

## Can wire-guided cannulation prevent post-ERCP pancreatitis? A prospective randomized trial CME

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**Background:** Among the procedure-related factors associated with post-ERCP pancreatitis, selective cannulation of the common bile duct by insertion of a guidewire may be associated with fewer complications than conventional methods of cannulation with contrast injection to access the bile duct. However, the results of studies regarding the usefulness of wire-guided cannulation (WGC) are conflicting.

**Objective:** This prospective randomized trial was designed to determine whether WGC reduces the rate of post-ERCP pancreatitis.

**Design:** A prospective randomized controlled trial.

**Setting:** Tertiary-care academic medical center.

**Patients:** A total of 300 consecutive patients with native papilla and pancreaticobiliary disease who were candidates for therapeutic ERCP were randomized from June 2006 to May 2007.

**Interventions:** WGC without contrast injection or conventional cannulation with contrast injection.

**Main Outcome Measurements:** Post-ERCP pancreatitis, risk factors, and procedure-related complications were evaluated prospectively.

**Results:** A total of 3 patients (2%) in the WGC group and 17 patients (11.3%) in the conventional group had post-ERCP pancreatitis ( $P = .001$ ). Among the cases of acute pancreatitis in the WGC group, 2 patients with suspected sphincter of Oddi dysfunction (SOD) and unintentional main pancreatic duct (PD) guidewire cannulation showed post-ERCP pancreatitis despite the use of WGC. In multivariate analysis, WGC was a protective factor (odds ratio 0.1; 95% CI, 0.024-0.490,  $P = .004$ ), whereas female sex and SOD were risk factors for post-ERCP pancreatitis.

**Limitation:** Our study population was a low-risk cohort.

**Conclusions:** WGC is associated with a lower rate of post-ERCP pancreatitis. However, WGC may not prevent post-ERCP pancreatitis in patients with suspected SOD and unintentional PD guidewire cannulation. (Gastrointest Endosc 2009;69:444-9.)

Post-ERCP pancreatitis is a dreaded and not uncommon complication because of its association with substantial morbidity, occasional mortality, and increased hospitaliza-

*Abbreviations: CBD, common bile duct; OR, odds ratio; PD, pancreatic duct; SOD, sphincter of Oddi dysfunction; WGC, wire-guided cannulation.*

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tion rates. The expected rate of post-ERCP pancreatitis ranges from 1% to 7% to as high as 12% to 31%.<sup>1-7</sup> Numerous risk factors, both patient and procedure related, contribute to the development of pancreatitis, and many studies have been performed to minimize the incidence and severity of post-ERCP pancreatitis. These include developing endoscopic intervention and training<sup>6,8,9</sup> and the administration of pharmacologic agents such as gabexate mesilate, corticosteroids, and octreotide.<sup>10-12</sup> Among procedure-related factors, selective cannulation of the common bile duct (CBD) by insertion of a guidewire may lead to fewer complications than do conventional methods with a contrast injection to

access the bile duct.<sup>13,14</sup> However, the results of the studies on the usefulness of wire-guided cannulation (WGC) are conflicting.<sup>7,13,14</sup>

This prospective randomized trial was designed to determine whether WGC can reduce the rate of post-ERCP pancreatitis.

## PATIENTS AND METHODS

### Patients

This study was designed as a prospective randomized trial. The ethics committee at the Soonchunhyang University Cheonan Hospital approved the study protocol. All participants gave their informed consent, and patients with native papilla and pancreaticobiliary disease who were candidates for therapeutic biliary ERCP were invited to participate in the study. All patients underwent transabdominal or endoscopic US, abdominal CT scans, and MRCP before ERCP. Exclusion criteria were as follows: (1) age less than 18 years, (2) refusal of the study protocols, (3) allergy to contrast, (4) history of acute pancreatitis, (5) Billroth II gastrectomy, (6) use of needle-knife fistulotomy for biliary sepsis with impacted stones, (7) ampullary tumors, and (8) pancreaticobiliary malunion (long common channel) on EUS or MRCP before ERCP. From June 2006 to May 2007, a total of 300 patients met the eligibility criteria. No patient was lost during follow-up.

All ERCP procedures were performed by a single experienced endoscopist (D. H. P., >2500 career ERCPs with a workload of 350 ERCPs annually). The guidewire was controlled by a skilled assistant with 2 years of training (E. O. K. or Y. S. L.).

