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ORIGINAL ARTICLE

The Comparison of Two Different 5.5 Fr Sphincterotomes for Selective Cannulation of the Common Bile Duct: A Prospective, Randomized Study

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Abstract
Background and Aim There are scarce data regarding the impact of sphincterotome design on cannulation success. We aimed to compare two different 5.5 Fr standard sphincterotomes to determine initial cannulation success.
Methods Adult patients with naive papillae were enrolled in a prospective, randomized, crossover study. Two different 5.5 Fr sphincterotomes preloaded with guidewire (GW) were used in two groups with 140 patients included per group. A total of five papillary attempts and two pancreatic channel entries were allowed as maximum targets. In a case of more than two pancreatic entries, a double GW technique was attempted before crossover. If choledochal cannulation was not achieved within ten papillary attempts or more than four pancreatic entries despite crossover, access papillotomy was performed. Successful biliary cannulation was the primary outcome. Secondary outcomes were incidence of early complications and overall cannulation success.
Results Higher initial cannulation success was achieved in group I compared with group II (88.5 vs. 77.1 %, $p = 0.011$). The crossover and double GW techniques reduced the need for precut from 11.7 to 5.3 %. The overall cannulation success including precut for failed cases was 99.2 % (group I) and 98.5 % (group II). Sphincterotome type, presence of crossover, and number of cannulation attempts were predictors of successful cannulation in multivariate analysis.
Conclusions There was a significant difference in cannulation success between two different 5.5 Fr sphincterotomes. The cannulation success was mainly governed by sphincterotome design which serves a proper spatial orientation during the procedure. The combined use of crossover and double GW techniques may substantially decrease precut necessity.

Keywords ERCP · Cannulation · Sphincterotome · Biliary

Abbreviations

ERCP	Endoscopic retrograde cholangio pancreatography
CBD	Common bile duct
PEP	Post-ERCP pancreatitis
GW	Guidewire
CBC	Complete blood count
CT	Computed tomography
DGW	Double guidewire
PD	Pancreatic duct
C	Cannula, catheter
S	Sphincterotome

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Introduction

Repeated attempts at biliary cannulation have been associated with an increased risk of post-ERCP pancreatitis (PEP) [1]. Moreover, by prolonging the procedure, difficult cannulation may lead to sedation-related complications. The use of rescue methods such as precut (access) sphincterotomy and pancreatic duct (PD) stent placement may be undesirable for inexperienced operators.

Successful cannulation is achieved in >80 % of cases and >95 % when performed by experts [2]. Recently, the preferred method of biliary cannulation has become wire-guided using a sphincterotome preloaded with a guidewire (GW) instead of the conventional catheter with the injection of contrast medium. This approach results in superior cannulation success rates and decreased incidence of PEP [3–6].

There are a paucity of data regarding cannulation success with different sphincterotomes [7]. In a prospective, nonrandomized study, cannulation rate was higher by using a 3-Fr sphincterotome compared with a 5.5-Fr sphincterotome [8]. In contrast, a randomized, controlled trial found no difference in cannulation rates, procedure time, or complication rates between 4 and 5 Fr sphincterotomes [9]. Recently, our group tested the cannulation success by same size sphincterotomes of different manufacturers [10] and found the 5.5-Fr Ultratome with GW was superior to 5.5 Fr Endo-flex sphincterotome with GW in achieving initial selective CBD cannulation (92 vs. 81 %). We decided to perform a prospective, randomized, crossover study using these two sphincterotomes to determine initial cannulation success and adverse events in patients with naive papillae. Moreover, we sought to explore the causes of cannulation failure related to the device and/or papilla (Fig. 1).

Methods

Patients and Study Design

Patients with naive papilla who underwent ERCP at our hospital (Ankara Numune Education and Research Hospital, Department of Gastroenterology, Turkey) between November 2012 and July 2013 were prospectively enrolled. Exclusion criteria were as follows: age younger than 18 years, pregnancy, previous sphincterotomy, surgically altered gastric anatomy, severe comorbidity, visible tumoral infiltration at the periampullary area, visible impacted stone, resolving acute pancreatitis, and refusal to provide informed consent. After applying exclusion criteria, patients were randomly allocated to one of two groups (Fig. 2): Ultratome, group I or the Endo-flex, group II. Randomization was performed by computer-generated method 1:1. The study protocol was approved by Turgut Ozal (formerly Fatih) University review board (No. 1490). All authors having had access to and approving the study data.

