は全体の41.8%で，修練医（48.2%）は指導医（31.7%）に比し有意に高かった（p<0.001）．修練医はProtrusion-R（p<0.001），Papilla-A（p<0.028），Papilla-LO（p<0.043），Papilla-G（p<0.033）の4型において，指導医に比し胆管挿管困難例の割合が高かった．指導医が実施した症例を対象にロジスティック回帰分析を行うと，単変量解析ではProtrusion-L（オッズ比：2.956，95%CI：1.115-7.84，p=0.029）が，多変量解析でも同様にProtrusion-Lが独立した胆管挿管困難のリスク因子として抽出された(オッズ比：3.772，95% CI：1.359-10.464，p=0.011)．

【考察】

胆管挿管の成否と関連を有する新たな十二指腸乳頭形態の分類の作成に成功した．本分類法は，胆管挿管の際にその場で迅速な判定が可能であることから，特に胆管挿管困難であるProtrusion-Lでは，迅速な胆管挿管と処置後の膵炎の予防のため，主実施医や第一助手を指導医に変更するなどの十分な対応が必要である．

目次

Introduction

More than half a century since endoscopic retrograde cholangiopancreatography (ERCP) was first reported by McCune et al. [1] in 1966, it still plays an important role in the diagnosis and treatment of biliopancreatic disease. To date, approaches, such as wire-guided cannulation [2, 3], precutting [4], double-guidewire technique [5–7], the two devices in one channel method [8], and others, have been proposed to improve the biliary cannulation rate. However, a recent meta-analysis showed that the success rate of biliary cannulation is 89.3% [95% confidence interval (CI) 0.866–0.919] [9], thus indicating a significant number of failures. Furthermore, it has been reported that ERCP procedures conducted at hospitals with small ERCP volumes have significantly increased adverse event rates [10]. Therefore, providing appropriate guidance and education for an inexperienced endoscopist with relatively little ERCP experience is important for high-volume centers. In Japan, the importance of classifying the structure of the opening of the duodenal papilla for biliary cannulation has long been recognized [11]. Haraldsson et al. [12] proposed a classification method that places particular emphasis on the size of duodenal papillae and reported the biliary cannulation and post-ERCP pancreatitis (PEP) rates based on this method [13]. However, insufficient attention has been given to recognizing the papilla morphological forms, for which biliary cannulation is difficult. Therefore, we proposed a new classification approach based on the premise that both the oral protrusion pattern and papilla pattern are important factors that affect the success of biliary cannulation. In this study, we compared the results of biliary cannulation based on the concordance rates of classification by multiple experienced endoscopists and the differences in experiences with ERCP (experienced endoscopists versus inexperienced endoscopists). Furthermore, we identified papilla morphological forms, for which biliary cannulation is difficult, according to the new classification to examine its versatility.

Methods

Patients

Our study was reviewed and approved by our institutional ethics committee, and it conformed to the provisions of the Declaration of Helsinki. The study population comprised 3052 patients who underwent ERCP at Kitasato University Hospital or Kitasato University East Hospital between September 1, 2013, and June 30, 2017, and whose details were recorded in the ERCP Database of the Department of Gastroenterology at Kitasato University School of Medicine. Those who had previously undergone treatment of the duodenal papilla, and therefore did not possess a naïve major duodenal papilla, were excluded. In addition, we excluded patients who had undergone surgical intestinal reconstruction or ERCP for pancreatic duct cannulation, those with the papilla inside a peripapillary duodenal diverticulum, those with unclassifiable papillary morphology due to tumor invasion, and those with unclear endoscopic images.

