Feasibility of Temporary Pancreatic Stenting after Early Endoscopic Retrograde Cholangiopancreatography in Patients with Acute Biliary Pancreatitis

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Background/Aims: To assess the safety and effectiveness of temporary pancreatic stenting after early endoscopic retrograde cholangiopancreatography (ERCP) in patients with acute biliary pancreatitis regardless of the severity or concomitant cholangitis.

Methods: Temporary pancreatic stenting was performed in 79 patients with visualized pancreatic duct during ERCP. The outcomes of 64 patients with adequate pancreatic stenting (PS) and 15 patients with inadequate pancreatic stenting (no PS) were compared in this prospective, observational trial.

Results: The baseline characteristics were similar. Development of systemic inflammatory response syndrome (7.8% for PS vs. 13.3% for no PS; p=0.50) and mortality (none for both groups; p=0.99) did not differ. However, fewer local complications occurred in PS than in no PS (4.7% for PS vs. 20.0% for no PS; p=0.04) and the difference was most outstanding in necrosis (1.6% for PS vs. 13.3% for no PS; p=0.03).

Conclusions: Temporary pancreatic stenting after early ERCP should be considered safe, as complications did not increase even in cases of inadequate stenting. However, if successful, there appears to be a reduction in local complications. (Korean J Gastroenterol 2017;70:247-252)

Key Words: Acute biliary pancreatitis; Endoscopic retrograde cholangiopancreatography; Pancreatic stenting

INTRODUCTION

Early endoscopic retrograde cholangiopancreatography (ERCP) has proven to be helpful in patients with acute biliary pancreatitis (ABP), especially when severe disease is predicted or combined with cholangitis.1-7 However, early ERCP remains to be controversial for other patients since improvement in prognosis has not always been observed when compared with conservative treatment. The rationale behind conservative treatment is that the stones that are small enough to obstruct the pancreatic duct tend to pass spontaneously and manipulations of ERCP itself might aggravate the papillary edema and do more harm to the vulnerable pancreas. However, the development of complications from conservative treatment is not negligible. Neoptolemos et al.1 and Fan et al.2 reported that 12% and 7% of their patients, respectively, developed complications.
spectively, experienced systemic and local complications, even when mild disease was predicted. Furthermore, because all of the patients with ABP presents with upper abdominal pain, and leukocytosis and jaundice are seen in most of them regardless of severity, concomitant cholangitis, which is diagnosed on the basis of Charcot’s triad, cannot easily be excluded. In practice, rescue ERCP is frequently performed during conservative treatment for patients with predicted mild disease. In addition, more complications develop if the duration of ampullary obstruction by a sustained stone exceeds 48 hours. Therefore, if feasible, it is crucial to perform ERCP as early as possible, irrespective of severity, for patients with ABP.

Meanwhile, 1% to 7% of patients who receive ERCP in the absence of pancreatitis experience post-ERCP pancreatitis (PEP), and the risk may exceed 25% amongst the high risk populations. There are several potential procedure-related risk factors; among them, pancreatic injection, which frequently occurs during biliary cannulation and removal of stones, is considered to be a definitive one. To overcome this risk factor, temporary pancreatic stenting after ERCP has been attempted, with success, to reduce the development of PEP; this method has been supported with concrete evidence. Moreover, its use for patients who are at high risk is recommended by the guidelines put forth by the European Society of Gastrointestinal Endoscopy. However, to the best of our knowledge, there has only a limited number studies evaluating the safety of leaving a pancreatic stent temporarily after ERCP in a patient who was already affected by acute pancreatitis. Therefore, this current study was designed to explore this safety and to determine its influences on clinical outcomes.