### Study protocol

Enrolled patients were randomly assigned to 2 groups (group A, WGC group; group B, conventional group) by means of computer-generated numbers. After an overnight fast, all patients underwent ERCP in the prone position with a standard duodenoscope (TJF 240, Olympus Optical, Tokyo, Japan) after sedation with intravenous midazolam (0.05 mg/kg) or propofol (0.5 mg/kg). Prophylactic antibiotics and analgesics were permitted.

**WGC.** In the WGC group, a hydrophilic-tipped guidewire (Jagwire, Boston Scientific, Natick, Mass), 0.035 inch in a diameter, was preloaded into a pull-type papillotome (flow cut, Olympus Optical). The papillotome was oriented from the 11 to 12 o'clock position on the papilla and bowed to align it correctly with the axis of the bile duct. After a minimal insertion (2-3 mm) of the pull-type papillotome in the ampulla, the guidewire was carefully advanced through the CBD under fluoroscopy until it was seen to enter the bile duct. If the pancreatic duct (PD) was entered, the guidewire was simply withdrawn and attempts to redirect it toward the CBD were made.

### Capsule Summary

#### What is already known on this topic

- Post-ERCP pancreatitis, with an incidence of 1% to 31%, may be related to many factors associated with contrast injection.

#### What this study adds to our knowledge

- In a single-center prospective trial of 300 patients randomized to wire-guided cannulation (WGC) or conventional cannulation with contrast injection, the WGC group had a lower rate of post-ERCP pancreatitis.

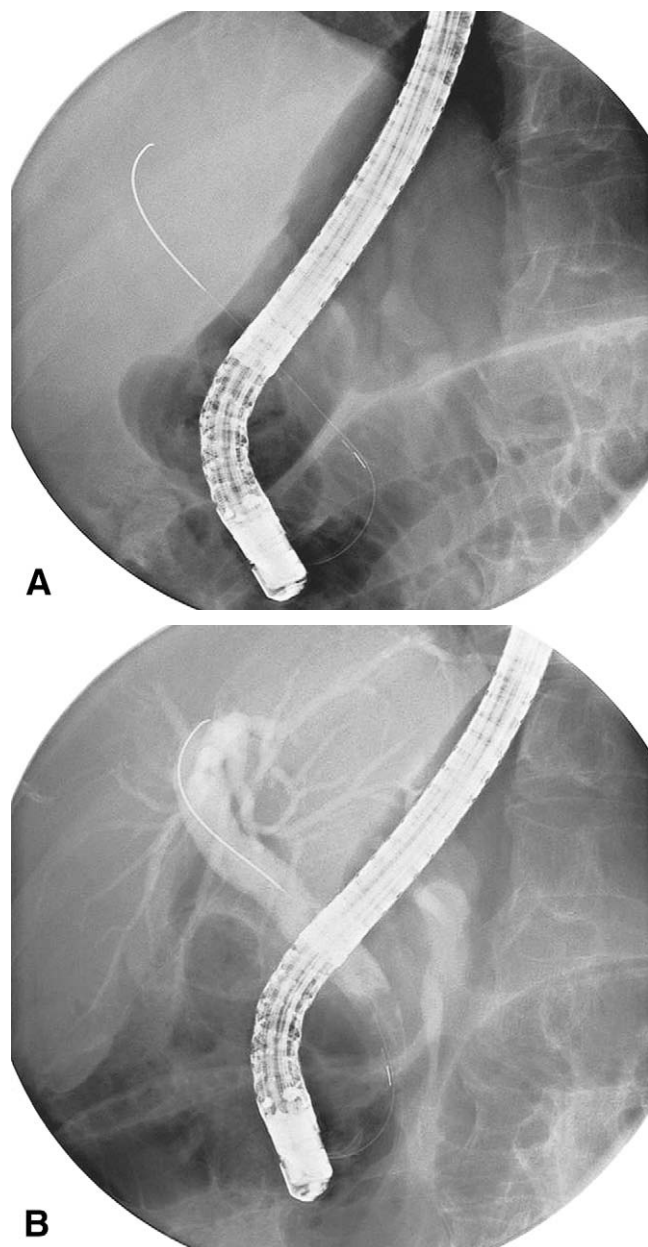
After biliary cannulation was achieved through guidewire insertion, contrast injection was allowed (Fig. 1).

**Conventional cannulation.** In the conventional group, the standard method for cannulation of the bile duct with a papillotome and injection of contrast media was used.