ERCP Devices and Cannulation Methods

The first endoscopist to perform ERCP was chosen by an experienced endoscopist. Endoscopists with ≤ 5 years of experience using ERCP were classed as inexperienced endoscopist, and those with ≥ 6 years were classified as experienced endoscopist. The experienced endoscopist had completed over 300 more cases of ERCP than the inexperienced endoscopists. When the first endoscopist was inexperienced and was unable to achieve successful cannulation within 10 min or after 5–10 attempts, an experienced endoscopist took over the procedure. JF-260V and TJF-260V duodenoscopes were used (Olympus Medical Systems, Tokyo, Japan). For biliary cannulation and injection of contrast media, a conventional ERCP catheter (PR- 4Q-1; Olympus Medical Systems; and S01-20-70-1; MTW Endoskopie Manufaktur, Wesel, Germany) or a papillotomy knife (Clever Cut 3V; Olympus Medical Systems) was used. The initial choice between conventional contrast, wire-loaded, and wire-guided cannulation was decided by the experienced endoscopist. Either a 0.025-inch (G-240-2545A, Visiglide2; Olympus Medical Systems) or a 0.035- inch disposable guidewire (RF-GA35403, Radifocus; Terumo Corporation, Tokyo, Japan) was used. If cannulation was difficult to perform with a guidewire, then we used the double-guidewire technique or precutting with a needle knife (Single Use 3-Lumen Needle Knife V; Olympus Medical Systems).

Classification of Duodenal Papilla

Our new proposed classification (Figs. 1, 2) was defined in terms of two subclassifications, oral protrusion pattern (Fig. 1), which indicates the ratio of length of oral protrusion to transverse diameter of the papilla, and papilla pattern (Fig. 2), which indicates the surface pattern of the orifice. Oral protrusion pattern was classified into three types: small (Protrusion-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 (Protrusion-R), for which the ratio was one-half or more but less than 2; and large (Protrusion- L), for which the ratio is 2 or more. The papilla pattern was classified into the following five types: annular (Papilla-A), which comprised typical papilla with an 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; unstructured (Papilla-U), which were without a clear orifice; longitudinal (Papilla-LO), which comprised longitudinal grooves continuous with the orifice, with the length of the grooves being longer than the transverse diameter of the biliary duct axis of the papilla; isolated (Papilla- I), which comprised two separate isolated orifices of the biliary and pancreatic ducts (the orifice on the oral or left side is that of the biliary duct, and that on the anal or right side is that of the pancreatic duct); and gyrus (Papilla-G), which had a gyrate structure. This system was a modification of Inomata's classification [11].

Evaluation of Cannulation Difficulty

We evaluated the results of using our classification (the proportions of each type and intra-evaluator concordance), the results of biliary duct cannulation for each type of duodenal papilla classified according to our classification by selected evaluators (successful biliary duct cannulation rates and number of attempts), and the comparative results of biliary duct cannulation depending on the operator's experience with ERCP (experienced endoscopist versus inexperienced endoscopist). Patients were classified according to our method by three physicians who were certified by the Japan Gastroenterological Endoscopy Society and were highly experienced with ERCP; they had no access to the patients' medical information. Each of the evaluators classified the papillae independently based on the frontal view images (1–3 per patient) acquired immediately before attempting biliary duct cannulation. Classifications of both the oral protrusion pattern and papilla pattern were determined by a majority of at least two of the three evaluators. Following the clinical guidelines of the European Society of Gastrointestinal Endoscopy, difficult biliary duct cannulation was defined as at least five attempts with the papilla to achieve successful cannulation [14]. The number of attempts was determined according to the ERCP database. Cases in which difficulty performing cannulation during ERCP resulted in an inexperienced endoscopist

conceding to an experienced endoscopist as the main endoscopist were analyzed as "inexperienced endoscopist first."

Statistical Analysis

Concordance between our classifications determined by three evaluators was analyzed using the Fleiss kappa. Fisher's exact test was used to compare the effectiveness between the two groups (inexperienced endoscopist first versus experienced endoscopist). Logistic regression was used for univariate and multivariate analyses of independent risk factors for difficult biliary duct cannulation. Statistical analyses were performed using the SPSS Base 17.0 statistical package (SPSS Inc., Chicago, IL) and R version 3.2.4. $p < 0.05$ was considered statistically significant.