All ERCP procedures were performed by one experienced endoscopist (E.O.) who performed >400 ERCPs per year. All ERCPs were done as inpatient procedures to our institutional policy, using a side-view duodenoscope (Fujinon ED-250XT5), with anesthesia assistance. All patients were evaluated for ERCP-related adverse events (Aes) by repeated clinical examinations, serum studies (CBC,

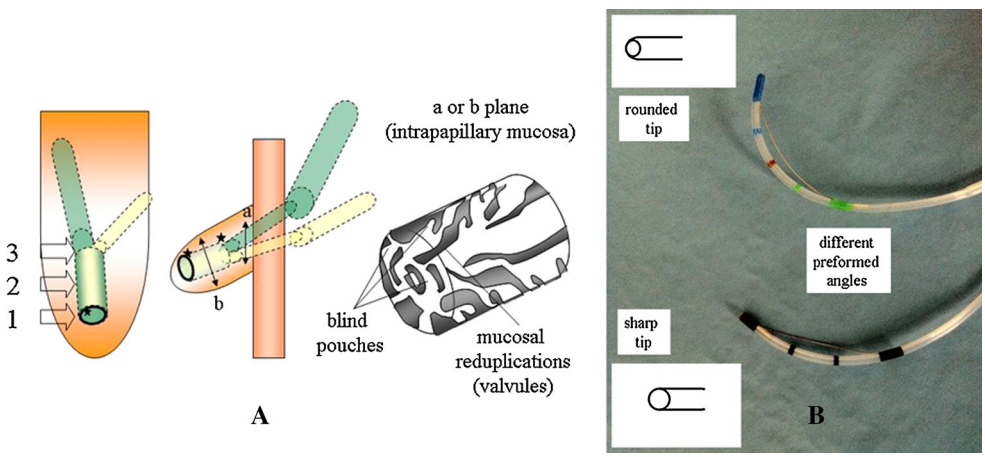

Fig. 1 **a** Illustration of major papilla anatomy. *1* Papillary orifice, *star* depicts the ideal point of first touch during cannulation, *2* intrapapillary common channel, and *3* the union of common bile duct–pancreatic duct. **b** Different features of same size (5.5 Fr) standard sphincterotomes in the relaxed position (Ultratome: *upper*, Endo-flex: *below*). Ultratome has a higher precurved angulation, and a rounded tip compared with sharp-edged tip of Endo-flex

amylase, liver chemistries), and ultrasound or CT imaging, if indicated.

Sample Size Calculation

In designing the study, power analysis was conducted by using the chi-square test to detect differences at a 5 % significance level at a power of 80 %, considering the cannulation success rates of wire-guided methods, 82 versus 95 % on lower and upper averages of reported literature, respectively [10–14]. Each group required nearly 140 patients based on power analysis. MedCalc version 12 was used for calculation.

ERCP and Cannulation Procedure

Cannulation was performed using a sphincterotome with GW assistance (in group I: Ultratome 5.5 Fr, 5-mm nose, double lumen type, Boston Scientific, Natick, MA, USA; in group II: Endo-flex 5.5 Fr, standard, 5-mm nose, double lumen type, Endo-flex GmbH, Düsseldorf, Germany). The sphincterotome wire length was 3 cm in the majority of cases (134 cases of group I and 135 cases of group II), while it was 2 cm in the remaining cases where there was a confined duodenal space. A standard 0.035″ straight type GW was used in all procedures (Jagwire, straight type; Boston Scientific). The sphincterotome with preloaded GW was aligned with the CBD and advanced carefully through the papillary channel. Once the papillary channel was entered, the GW was carefully advanced under fluoroscopy to determine which duct was cannulated based on anatomic course. When the GW was seen in the CBD, the sphincterotome was advanced and contrast injected to verify biliary cannulation. If the GW passed into the PD, it was withdrawn and further attempts to cannulate the CBD were made. Each attempt to cannulate the papilla or adjust/reintroduce the sphincterotome through the papillary channel, with or without GW advancement, before successful deep cannulation of the CBD, regardless of the time spent, was counted as 1 cannulation attempt. Number of cannulation attempts and those of PD entrances were counted in each case. A total of five papillary attempts and two pancreatic channel entries were allowed as maximum targets (Fig. 2). When there were more than two pancreatic entries, double guidewire (DGW) technique was tried before crossover, as previously described [15]. Unsuccessful initial cannulation was followed by crossover to other sphincterotome. If selective CBD cannulation was not achieved within 10 papillary attempts or more than four pancreatic entries, access papillotomy was performed. Time to successful cannulation was noted as seconds for each procedure. Access sphincterotomy was performed using a double lumen needle knife papillotome. The choice