SUBJECTS AND METHODS

1. Patients

Patients who underwent early ERCP under the diagnosis of ABP with cholangitis were prospectively enrolled. The diagnosis of acute pancreatitis was made if there were two or more of the following features: (1) abdominal pain consistent with acute pancreatitis; (2) at least a 3-fold elevation of serum amylase lipase and/or amylase activity; and (3) characteristic imaging findings. Pancreatitis was causally attributed to the biliary origin if common bile duct (CBD) stones were discovered on an ultrasonography or computed tomography in the absence of other causes of acute pancreatitis, such as excessive alcohol intake or hypertriglyceremia. Patients with the following conditions were excluded from the study: under the age of 18 years, pregnancy, hepatic cirrhosis, history of pancreaticobiliary surgery other than cholecystectomy, and previous ERCP. The study population was categorized into two groups in accordance with the success of insertion (the PS group and no PS group). The local institutional review boards approved this study (DUHHRB 2013:105).

2. Procedures

Unified procedural strategy was maintained throughout the study period for all patients as follows. Once the diagnosis was made, ERCP was performed within 24 hours from hospi-
talization with a side-view of duodenoscope (JF-240, TJF-260, Olympus Corporation, Tokyo, Japan). Patients were sedated with midazolam (2.5-5.0 mg) and meperidine (25-50 mg), which were administered by registered nurses. Duodenal relaxation was obtained with scopolamine butylbromide. Continuous cardiopulmonary monitoring was used for all patients. The operator chose freely the device and technique for cannulation and removal of stones. When stones were visible after selective probing of CBD, endoscopic sphincterotomy was commonly performed with a pull-type sphincterotome, and stones were removed with baskets and/or retrieval balloons. If the pancreatic duct was unexpectedly visualized by a contrast injection during the procedure, a pancreatic stent was inserted after removing the stones. To minimize possible insults, recannulation of the pancreatic duct by a guide-wire was limited to 5 attempts. If successful, a 3 cm-long, 3 Fr polyethylene stent with 2 flanges on both the pancreatic ductal and duodenal sides was inserted (GPSO-3-3, Cook Endoscopy, Inc., Winston-Salem, NC, USA). Placement of the pancreatic stent was regarded adequate if the stent was adequately positioned in the pancreatic duct with its distal end in the duodenal lumen. Fig. 1 shows the typical computed tomography image and describes the procedure. Spontaneous dislodgement of the pancreatic stent was assessed with plain abdominal radiographs taken on the following day, 7th day, and 14th day after ERCP. If the pancreatic stent was not passed out spontaneously by the 14 days, it was removed endoscopically.

3. Outcome measure

The primary outcomes of interests were mortality and overall complications within 90 days after enrollment. Complications of pancreatitis were classified, and organ failure was defined according to the revised Atlanta classification.26

The clinical courses were assessed as secondary outcomes; the mean changes in serum amylase and lipase levels between the initial and the next day of ERCP, time elapsed for patients to become eligible for cholecystectomy or discharge. Moreover, adverse events from the procedure, such as bowel-wall and sphincterotomy-related perforations or bleeding, were closely monitored. Significant bleeding was defined as the need for blood transfusion; a decrease in the hemoglobin level of greater than 2 g/dL; or hematochezia, melena or hematemesis within 24 hours after the procedure.27

4. Statistical analysis

The differences in categorical variables were analyzed using chi-square test with Yates’ correction or Fisher’s exact test, as applicable. The mean values were expressed as the means±standard errors (SE) and compared using the Student’s t-test. All data were analyzed using SPSS version 12.0 for Windows (SPSS Inc., Chicago, IL, USA). Differences were considered statistically significant when p-values were less than 0.05.

RESULTS

During the study period, ERCP was successfully performed in 587 patients with ABP and insertion of a pancreatic stent was attempted in 79 patients, in whom the pancreas was injected. Pancreatic stenting was adequate in 64 (81.0%) patients (the PS group); they were compared with 15 patients with unsuccessful—or inadequate—stenting (the no PS group). The two groups showed no meaningful differences in the baseline demographic and clinical characteristics (Table 1).