Results

Of the 3052 patients in the study population, 1968 had previously undergone duodenal papilla treatment and lacked naïve major duodenal papilla, 198 had undergone surgical intestinal reconstruction, 201 had undergone ERCP for pancreatic duct cannulation, 10 had papilla located inside a peripapillary duodenal diverticulum, 36 had unclassifiable papillary morphology because of tumor invasion, and 50 had unclear endoscopic images. The final analysis included 589 patients (Fig. 3): 377 men and 212 women with a median age of 70 years (range 6–96). Biliary stones were the most common pathology (n = 230; 39%), followed by pancreatic neoplasm (n = 125; 21.2%), biliary neoplasm (n = 122; 20.7%), biliary stricture due to non-pancreaticobiliary malignancy (n = 44; 7.5%), pancreaticobiliary maljunction and/or congenital biliary dilatation (n = 16; 2.7%), cholecystitis (n = 11, 1.9%), primary sclerosing cholangitis (n = 10; 1.7%), autoimmune pancreatitis (n = 9; 1.5%), chronic pancreatitis (n = 4; 0.7%), and other benign diseases (n = 18; 3.1%).

Distribution of Classifications

Patients were classified according to our system, with at least two of the three evaluators agreeing on the oral protrusion pattern in 100% of cases and on the papilla pattern in 98.3% of cases (579/589) (Table 1). In terms of oral protrusion pattern, 11.7% of patients (69/589) had Protrusion- S, 77.9% (459/589) had Protrusion-R, and 10.4% (61/589) had Protrusion-L. In terms of papilla pattern, Papilla-A was observed in 67.1% of patients (395/589), Papilla-U was observed in 7.0% (41/589), Papilla-LO was observed in 7.5% (44/589), Papilla-I was observed in 1.2% (7/589), and Papilla-G was observed in 15.6% (92/589), with a discordance rate of 1.7% (10/589) for the three evaluators.

Concordance Rate of Classifications

The concordance rates (Fleiss kappa) among the three evaluators for each subclassification were 0.788 (95% CI 0.753–0.824; $p < 0.001$) for the oral protrusion pattern and 0.750 (95% CI 0.719–0.781; $p < 0.001$) for the papilla pattern (Table 1).

Cannulation Rates According to Subclassifications

The first endoscopist to perform ERCP was an inexperienced endoscopist in 61.0% of cases (359/589). The overall biliary duct cannulation success rate was 97.6%, and there was no significant difference according to the first endoscopist's experience [inexperienced endoscopist first, 97.5% (350/359); experienced endoscopist first, 97.8%

(225/230)]. The success rates according to the oral protrusion pattern were as follows: Protrusion-S, 100% (69/69); Protrusion-R, 97.6% (448/459); and Protrusion-L, 95.1% (58/61). In terms of the papilla pattern, the rates were as follows: Papilla-A, 98.0% (387/395); Papilla-U, 97.6% (40/41); Papilla-LO, 93.2% (41/44); Papilla-I, 100% (7/7); and Papilla-G, 98.9% (91/92). Whether the first endoscopist was an experienced or inexperienced endoscopist made no significant difference (Table 2).

Number of Cannulation Attempts According to Subclassifications

Five or more attempts were needed to achieve successful cannulation in 41.8% of cases (246/589), and this was significantly more common when the first endoscopist was an inexperienced endoscopist [inexperienced endoscopist, 48.2% (173/359); experienced endoscopist, 31.7% (73/230); $p < 0.001$)]. The rates of difficult biliary duct cannulation according to the oral protrusion pattern were as follows: Protrusion-S, 40.6% (28/69); Protrusion-R, 39.0% (179/459); and Protrusion-L, 63.9% (39/61). In terms of the papilla pattern, the rates were as follows: Papilla-A, 41.5% (164/395); Papilla-U, 36.6% (15/41); Papilla-LO, 40.9% (18/44); Papilla-I, 28.6% (2/7); and Papilla-G, 43.5% (40/92). The rates according to the first endoscopist's experience and oral protrusion pattern were as follows: Protrusion-S, inexperienced endoscopist first 43.2% (16/37) and experienced endoscopist first 37.5% (12/32); Protrusion-R, inexperienced endoscopist first 45.9% (128/279) and experienced endoscopist first 28.3% (51/180); and Protrusion-L, inexperienced endoscopist first 67.4% (29/43) and experienced endoscopist first 55.6% (10/18). In terms of the papilla pattern, the rates were as follows: Papilla-A, inexperienced endoscopist first 46.1% (111/241) and experienced endoscopist first 34.4% (53/154); Papilla-U, inexperienced endoscopist first 42.3% (11/26) and experienced endoscopist first 26.7% (4/15); Papilla-LO: inexperienced endoscopist first 51.6% (16/31) and experienced endoscopist first 15.4% (2/13): Papilla-I: inexperienced endoscopist first 50.0% (2/4) and experienced endoscopist first 0% (0/3); and Papilla-G: inexperienced endoscopist first 53.8% (28/52) and experienced endoscopist first 30.0% (12/40). Patients with Protrusion-R required significantly more cannulation attempts when an inexperienced endoscopist attempted the procedure first compared with when an experienced endoscopist attempted the procedure first ($p < 0.001$). In terms of the papilla pattern, all patients with Papilla-A ($p = 0.028$), Papilla-LO ($p = 0.043$), and Papilla-G ($p = 0.033$) required significantly more attempts when an inexperienced endoscopist attempted the procedure first (Table 4). A logistic regression analysis of patients who underwent ERCP by experienced endoscopist using the difficulty of biliary duct cannulation as the target variable identified Protrusion-L as a significant risk factor [odds ratio (OR) 2.956; 95% CI 1.115–7.84; $p = 0.029$]. A