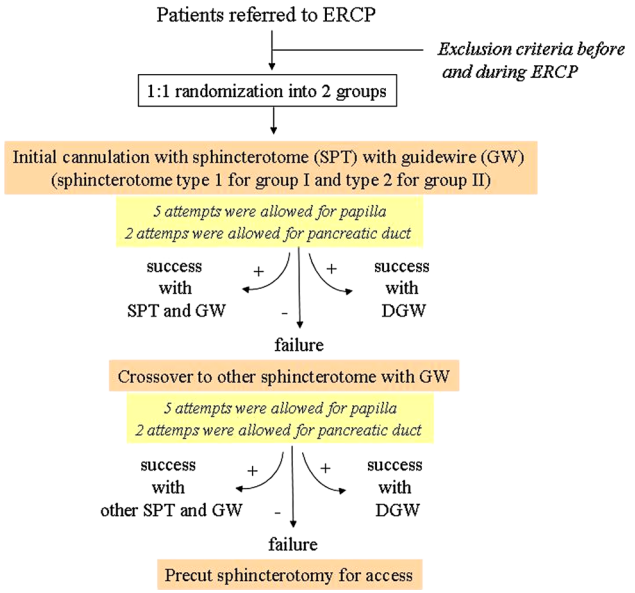

Fig. 2 Study design. *GW* guidewire

of precut method was left to endoscopist discretion. A PD stent was inserted in cases of more than four pancreatic channel entries or presumed high probability of PEP such as suspected Oddi sphincter dysfunction in cases of papillary stenosis. Prophylactic PD stents were removed endoscopically 5–7 days after placement. No patients received pharmacologic prophylaxis for PEP.

We tried to define the presumed mechanism of cannulation failure in each case based on the endoscopist' perception.

Definitions

Primary CBD cannulation success was defined as free cannulation of the CBD with the initial sphincterotome and GW (in group I: sphincterotome 1, Ultratome; in group II: sphincterotome 2, Endo-flex). The added cannulation rates of DGW and crossover were also noted. Overall final CBD cannulation success was defined as the sum of primary cannulation, crossover, and after the use of precut.

The predicted rate of precut is defined as "the number of cases with unsuccessful cannulation via sphincterotome" divided by "the number of total cases." In other words, it describes the probability of precut need for cases, cannulation tried by only sphincterotome, and the crossover and DGW techniques were not applied subsequently. The actual rate of precut is defined as "the number of cases with unsuccessful cannulation after the use of sphincterotome, crossover, and DGW" divided by "the number of total cases." In other words, it describes the precut applied cases, after the use of all efforts (sphincterotome, crossover, and DGW techniques).

Post-ERCP pancreatitis (PEP) was defined as new-onset or increased abdominal pain persisting for at least 24 h after the procedure with serum amylase levels increasing to more than 3× the upper limit of normal [16].

Statistical Analysis

Data were collected prospectively and entered into a database program (Excel, Microsoft) and analyzed with a statistical package (SPSS 18.0 software). Kolmogorov–Smirnov/Shapiro–Wilks test were used as normality test of variables. Comparisons between the two groups were made by using the Mann–Whitney *U* test for continuous variables and the chi-square test or, when appropriate, the Yates's continuity correction test for categorical variables. Median, minimum, and maximum were used for continuous variables and percentages for categorical variables. Possible factors identified with univariate analysis were then entered into multivariate analysis to determine independent predictors. Hoshmer–Lemeshow fitness was used to evaluate model fit. All differences were considered significant with a two-sided p value <0.05.

Results

A total of 382 patients were enrolled in the study, and 102 were excluded. The remaining 280 were randomized in two groups. The study groups included 140 patients in each arm; 102 cases were excluded due to previous sphincterotomy ($n = 57$), operated stomach ($n = 9$), visible impacted stone ($n = 16$), visible tumoral infiltration at the periampullary area ($n = 7$), ectopic opening of the papilla into the duodenal bulb ($n = 3$), post-bulbar narrowing ($n = 3$), inability to identify the papillary orifice within a periampullary diverticula ($n = 1$), severe comorbidity ($n = 4$), and premature termination of the procedure due to anesthesia-related difficulties ($n = 2$). The median age of the patients was 56 (18–93) years [group I: 58 (18–93), group II: 55 (21–92)]; 51 % of the patients were women (group I: m/f 64/76; group II: m/f 74/66).