To avoid clouding the results with additional risk factors such as prolonged attempts on the papilla or multiple pancreatic cannulations resulting in the late institution of precutting for difficult biliary cannulation,<sup>15</sup> certain parameters were instituted. In the WGC group, 10 minutes for biliary cannulation or up to 5 attempts of unintentional PD cannulation by guidewire (5 passes) were allowed, whereas in the conventional group 10 minutes for biliary cannulation or up to 5 attempts of unintentional PD cannulation with 2 contrast injections into the PD were allowed. A fistulotomy with a needle-knife (Microtome, Boston Scientific, Microvasive, Marlboro, Mass) as rescue management was performed when access to the CBD failed despite 5 attempts of pancreatic cannulation. This type of precut was started over the bulging portion of the papilla, extended downward, and stopped short of the papillary orifice to avoid the risk of duodenal perforation and injury to the pancreatic sphincter.<sup>15</sup> All endoscopic sphincterotomies were performed with a blended electrosurgical current (UES-30 generator, Olympus) in both groups after access to the CBD. A PD stent for prophylactic prevention of pancreatitis was not used in this study.

### Definition of outcomes

Suspected sphincter of Oddi dysfunction (SOD) was defined as unexplained abdominal pain of suspected pancreaticobiliary origin with elevation of serum hepatic enzymes (biliary type I or II). SOD was diagnosed on the basis of ERCP or manometric results. Difficult biliary cannulation was defined as the failure of biliary access despite 10 minutes of attempted biliary cannulation, or more than 5 attempted unintentional pancreatic cannulations.<sup>15</sup> The serum amylase level was measured before ERCP and 24 hours thereafter. Hyperamylasemia after ERCP was



**Figure 1.** After a minimal insertion of the pull-type papillotome in the ampulla, the guidewire was advanced through the CBD under fluoroscopy (**A**). Guidewire cannulation followed by contrast injection shows filling defects on distal CBD (**B**).

defined as an elevation of the serum amylase level above the upper normal limit (160 IU/L). All complications were classified and graded according to consensus guidelines.<sup>16</sup> Definition and grade of post-ERCP pancreatitis was as follows: new or worsened abdominal pain with elevation of serum amylase at least 3 times above the upper normal limits for 24 hours after a procedure that requires at least 2 to 3 days (mild), 4 to 10 days (moderate), and more than 10 days (severe) of hospitalization or if any of the following occurred: hemorrhagic pancreatitis, pancreatic

necrosis, pseudocyst, or the need for percutaneous drainage or surgery.<sup>16</sup>

### Statistical analysis

In the design of this study, a sample size was estimated by using a  $\chi^2$  test to detect differences at a 5% level of significance with a power of 90% in rates of pancreatitis. The expected rate of post-ERCP pancreatitis was 15% in the standard group with prophylactic treatment of 4%. The analysis indicated that 150 patients would be required in each group. Statistical analysis was performed with SPSS 12.0 (SPSS, Chicago, Ill), and a 2-tailed *P* value of less than .05 was considered statistically significant. Variables for post-ERCP pancreatitis in the 2 groups were analyzed with a Student *t* test or Mann-Whitney *U* test according to the continuous data with normal or nonnormal distributions. Differences in categorical variables were analyzed by the  $\chi^2$  and Fisher exact tests. Logistic regression modeling was used to control confounding and estimate the odds ratio (OR) associated with each variable for the development of post-ERCP pancreatitis.

### RESULTS

Successful biliary cannulation was achieved in 148 patients (98.7%) in the WGC group and in 147 patients (97%) in the conventional group ( $P > .05$ ). The respective indications for ERCP in WGC group and conventional group were as follows: choledocholithiasis (102 patients vs 115 patients), cholangiocarcinoma with obstructive jaundice (21 vs 19), pancreas head cancer (15 vs 11), bile leak after cholecystectomy (2 vs 0), hepatoma with bile duct invasion (4 vs 4), and suspected SOD (6 vs 1) (Table 1). All patients in the latter group (suspected SOD) had confirmed SOD.

A hyperamylasemia at 24 hours after ERCP was lower in the WGC group (537.3 IU/L vs 938.1 IU/L,  $P = .016$ ). Unintentional main PD cannulations occurred in 39 patients (26%) in the WGC group and in 44 patients (29.3%) in the conventional group, respectively ( $P > .05$ ), in which cases the conventional group showed a variable extent of opacification of the PD system. For difficult biliary cannulation, a needle-knife fistulotomy was performed in 28 patients (18.7%) and 36 patients (24%), respectively ( $P > .05$ ). There were no significant differences between the 2 groups in rates of procedure-related complications, such as bleeding and perforation (Table 2).