multivariate analysis confirmed Protrusion-L as an independent risk factor (OR 3.772; 95% CI 1.359–10.464; p = 0.011; Table 4).

Discussion

We proposed a new classification based on the premise that both the oral protrusion pattern and papilla pattern are important factors affecting the success rate of biliary cannulation. In this study, we compared the concordance rates of classification by multiple experienced endoscopists as well as the differences of cannulation success rates with ERCP in experienced verses inexperienced endoscopists. Further, using the new classification, we identified the certain pattern of new classification that often make cannulation difficult.

The interevaluation concordance values (Fleiss kappa) of our classifications assigned by the three endoscopists who were highly experienced with ERCP were high for both subclassifications [oral protrusion pattern: 0.788 ($p < 0.001$); papilla pattern: 0.750 ($p < 0.001$)] (Table 1). This suggested that our classification may be a novel, general-purpose classification system. Training endoscopists is one of the most important missions of high-volume centers. When the first endoscopist conceded to an experienced endoscopist, according to our protocol, the ERCP biliary duct cannulation success rate was 97.6%, which is good. The absence of significant differences in cannulation rates for all our classification types depending on operator experience may have been due to appropriate supervision of the inexperienced endoscopist, with experienced endoscopist taking over the procedure when necessary, resulting in high cannulation rates.

Difficult biliary duct cannulation occurred in significantly more cases when an inexperienced endoscopist was the first endoscopist. Comparing the number of cannulation attempts according to our classification types also revealed significant differences between inexperienced and experienced endoscopists, with Protrusion-R, Papilla-A, Papilla-LO, and Papilla-G requiring significantly more cannulation attempts when an inexperienced endoscopist performed the procedure first (Table 3). These findings may reflect the differences in ERCP skills between inexperienced and experienced endoscopists. However, there were no significant differences between inexperienced and experienced endoscopists as the first endoscopists for other oral protrusion pattern types and papilla patterns. To investigate whether inexperienced and experienced endoscopists found these types equally easy or equally difficult, we assumed that the duodenal papilla types that are difficult for experienced endoscopists to cannulate are the ones that would cause genuine difficulty. Therefore, we performed univariate and multivariate logistic regression analyses on only those cases in which an experienced endoscopist performed ERCP in order to analyze independent risk factors for difficult biliary duct cannulation. Protrusion-L was identified as a

significant risk factor for difficult biliary duct cannulation by univariate and multivariate analyses (Table 4). According to our classification system, Protrusion-L is very similar to the type 3 classification of Haraldsson et al. [12]. Furthermore, according to our definition, Protrusion-L papillae have a large oral protrusion, indicating that the intramural distance travelled by the biliary duct is longer than that for other types. We speculated that it is easier for misalignment between the ERCP catheter and the biliary duct axis to occur during biliary duct cannulation, even if a guidewire is used, thus leading to penetration of the submucosa and rendering cannulation difficult. A recent study found that early precutting increases the rate of primary cannulation and reduces the risk of PEP [15]. Even in our study, of the 61 cases of Protrusion-L, the most common method of biliary cannulation for the 39 difficult cases was precutting, which was performed in 16 cases (nearly half). This was followed by 13 cases treated with wire- guided cannulation and 8 treated with cannulation using the double-guidewire technique. Although that study used a different definition of difficult biliary duct cannulation, patients with Protrusion-L papillae may be good candidates for early precutting. The logistic regression analysis also found Protrusion-R to be significantly easier to cannulate. This was because most duodenal papillae not classified as Protrusion-L were classified as Protrusion-R; therefore, their rates were negatively correlated.