The most common indication for ERCP was known or suspected biliary lithiasis and/or lithiasis-related events (60 vs. 64 %). There were no significant differences between the groups in the number of patients, age, sex, indications for ERCP, and rate of periampullary diverticula (Table 1).

Primary cannulation was successful in 124 of group I and in 108 of group II (Fig. 3; Table 2). The primary CBD cannulation success was significantly higher in group I compared with group II ($n = 124$ vs. 108; 88.5 vs. 77.1 %, $p = 0.011$). Success of sphincterotome 1 persisted after crossover ($n = 144$ vs. 121; 88.8 vs. 80.1 %, $p = 0.032$). There was no statistical difference in either the number of cannulation attempts or mean time to cannulation (Table 2). The crossover and DGW techniques reduced the need for precut from 11.7 to 5.3 % ($p = 0.01$), with no difference between groups. Six cases in group I and nine cases in group II underwent access sphincterotomy with overall precut success of 80 %. Precut was performed nearby after placement of a pancreatic stent ($n = 11$) or as a fistulotomy ($n = 4$). In three patients, cannulation failed despite precut and two cases underwent percutaneous transhepatic cholangiography and the remaining one patient did not undergo further intervention and was observed. There was no significant difference in overall final CBD cannulation success rate between the two groups (99.2 vs. 98.5 %).

Table 1 Demographics and ERCP indications in study groups

	Group I ($n = 140$)	Group II ($n = 140$)	p value
M/f	64/76	74/66	n.s.
Age, years, median (min–max)	58 (18–93)	55 (21–92)	n.s.
Diverticula	15	17	n.s.
Choledocholithiasis	84	89	n.s.
Stone	62	65	
Probable passed stone	7	7	
Acute biliary pancreatitis	8	6	
Papillary stenosis	4	5	
More than one of above	3	6	
Malignant stricture	29	25	n.s.
Proximal-middle	19	12	
Distal	10	13	
Postoperative[a]	24	21	n.s.
Others[b]	3	5	n.s.

[a] Postoperative biliary leaks/strictures/retained stones/hydatid surgery

[b] Chronic pancreatitis, toxic, and other liver disease, pancreatic hydatid cyst, hemobilia

At multivariate regression analysis, the sphincterotome type ($p = 0.048$), number of cannulation attempts ($p < 0.001$), and presence of crossover ($p < 0.001$) were found as predictors of cannulation success.

To the endoscopist' perception, the most common presumed mechanism of cannulation failure was improper spatial orientation of the sphincterotome deviating from the left upper quadrant of the papilla that inadvertently oriented toward the apex or to the center despite manipulation (Table 3).

Regarding ERCP-related adverse events, there was no perforation or major bleeding, while PEP occurred in overall 2.1 %. There were no significant differences in PEP rates between the two groups (group I 1.5 vs. group II 2.9 %). Based on clinical and laboratory criteria, two documented cases of pancreatitis were identified in group I (both mild) and four cases in group II (three mild and one moderate)