A total of 3 patients (2%; 1 mild, 1 moderate, 1 severe) in the WGC group and 17 patients (11.3%; 14 mild, 2 moderate, 1 severe) in the conventional group had post-ERCP pancreatitis ( $P = .001$ ), according to the consensus guideline definition of ERCP-related pancreatitis.<sup>16</sup> Between the 2 groups, there were no significant differences in patient-related or technical factors for post-ERCP pancreatitis (Table 3). Among the cases of acute pancreatitis in the

**TABLE 1. Baseline patient characteristics and indications**

	A (n = 150)	B (n = 150)	P value
Mean age (y [SD])	63.6 (16.2)	62.7 (16.0)	.626
Male/female ratio	83:67	72:78	.204
Periampullary diverticulum	26	26	1.000
Indications (No.)			
Cholelithiasis	102	115	.093
Cholangiocarcinoma	21	19	.734
Pancreas head cancer	15	11	.412
Bile leak after cholecystectomy	2	0	.498
Hepatoma with bile duct invasion	4	4	1.000
Suspected SOD	6	1	.121

A, Guidewire group; B, conventional group.

**TABLE 2. Patient outcomes**

	A (n = 150)	B (n = 150)	P value
Amylase (IU/L [SE])	292.8 (37.9)	464.9 (68.5)	.683
Hyperamylasemia (IU/L [SE])	537.3 (73.3)	938.1 (132.3)	.016
Unintentional PD cannulation/contrast injection (%)	39 (26)	44 (29.3)	.519
Use of fistulotomy for biliary access (%)	28 (18.7)	36 (24)	.260
Pancreatitis (%)	3 <sup>a</sup> (2)	17 <sup>b</sup> (11.3)	.001
Bleeding	0	0	
Perforation	0	0	
Mortality rate	0	0	

Grade of pancreatitis: mild/moderate/severe; a (1/1/1) versus b (14/2/1). A, Guidewire group; B, conventional group.

**TABLE 3. Risk factors for pancreatitis**

	A (n = 75)	B (n = 82)	P value
Female, age <35 years (%)	2 (1.3)	1 (0.7)	.624
Suspected SOD	6 (4)	1 (0.7)	.121
Difficult cannulation	28 (18.7)	36 (24)	.260
Unintentional PD cannulation/contrast injection	39 (26)	44 (29.3)	.519

A, Guidewire group; B, conventional group.

**TABLE 4. Results of logistic regression on post-ERCP pancreatitis with regard to variables**

	OR	95% CI	P value
Guidewire	0.1	0.024-0.490	.004
Female sex	3.2	1.109-9.401	.032
SOD	23.7	2.437-230.175	.006

## DISCUSSION

Numerous mechanisms have been postulated for the induction of post-ERCP pancreatitis. Multifactorial (mechanical, chemical, hydrostatic, enzymatic, microbiologic, allergic, and thermal) issues may act independently or in concert to induce post-ERCP pancreatitis.<sup>3,4,17</sup> Among etiologic factors, hydrostatic pressure on the PD contributes to ductal epithelial or acinar injury.<sup>4,18</sup> Accessing the bile duct with the aid of a guidewire may reduce traumatic injury to the pancreatic duct and papilla or avoid hydrostatic pressure associated with contrast injection, thereby reducing ERCP-related pancreatitis.<sup>13,14,18</sup> In our study, rates of post-ERCP pancreatitis were 2% in the WGC group and 11.3% in the conventional group ( $P = .001$ ), and the overall rates were about 6.6%. The rate of post-ERCP pancreatitis is in close agreement with the expected rates<sup>19</sup> and corresponds with the results of earlier studies that reported that post-ERCP pancreatitis can be reduced by WGC.<sup>13,14</sup>

In the study by Lella et al,<sup>14</sup> none of the patients in a cohort of 200 patients randomly selected for bile duct cannulation with a soft polytetrafluoroethylene (Teflon, DuPont, Wilmington, Del)-tipped guidewire had pancreatitis (4.1% in the control group,  $P < .01$ ). That study concluded that this reduced the possibility of chemical- and pressure-related pancreatic injury by preventing unintentional injection of contrast media into the main PD or the papilla itself (submucosal injection).<sup>14</sup> However, the authors did not assess post-ERCP pancreatitis according to the

WGC group, 2 patients with suspected SOD demonstrated pancreatitis (one moderate, and another severe) despite the use of WGC. In multivariate analysis, WGC was a protective factor (OR 0.1; 95% CI, 0.024-0.490,  $P = .004$ ), whereas female sex (OR 3.2; 95% CI, 1.109-9.401,  $P = .032$ ) and SOD (OR 23.7; 95% CI, 2.437-230.175,  $P = .006$ ) were risk factors for post-ERCP pancreatitis (Table 4).