When Protrusion-L papillae are encountered during ERCP, operators should be aware that difficult biliary duct cannulation is common. Conversely, having an experienced, rather than an inexperienced endoscopist, performance of biliary duct cannulation for patients with Protrusion-R, Papilla-A, Papilla-LO, and Papilla-G papillae may be a simple method for avoiding risk. However, this may not be compatible with the educational mission of high-volume centers. Other options include reducing the time allotted to inexperienced endoscopists (i.e., starting biliary duct cannulation with an early switch in mind), using an experienced endoscopist as the first assistant, and enforcing sufficient measures to avoid PEP, which is one of the most lethal adverse events. The most important methods of preventing PEP in high-risk patients include indomethacin [16], a combination of indomethacin and sublingual nitrates [17], and prophylactic pancreatic duct stenting [18–20].

This study had a number of limitations. First, this was a retrospective study performed at two institutions. When inexperienced endoscopists were the first to perform ERCP, it was unclear whether they themselves succeeded at cannulating the biliary duct or whether an experienced endoscopist replaced them after a certain time or a certain number of attempts. Therefore, a logistic regression analysis to identify types of duodenal papilla that are genuinely difficult to cannulate was limited to those

that involved an experienced endoscopist performing ERCP. However, this meant that a smaller patient population was analyzed. Additional large scale prospective studies are required to ascertain the results of inexperienced endoscopists. Second, although the Fleiss kappa vales for our classifications, which were assigned by three endoscopists highly experienced with ERCP, demonstrated that this classification system is highly versatile, further studies are required to investigate whether similar concordance rates can be achieved by inexperienced and experienced endoscopists or by endoscopists working at other institutions. Third, we could not determine the association between the various classification types and the incidence of PEP. This was because the analyzed population included patients who had undergone preventive procedures and those who had not, rendering evaluation impossible. Haraldsson et al. [13] reported that there was an increased tendency for PEP with Type 2 papillae, which closely resembled Protrusion-S in this study. Our classification, which was defined by the oral protrusion pattern and papilla pattern, should be verified by multicenter prospective studies with regard to its relevance to PEP development.

In conclusion, we proposed a new general-purpose classification for the morphology of the duodenal papilla and successfully analyzed the association between the various classification types and difficult biliary duct cannulation. The classification system was based on the premise that both the aforementioned factors are important and affect the success of biliary cannulation. This system enables assessments to be made instantaneously during ERCP and does not require any special equipment. When classification types that make it particularly difficult for an inexperienced endoscopist to achieve biliary duct cannulation are encountered, ERCP should be performed with the full support of an experienced endoscopist.

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Figures and Legends

Figure.1 Oral protrusion pattern according to our classification criteria.

Oral protrusion pattern is classified into three types depending on the ratio of the length of the oral protrusion to the transverse diameter of the papilla expressed in terms of the length of the oral protrusion (L) and the diameter of the papilla (D): small (Protrusion-S), L/D < 0.5; regular (Protrusion-R), 0.5 ≤ L/D < 2; and large (Protrusion-L), L/D ≥ 2

Figure.2 Papilla pattern according to our classification.

The papilla pattern is classified into the following five types: Papilla-A, comprising typical papilla with an annular shape, with some having nodular changes at the oral side of the center (10–11 o'clock) and others for which these were difficult to discern; Papilla-U, unstructured without a clear orifice; Papilla-LO, comprising longitudinal grooves continuous with the orifice, with the length of the grooves being longer than the transverse diameter of the biliary duct axis of the papilla; Papilla- I, comprising two separate, isolated orifices of the biliary and pancreatic ducts, with the opening on the oral or left side being that of the biliary duct and that on the anal or right side being that of the pancreatic duct; and Papilla-G, with a gyrate structure.