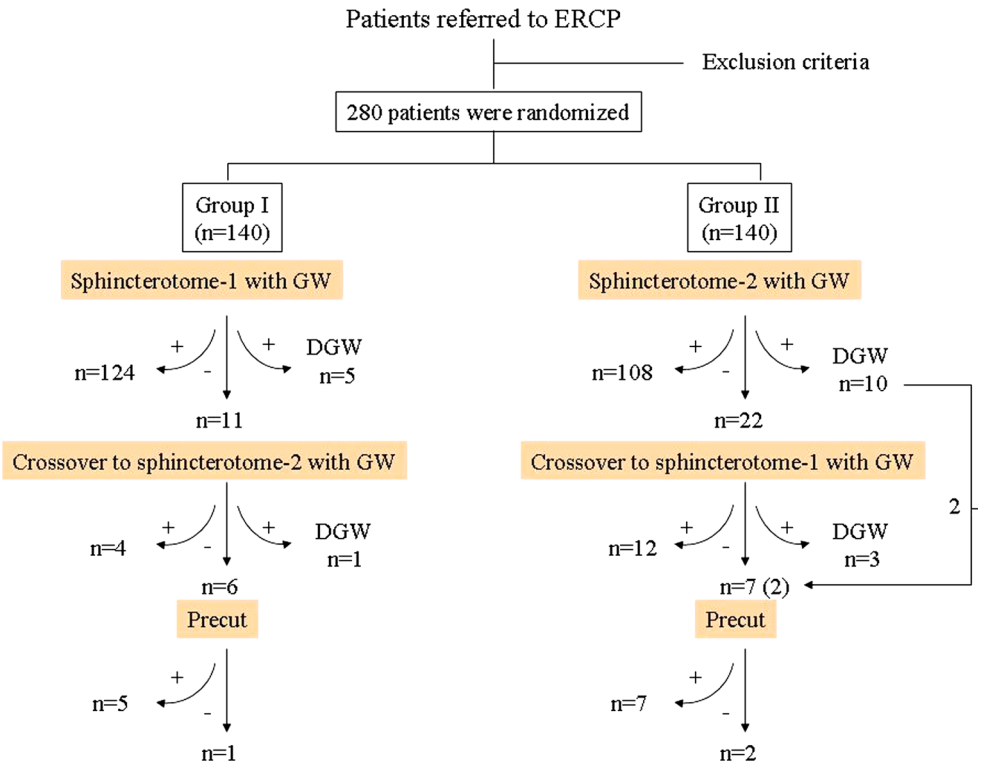

Fig. 3 Flow-chart showing the results of the study including initial, crossover, and precut phases. *DGW* double guidewire

Table 2 Results of cannulation in study groups

	Total	Group I	Group II	*p* value
Primary cannulation success	232/280 (82.9 %)	124/140 (88.5 %)	108/140 (77.1 %)	**0.011**
No. of attempts before crossover (median, min–max)	3.0 (1–10)	2.9 (1–5)	3.1 (1–5)	n.s.
Time to cannulation (s) (median, min–max)	204 (3–960)	190 (3–680)	212 (3–960)	n.s.
Success including crossover		144/162 (88.8 %)	121/151 (80.1 %)	**0.032**
No. of attempts after crossover (median, min–max)	3.7 (1–10)	3.3 (1–10)	3.9 (1–10)	n.s.
Time to cannulation (s), after crossover (median, min–max)	233 (3–1,520)	212 (3–1,200)	256 (3–1,520)	n.s.
Predicted precut rate[a]	33/280 (11.7 %)	11/140 (7.8 %)	22/140 (15.7 %)	**0.042**
Actual precut rate	15/280 (5.3 %)	6/140 (4.3 %)	9/140 (6.4 %)	n.s.
Overall cannulation success	277/280 (98.9 %)	139/140 (99.2 %)	138/140 (98.5 %)	n.s.

Statistically significant values ($p < 0.05$) are given in bold

SPT sphincterotome and *DGW* double guidewire

[a] The predicted rate of precut: if the crossover and double guidewire techniques were not applied

($p > 0.05$). Twenty-six patients in group I (19 %) and thirty-one patients in group II (22 %) demonstrated asymptomatic increase in serum amylase levels ($p > 0.05$) within 24 h following ERCP. At univariate regression analysis, the combined rates of hyperamylasemia and pancreatitis were related to cannulation success, number of attempts, number of PD entries, time to cannulation, presence of crossover, and use of precut in both groups (data not shown). However, at multivariate regression analysis, only the presence of PD entries remained as a predictor of hyperamylasemia/PEP (OR 3.5, 95 % CI $p = 0.001$).

Discussion

The success rates of CBD cannulation vary greatly depending on the type of cannulation device [3, 4, 10–14, 17, 18]. An approximation of 60, 70, 80, and 90 % can be made regarding the primary cannulation success of C (standard catheter), C + GW, S (sphincterotome), and S + GW, respectively. In general, although not perfect, S + GW is the recommended initial approach for selective CBD cannulation. However, there are large differences between primary cannulation rates even with S + GW