**TABLE 5. Prospective trials of WGC to reduce the incidence of post-ERCP pancreatitis**

No.	Design	Suspected SOD	Pancreatitis/SOD (WGC) (No.)	Pancreatitis/unintentional PD (WGC vs CC) (No.)*	Pancreatitis (WGC)	Pancreatitis (CC)
Vandervoort et al <sup>7</sup>	1223 Prospective	83/1223 (6.8%)	16/83†	NA	33/322 (10.2%)	55/896 (6.1%)
Lella et al <sup>14</sup>	400 Prospective randomized	5/400 (1.3%)	0/4	0/82, <sup>a</sup> 5/113 <sup>b</sup>	0/197 (0%)	8/195 (4.1%)
Artifon et al <sup>13</sup>	300 Prospective randomized	20/300 (6.7%)	0/16	0/27, <sup>c</sup> 4/21 <sup>d</sup>	13/150 (8.6%)	25/150 (16.6%)
Current study	300 Prospective randomized	7/300 (2.3%)	2/6	2/39, <sup>e</sup> 8/44 <sup>f</sup>	3/150 (2%)	17/150 (11.3%)

*P* values: a vs b, .08; c vs d, .05; e vs f, .09 by Fisher exact test. *P* values for *Pancreatitis (WGC)* versus *Pancreatitis (CC)* shown in table.

CC, Conventional cannulation; NA, not available.

\*The number of cases of post-ERCP pancreatitis after unintentional PD injection or cannulation in CC and WGC groups.

†The number was not associated with whether the procedure was conventional or wire guided.

difficulty of CBD cannulation (number of attempts). Artifon et al<sup>13</sup> also showed that the guidewire technique for bile duct cannulation lowers the likelihood of post-ERCP pancreatitis (8.6% in the guidewire group vs 16.6% in the conventional group,  $P = .02$ ). They assessed the difficulty of CBD cannulation and unintentional PD cannulations and concluded that the reduction in post-ERCP pancreatitis was mainly the result of preventing the injection of contrast media into the PD. The guidewire technique also reduced the risk for pancreatitis by facilitating cannulation and by potentially limiting papillary trauma and the need to precut sphincterotomies. Although the range of cannulation attempts was classified as 0 to 3, 4 to 6, and 7 to 10 attempts, the investigators did not provide the results of post-ERCP pancreatitis in these subgroups according to various ranges of attempts. Even with soft hydrophilic-tipped wire cannulations, difficult wire passages or frequent pancreatic manipulations may result in injury to the papilla, increasing the likelihood for post-ERCP pancreatitis. On the contrary, in the study by Vandervoort et al,<sup>7</sup> guidewire or sphincterotome cannulation were probably used as a rescue method in high-risk patients who had failed conventional cannulation. This explains why the rate of post-ERCP pancreatitis was higher in association with guidewire cannulation in this study (Table 5).

In the studies by Lella et al<sup>14</sup> and Artifon et al,<sup>13</sup> there were no episodes of post-ERCP pancreatitis in those who underwent unintentional PD cannulation by guidewire. Although these studies and our study did not show statistically significant differences, there was a tendency toward a lower frequency of post-ERCP pancreatitis in un-

intentional guidewire cannulation of the PD in WGC compared with that of post-ERCP pancreatitis in unintentional PD opacification by contrast injection in the conventional group (0% vs 4.4%,  $P = .08$ ; 0% vs 19%,  $P = .05$ ; and 5% vs 18%,  $P = .09$ ), respectively, Table 5). These data may indicate that unintentional PD cannulation by WGC may be safer than accidental opacification of contrast injection with regard to post-ERCP pancreatitis because unintentional PD cannulation by WGC reduces hydrostatic pressure on the main PD (Table 5). However, post-ERCP pancreatitis also occurred in patients without unintentional guidewire cannulation into the PD, as our study and other studies show.<sup>13,14</sup> This is probably because multiple attempts at cannulation of the bile duct may also cause mechanical trauma at the pancreatic orifice.<sup>19</sup>

In our study, the indication of choledocholithiasis occurred in 217 patients of our cohort of 300 enrolled patients, and suspected SOD occurred in only 7 patients (2.3%). Therefore, our patient population may represent a low-risk cohort, as in the previous study<sup>14</sup> (Table 5).