Figure.3 Patient enrollment and reasons for exclusion.

Of the 3052 patients in the study population, 1968 had previously undergone duodenal papilla treatment and lacked a naïve major duodenal papilla, 198 had undergone surgical intestinal reconstruction, 201 had undergone endoscopic retrograde cholangiopancreatography for pancreatic duct cannulation, 10 had papilla located inside a peripapillary duodenal diverticulum, 36 had unclassifiable papillary morphology because of tumor invasion, and 50 had unclear endoscopic images.

Figure.1

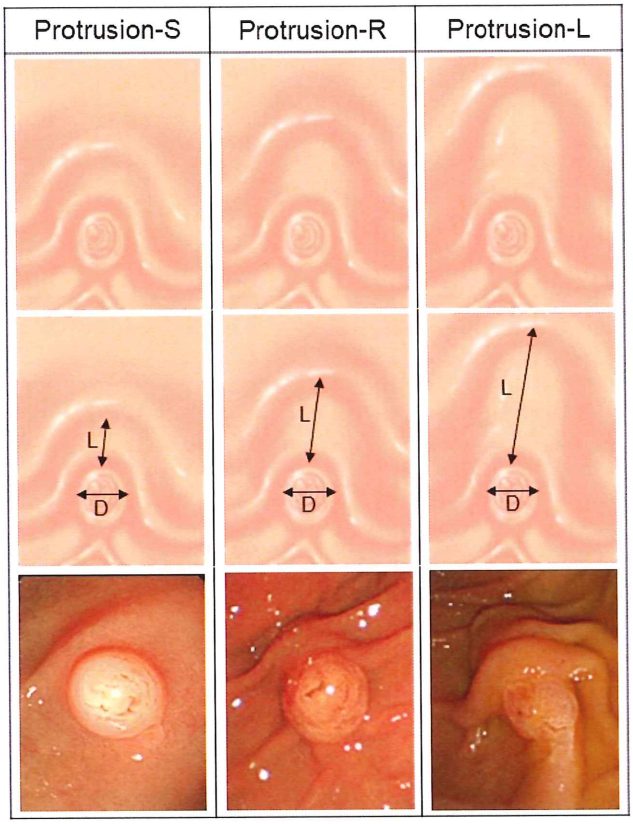


Figure.2

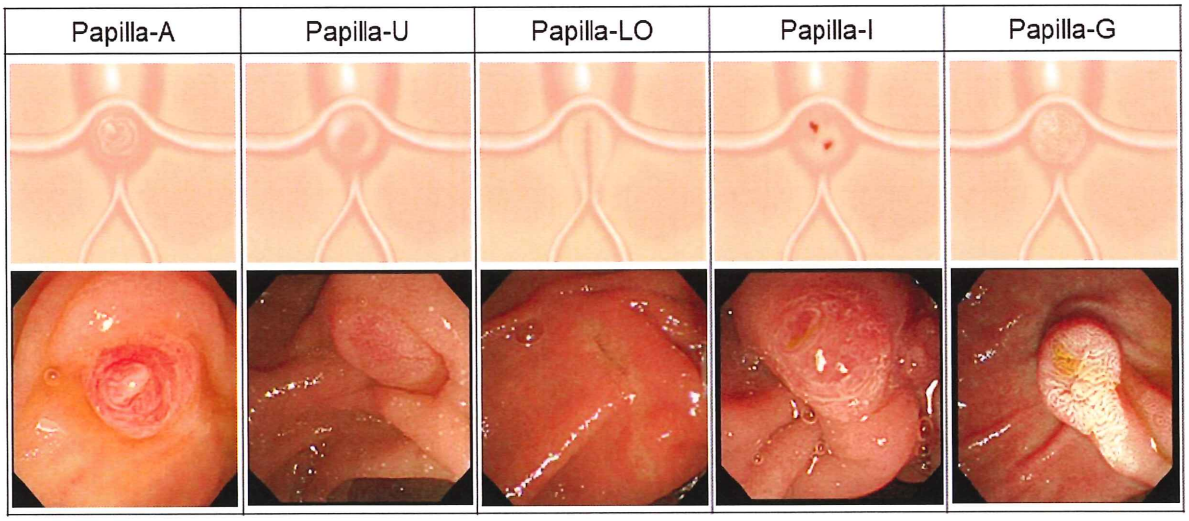
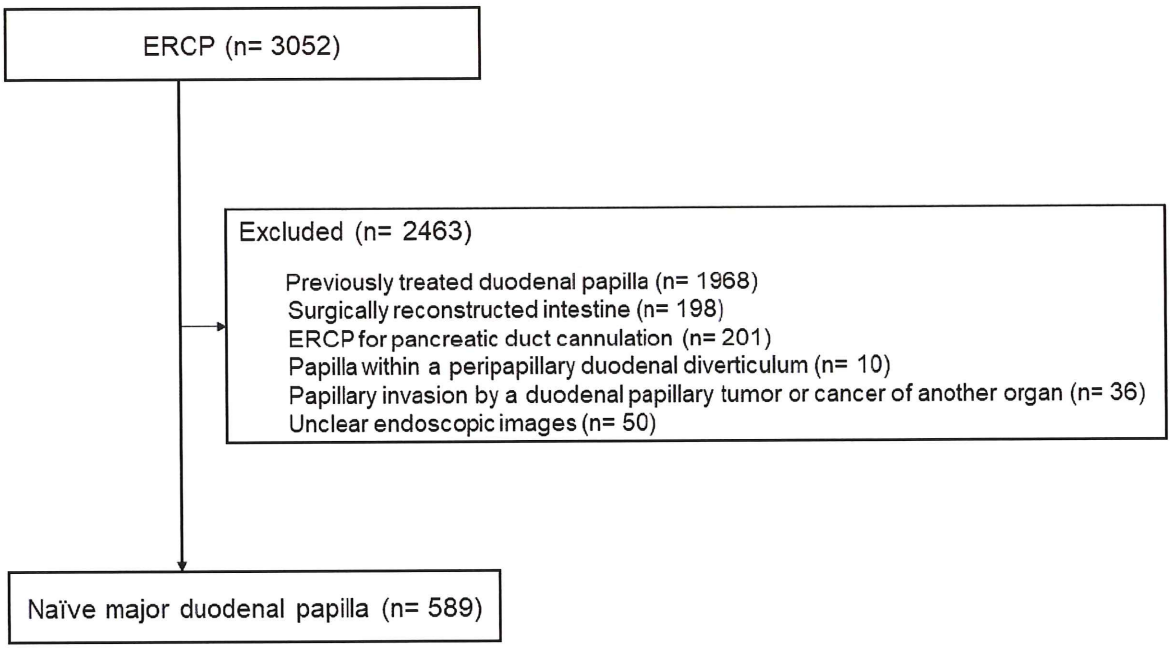


Figure.3


ERCP (n= 3052)
Excluded (n= 2463)
Previously treated duodenal papilla (n= 1968)
Surgically reconstructed intestine (n= 198)
ERCP for pancreatic duct cannulation (n= 201)
Papilla within a peripapillary duodenal diverticulum (n= 10)
Papillary invasion by a duodenal papillary tumor or cancer of another organ (n= 36)
Unclear endoscopic images (n= 50)
Naïve major duodenal papilla (n= 589)

Tables

Table 1. Distribution and concordance rates of classifications

	% (n)	Fleiss kappa (A vs. B vs. C)	95% CI	*p* value
Oral protrusion pattern (n = 589)				
Small type (Protrusion-S)	11.7 (69)			
Regular type (Protrusion-R)	77.9 (459)	0.788	0.753-0.824	< 0.001
Large type (Protrusion-L)	10.4 (61)			
Papilla pattern (n = 589)				
Annular type (Papilla-A)	67.1 (395)			
Unstructured type (Papilla-U)	7.0 (41)			
Longitudinal type (Papilla-LO)	7.5 (44)			
Isolated type (Papilla-I)	1.2 (7)	0.750	0.719-0.781	< 0.001
Gyrus type (Papilla-G)	15.6 (92)			
Unclassified	1.7 (10)			

Abbreviations: CI, confidence interval.