Table 3 Presumed causes of cannulation failure related to device and/or papilla

Presumed mechanism of failure to the endoscopist' perception	Group I ($n = 16$)	Group II ($n = 32$)
A: Improper spatial orientation of sphincterotome	4	16
B: Visible intrapapillary incision via false passage of GW through blind pouches	3	4
C: Very loose/floppy papilla, S + GW can not fasten onto properly	4	–
D: "True stuck"(no movement of S + GW due to stuck of mucosal valvules or membranous septum)	4	8
E: Difficult angulation of distal CBD at the common channel union	1	2
F: Intrapapillary distorted anatomy (fibrosis, edema etc.) revealed after EST	–	2

A–C are more objective and sensible than D–F, and multiple mechanisms may occur in a single case

(77.9–98.5 %) [3, 4, 13, 14]. In the current prospective study, we compared two different 5.5 Fr sphincterotomes available from different manufacturers. A significant cannulation success was observed between two different same sized sphincterotomes (88.5 vs. 77.1 %).

A greater capability of a sphincterotome to adjust to the papillary orifice favors the use of the sphincterotome with GW approach over a standard cannula [18]. However, in most studies, use of different sphincterotomes of different sizes from various manufacturers has been used. Sphincterotomes of identical size were not compared. Our results favor the use of one type of sphincterotome which we believe has advantageous features such as a higher degree of flexibility, a more suitable precurved angulation, and a rounded tip compared with the other device studies which has a sharp-edged tip (Fig. 1). The most common suggested mechanism in failed cases was improper spatial orientation of the sphincterotome deviating from the left upper quadrant of the papilla that inadvertently oriented toward the apex or to the center despite manipulation. This was due to the intrinsic preformed angle of the sphincterotome and/or limited flexibility (Table 3).

However, the Ultratome was also not perfect for all cases and the Endo-flex worked well in some cases where cannulation failed with the Ultratome after crossover (Fig. 3). So, the papillary features may also determine cannulation success. In general, cannula/sphincterotome becoming stuck in the folds is reported as the most common problem in failed cases [19]. However, any explanation hidden behind this was not obvious in previous clinical studies. In anatomy literature, the complex intrapapillary mucosal features can be summarized as follows (Fig. 1) [20–23]: First, the papillary os is not visible as a single opening, but cauliflower-like or rosebud-/rose-like pattern with numerous mucosal duplications splitting off from the limbus that are distributed unevenly [21, 23]. Second, the lumen of the ampulla Vateri is filled almost entirely with mucosal duplications. The mucosal reduplications protrude into the lumen in a valviform pattern and also named as valvules. Third, numerous fissural orifices (cul-de-sacs or blind pouches) open into the duodenum between the mucosal duplications. These structures relax and contract and close the common channel [22]. Our study gives some indirect observations to believe these complex intrapapillary features are the reason for cannulation difficulty (Table 3). For example, false passage of the GW occurred through blind pouches between mucosal valvules or the S + GW could not be advanced in some cases, despite its proper hold in the papilla due to probable filling of mucosal valvules into the sphincterotome lumen.

The incidence of PEP in studies where sphincterotome with GW was used is reported to be from 0 to 8.7 % [3–5, 24, 25], reaching a figure of 12.2 % in high-risk patients [25]. The overall rate of PEP was 2.1 % in our study, at the lower end of cited studies which applied wire-guided cannulation. This may be due to very low number of high-risk patients (sphincter of Oddi dysfunction, recurrent pancreatitis), limiting the number of cannulation attempts to 10 and PD entries to four, and using the pancreatic stent in the majority of precut cases. Moreover, no significant differences were found between sphincterotome groups, despite a higher figure in group II. If the number of enrolled patients could be increased over the number in this study, there may be potentially significant differences in PEP.

The present study has some limitations in design. First, endoscopist skill may be a bias in clarifying the superiority of cannulation devices. Various levels of participants in a RCT in multiple centers with multiple endoscopists may reduce the skill bias and for generalizing the results of such study to estimate the cannulation success. Second, our definition of presumed mechanisms regarding cannulation failure is subjective and speculative. This issue needs further research for clarification by international experts.

In conclusion, we found a 5.5 Fr Ultratome with GW approach was more successful than 5.5 Fr Endo-flex sphincterotome with GW in achieving initial selective cannulation of CBD. In failed cases, crossover to the other sphincterotome resulted in a further increase in cannulation success. Although the cannulation success was mainly governed by sphincterotome design, we believe that mucosal features of papilla and intrapapillary ducts may

also determine cannulation success. Our findings should be explored in further studies. Lastly, the combined use of crossover and DGW techniques may substantially decrease precut necessity.

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Conflict of interest None.

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