Among patients with SOD, post-ERCP pancreatitis is a well-recognized complication with rates ranging between 10% and 20%.<sup>16,19</sup> SOD independently increases the risk of post-ERCP pancreatitis as a result of heightened hypersensitivity of the papilla to trauma or an increase in hydrostatic pressure on the main PD.<sup>5,6,9,19,20</sup> In our study, post-ERCP pancreatitis occurred in 2 patients with suspected SOD and the use of WGC (3 and 4 unintentional PD guidewire pass). Although SOD shows a statistically significant difference as a risk factor for post-ERCP pancreatitis in our study, it has a wide range of confidence intervals (OR 23.684; 95% CI, 2.437-230.175,  $P = .006$ ). This

result may be because of the small number of patients with SOD. Therefore, a larger study with more suspected SOD cases may be required to resolve this issue. In the studies by Lella et al<sup>14</sup> and Artifon et al,<sup>13</sup> no episodes of pancreatitis occurred in patients with SOD in the WGC group. Although we could not analyze the data of post-ERCP pancreatitis regarding SOD in previous studies,<sup>13,14</sup> we can assume that successful biliary access without unintentional PD guidewire cannulation may be easily achieved in this subgroup with a high risk of post-ERCP pancreatitis.<sup>21</sup> In high-risk patients, such as those with SOD, repeated unintentional PD guidewire cannulation, therefore, may develop into post-ERCP pancreatitis by mechanical trauma or an increase in hydrostatic pressure by the repeated introduction of a guidewire into the main PD. In cases of unintentional PD guidewire cannulation, therefore, WGC followed by a temporary placement of a PD stent may be more advantageous than WGC alone to prevent an increase in pancreatic enzymes and reduce the frequency of ERCP-related pancreatitis in high-risk patients.<sup>7-9,22</sup>

In conclusion, we found that WGC can reduce the rate of post-ERCP pancreatitis in a low-risk cohort. However, WGC may not prevent post-ERCP pancreatitis in patients with suspected SOD and unintentional PD guidewire cannulation. Further prospective comparative studies (WGC with prophylactic PD stenting vs WGC alone) in high-risk cohorts should be conducted to confirm our study.

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## Wire for hire? The impact of wire-guided cannulation in ERCP

Today many noninvasive imaging modalities used in defining pancreatobiliary pathologies are replacing purely diagnostic ERCP examinations. However, ERCP remains a therapeutic option in the management of patients with pancreatobiliary diseases. Pancreatitis is considered the most dreaded but common complication of ERCP and results in significant morbidity and occasional mortality. For this reason, many studies focused on methods to prevent this complication. Pharmacologic agents, such as gabexate mesilate,<sup>1</sup> somatostatin,<sup>1</sup> and octreotide,<sup>2</sup> were examined in clinical trials, but the effects of these medications in preventing post-ERCP pancreatitis (PEP) only produced mixed results. Other methods to prevent PEP included insertion of pancreatic stents<sup>3</sup> and use of a pure-cut (instead of a blended) current for papillotomy.<sup>4</sup>

In ERCP, cholangiopancreatography is obtained by injecting contrast into the respective duct(s) to define the anatomy (and underlying pathologies) and to guide subsequent procedures (if any), such as removing stones or inserting stents. The risk of PEP is high, especially after multiple injections of the pancreas in an attempt to visualize the common bile duct (CBD). It is well known that difficulty with CBD cannulation is associated with an increased risk of pancreatitis. In a prospective multicenter study, Freeman et al<sup>5</sup> reported that PEP occurred in 0% of patients in whom CBD cannulation was not attempted (eg, unable to access papilla or injection through previous biliary stent), 4.3% of patients with easy cannulation, 10.4% with moderately difficult cannulation, and 12.5% of patients in whom bile-duct cannulation was difficult. Because of the risk of post ERCP pancreatitis, a number of recent studies addressed ways to improve the success of selective CBD cannulation.