Table 2. Biliary duct cannulation rates according to subclassifications

	% (n)			*p*-value*
	All	Inexperienced endoscopist first	Experienced endoscopist	
Oral protrusion pattern				
Protrusion-S	100 (69/69)	100 (37/37)	100 (32/32)	1.000
Protrusion-R	97.6 (448/459)	97.5 (272/279)	97.8 (176/180)	1.000
Protrusion-L	95.1 (58/61)	95.3 (41/43)	94.4 (17/18)	1.000
Papilla pattern				
Papilla-A	98.0 (387/395)	98.3 (237/241)	97.4 (150/154)	0.717
Papilla-U	97.6 (40/41)	96.2 (25/26)	100 (15/15)	1.000
Papilla-LO	93.2 (41/44)	90.3 (28/31)	100 (13/13)	0.544
Papilla-I	100 (7/7)	100 (4/4)	100 (3/3)	1.000
Papilla-G	98.9 (91/92)	100 (52/52)	97.5 (39/40)	0.435
Unclassified	90.0 (9/10)	80.0 (4/5)	100 (5/5)	1.000

*The *p*-values were determined using the Fisher exact probability test.

Table 3. Number of biliary duct cannulation attempts according to subclassifications

	% (n)			*p*-value*
	All	Inexperienced endoscopist first	Experienced endoscopist	
Oral protrusion pattern				
Protrusion-S				0.806
<5 times	59.4 (41/69)	56.8 (21/37)	62.5 (20/32)	
≥5 times	40.6 (28/69)	43.2 (16/37)	37.5 (12/32)	
Protrusion-R				< 0.001
<5 times	61 .0 (280/459)	54.1 (151/279)	71.7 (129/180)	
≥5 times	39 .0 (179/459)	45.9 (128/279)	28.3 (51/180)	
Protrusion-L				0.397
<5 times	36.1 (22/61)	32.6 (14/43)	44.4 (8/18)	
≥5 times	63.9 (39/61)	67.4 (29/43)	55.6 (10/18)	
Papilla pattern				
Papilla-A				0.028
<5 times	58.5 (231/395)	53.9 (130/241)	65.6 (101/154)	
≥5 times	41.5 (164/395)	46.1 (111/241)	34.4 (53/154)	
Papilla-U				0.502
<5 times	63.4 (26/41)	57.7 (15/26)	73.3 (11/15)	
≥5 times	36.6 (15/41)	42.3 (11/26)	26.7 (4/15)	
Papilla-LO				0.043
<5 times	59.1 (26/44)	48.4 (15/31)	84.6 (11/13)	
≥5 times	40.9 (18/44)	51.6 (16/31)	15.4 (2/13)	
Papilla-I				0.429
<5 times	71.4 (5/7)	50.0 (2/4)	100 (3/3)	
≥5 times	28.6 (2/7)	50 .0 (2/4)	0	
Papilla-G				0.033
<5 times	56.5 (52/92)	46.2 (24/52)	70 .0 (28/40)	
≥5 times	43.5 (40/92)	53.8 (28/52)	30.0 (12/40)	

*The *p* values were determined using the Fisher exact probability test.

Table 4. Risk factors related to difficult biliary duct cannulation in cases performed by an experienced endoscopist

	No. of difficult biliary duct cannulations	Univariate analysis			Multivariate analysis		
		OR	95% CI	*p*value *	OR	95% CI	*p*value *
Oral protrusion pattern							
Protrusion-S (n = 32)	12	1.348	0.62-2.93	0.452			
Protrusion-R (n = 180)	51	0.503	0.264-0.96	0.037			
Protrusion-L (n = 18)	10	2.956	1.115-7.84	0.029	3.772	1.359-10.464	0.011
Papilla pattern							
Papilla-A (n = 154)	53	1.469	0.799-2.702	0.216			
Papilla-U (n = 15)	4	0.769	0.237-2.503	0.663			
Papilla-LO (n = 13)	2	0.374	0.081-1.732	0.208			
Papilla-I (n = 3)	0		n.c.				
Papilla-G (n = 40)	12	0.906	0.432-1.903	0.795			

Abbreviations: OR, odds ratio; CI, confidence interval; n.c., not calculated.

*The *p*values were determined using logistic regression.

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なし

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