Different accessories have been used to improve selective CBD cannulation, including taper-tipped catheters, papillotomes (with the advantage of tip deflection), papillotomes with a rotatable tip, and the use of regular, 0.035-inch, hydrophilic, coated-tip guidewires. In particular, a wire-guided papillotome has become a popular cannulation device, because it combines the advantage of tip deflection and cannulation with the atraumatic flexible-tipped guidewire. Another guidewire-assisted method involves the double-wire technique in which a guidewire is inserted into the

pancreatic duct (PD) (to straighten the common channel) and facilitate selective deep bile-duct cannulation.<sup>6</sup>

Wire-guided biliary cannulation was first described by Siegel and Pullano<sup>7</sup> in 1987. More recently, Lella et al<sup>8</sup> reported a cohort of patients in whom bile-duct access was achieved by using a soft-tipped polytetrafluoroethylene-coated guidewire, and they compared the results with a control group who underwent bile-duct cannulation by contrast injection only. No pancreatitis was detected in the former group, despite the fact that accidental insertion of the guidewire into the main PD was reported in 82 of 200 patients in the wire-cannulation group. On the contrary, 8 of

**One of the mechanisms by which guidewire cannulation reduces post-ERCP pancreatitis is avoiding an increase in hydrostatic pressure and/or chemical injury caused by contrast injection.**

200 patients in the control group developed acute PEP. Artifon et al<sup>9</sup> reported that guidewire cannulation was associated with a significantly lower risk of PEP (9%) compared with standard contrast cannulation (17%). However, in a separate study that examined risk factors for post-ERCP complications reported by Vandervoort et al,<sup>10</sup> univariate (but not multivariate) analysis showed that the use of guidewire cannulation was associated with an increased risk of PEP. Whether or not wire-guided cannulation (WGC) was used after the initial failure of the traditional contrast method was not clearly stated.<sup>10</sup> Further technologic adaptations include the use of smaller (0.025 inch and 0.021 inch), coated guidewires to improve the overall success rate of deep CBD cannulation and to minimize the risk of papillary and/or pancreatic trauma and PEP.

In this issue of *Gastrointestinal Endoscopy*, the effect of WGC was restudied. Lee et al<sup>11</sup> hypothesized that WGC can reduce PEP. Three hundred patients with native papilla who were to undergo therapeutic ERCP were randomized to either WGC (150 patients) or the conventional group (150 patients). In the WGC group, a hydrophilic-tipped guidewire was preloaded into a pull-type papillotome, and after a minimal insertion of the papillotome into the ampulla, the

guidewire was advanced through the CBD under fluoroscopy until it was seen to enter the bile duct. In the conventional group, the standard method for CBD cannulation with a papillotome and injection of contrast was used. In the WGC group, 10 minutes for biliary cannulation or up to 5 attempts of unintentional PD cannulation with the guidewire were allowed before pre-cut fistulotomy. In the conventional group, 10 minutes for biliary cannulation or up to 5 attempts of unintentional PD cannulation with 2 contrast injections into the PD were allowed. Pre-cut with a needle-knife was performed when access to the CBD failed, despite 5 unintentional PD cannulations.

PEP occurred in 2% of patients in the WGC group and 11.3% in the conventional group ( $P = .001$ ). Most of the patients in the conventional group had only mild pancreatitis (14 mild, 2 moderate, and 1 severe), and the severity of pancreatitis was evenly distributed in the WGC group (1 mild, 1 moderate, and 1 severe). There was a tendency toward a lower frequency of PEP with unintentional guidewire cannulation of the PD than contrast opacification of the PD, although it was not statistically significant (0% vs 4.4%,  $P = .08$ ). There were no statistical differences between the 2 groups in the percentage of patients who had successful biliary cannulation, unintentional PD cannulation, needle-knife fistulotomy, bleeding, and perforation. With multivariate analysis, WGC was determined to be a protective factor, whereas female sex and sphincter of Oddi were risk factors for PEP.

Contrast injection into the pancreas may contribute to increased hydrostatic pressure within the PD, which can cause ductal epithelial or acinar injury and PEP. In a multicenter study reported by Freeman et al,<sup>5</sup> the number of PD injections was associated with an increased risk of pancreatitis. The extent of PD filling with contrast is also important. Cheon et al<sup>12</sup> performed a retrospective analysis in which patients were divided into 4 groups, according to the extent of main PD opacification: group 1 had no opacification or failed pancreatic cannulation, group 2 had filling of the head only, group 3 had opacification to the body, and group 4 had filling to the pancreatic tail. Significantly more patients had PEP in group 4 (8.6%) than in group 1 (0.8%), group 2 (3.6%), or group 3 (4.5%),  $P < .001$ .<sup>12</sup> One of the mechanisms by which guidewire cannulation reduces pancreatitis is by avoiding an increase in hydrostatic pressure and/or chemical injury caused by contrast injection.

The technique of guidewire cannulation has not been standardized. Most endoscopists would suggest pushing gently and to stop if one encounters resistance or looping of the guidewire. Yet, much of the wire manipulation is done by GI assistants, and their experience in handling the guidewire can vary significantly. The use of short-wire technology allows the endoscopist to manipulate the guidewire without the assistant. This allows for optimal control to increase the chance of successful cannulation. Repeated attempts at wire cannulation, however, may lead to local trauma to the papilla with edema and obstruction to pan-

creatic drainage. This blinded pushing may result in accidental pancreatic cannulation and injury to the side branches of the pancreas.<sup>11</sup>

If trainees are involved with ERCP procedures, then improving the quality of training may reduce the risk of post-ERCP complications.<sup>13</sup> When it comes to teaching cannulation, the conventional contrast method may have some benefits in that trainees can better appreciate the respective ductal anatomy compared with the blinded WGC. Having a little contrast in the ductal system helps to guide and facilitate subsequent selective deep cannulation. Like a lighthouse, the contrast allows us to steer toward or away from the CBD, depending on whether the contrast is in the bile duct or the pancreas. Upon initial pancreatic filling, unless a full pancreatogram is necessary to identify the underlying pathologies, one should refrain from further or repeated injection of the pancreas to avoid overfilling and PEP.

In attempting selective cannulation, it is important to appreciate and recognize the respective axes of the bile duct and PD to properly orientate and align the accessory used for cannulation. For example, if the tip of the papillotome is clearly pointing in the pancreatic axis, ie, 1-o'clock or 2-o'clock direction, it is very unlikely that selective deep CBD cannulation will be successful, unless duodenoscope repositioning is performed to change such orientation. Choosing the appropriate accessory, varying tension on the papillotome wire, or even shaping the tip of the catheter and/or papillotome to achieve a better orientation may be necessary to improve the success of selective deep CBD cannulation. In addition to cannulation, configuration of the different papillotomes also impacts the results of papillotomy, which may lead to PEP, because the cutting wires of most papillotomes tend to deviate to the right (ie, pancreatic axis). Our previously reported papillotomy scoring scale and experts consensus also support the fact that cutting along the "perfect" biliary axis minimized the risk of post-papillotomy pancreatitis.<sup>14</sup>

A special clinical situation that may warrant WGC without fluoroscopy is in ERCP during pregnancy, to avoid fetal exposure to radiation. Shelton et al<sup>15</sup> reported 21 consecutive pregnant women who underwent therapeutic ERCP without fluoroscopy. Selective bile-duct cannulation was initially attempted by using a guidewire, followed by insertion of the catheter. Aspiration of bile confirmed deep CBD cannulation. However, 1 of the first 10 patients experienced mild PEP. The investigators modified the technique and used only the guidewire for deep cannulation, and observed bile flow around the guidewire. If necessary, insertion of a 5F, 2-cm-long stent was performed to confirm deep CBD cannulation and drainage. There was no pancreatitis reported in the remaining patients.

Another issue that is worth discussing is the use of pre-cut needle-knife fistulotomy for access. In the study by Lee et al,<sup>11</sup> because of the need for biliary therapy, such fistulotomy was performed in a high percentage of patients, 18.7% in the WGC group and 24% in the conventional

group. Even though it did not meet statistical significance, needle-knife fistulotomy was performed more often in the conventional group, which makes one wonder if this could have contributed to some of cases with PEP.<sup>11</sup> As commented before by many expert biliary endoscopists, access pre-cut papillotomy should be reserved for those with a strong indication for biliary therapy and should not be performed for diagnostic examination, because the risk and complications are significant.

In conclusion, therapeutic ERCP is here to stay, and there is an increasing expectation for endoscopists to perform successful selective deep CBD cannulation to conduct biliary endotherapy. Understanding the correct axis of the respective ductal system and manipulation of the duodenoscope to position accessories for selective cannulation is crucial. It does appear that use of an atraumatic tip guide-wire for cannulation achieves a lower complication of PEP. Injecting minimal contrast may still be necessary to serve as a guide for selective cannulation. Methods to promote drainage from the pancreas, including pancreatic stenting, reduce the intraductal pressure and minimize the risk of pancreatitis.

## DISCLOSURE

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*Abbreviations: CBD, common bile duct; PD, pancreatic duct; PEP, post-ERCP pancreatitis; WGC, wire-guided cannulation.*

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