### Table 1. Baseline Characteristics

|               | PS group (n=64) | No PS | p-value |
|---------------|----------------|-------|---------|
| Age, years    | 60.3±2.0       | 63.6±3.3 | 0.47    |
| Gender (male/female) | 35/29     | 10/5   | 0.40    |
| Body mass index | 23.8±0.4   | 23.3±0.7 | 0.60    |
| Time from onset of pain to ERCP, hours | 23.9±4.0 | 25.0±5.5 | 0.81    |
| Total bilirubin, mg/dL | 3.5±0.4 | 3.0±0.6   | 0.52    |
| Initial amylase, IU/L | 518.1±65.5 | 466.1±43.3 | 0.70    |
| Initial lipase, IU/L | 3,775.7±1,036.6 | 3,355.9±1,050.2 | 0.82    |
| C-reactive protein, mg/dL | 0.34 | 0.35 | 0.88    |
| Previous cholecystectomy, n (%) | 2 (3.1) | 0 (0.0) | 0.49    |

Values were expressed as means±standard errors (SE).

PS, pancreatic stenting; ERCP, endoscopic retrograde cholangiopancreatography.
Table 2. Primary Outcome of Interest

|                         | PS group (n=64) | No PS group (n=15) | p-value |
|-------------------------|-----------------|--------------------|---------|
| Overall complications   | 6 (9.4)         | 3 (20.0)           | 0.24    |
| Local complications     |                 |                    |         |
| Acute peripancreatic fluid collection or pseudocyst | 2 (3.1) | 2 (13.3) | 0.10    |
| Acute necrotic collection or walled-off necrosis | 1 (1.6) | 2 (13.3) | 0.03    |
| Infected necrosis       | 1 (1.6)         | 1 (6.7)            | 0.26    |
| Presence of SIRS*       | 5 (7.8)         | 2 (13.3)           | 0.50    |
| Persistent organ failure >48 hours | 4 (6.7) | 2 (13.3) | 0.35    |
| Mortality               | 0 (0.0)         | 0 (0.0)            | 0.99    |

Values are presented as n (%).
PS, pancreatic stenting; SIRS, systemic inflammatory response syndrome.
*SIRS was defined by presence of two or more criteria: heart rate >90 beats/min; core temperature <36°C or >38°C; white blood count <4,000 or >12,000/mm; respirations >20/min or PCO₂ <32 mmHg.

Table 3. Secondary Outcome of Interest

|                              | PS group (n=64) | No PS group (n=15) | p-value |
|------------------------------|-----------------|--------------------|---------|
| Change in amylase after ERCP, IU/L | -279.2±51.7     | -250.7±93.3        | 0.82    |
| Change in lipase after ERCP, IU/L  | -2,103.4±439.7  | -2,248.7±484.8     | 0.48    |
| Time elapsed for patients to become eligible for cholecystectomy or discharge, days | 12.5±1.0        | 15.0±1.6           | 0.20    |
| Adverse events related with ERCP, n (%) | 0 (0.0) | 0 (0.0) | 0.99    |
| Perforation                  | 0 (0.0)         | 0 (0.0)            | 0.99    |
| Bleeding                     | 0 (0.0)         | 0 (0.0)            | 0.99    |

Values were expressed as means±standard errors (SE).
PS, pancreatic stenting; ERCP, endoscopic retrograde cholangiopancreatography.

1. Primary outcome measure
There were no significant differences in the overall complications and systemic inflammatory response syndrome (SIRS) between the two groups (Table 2). However, fewer local complications occurred in the PS group than in the no PS group (4.7% for PS vs. 20.0% for no PS; p=0.04) and the difference was the most remarkable in necrosis (1.6% for PS vs. 13.3% for no PS; p=0.03). There was no case of mortality in both groups (p=0.99).

2. Secondary outcome measure
Serum amylase and lipase levels measured on the day after ERCP tended to decrease in both groups; no patient showed an increase in the levels after ERCP. There were no significant differences in time elapsed for patients to become eligible for cholecystectomy or discharge between the two groups. There was no case of perforation or significant bleeding (Table 3).

DISCUSSION
Although the benefit of early ERCP for patients with ABP other than predicted severe disease or concomitant cholangitis is debatable, the development of complications is not infrequent. Moreover, concurrent acute cholangitis is not excluded readily, and despite its absence at the time of diagnosis, rescue ERCP during conservative treatment is frequently performed due to the emergence of cholangitis not only in daily practices, but also in clinical trials. Neoptolemos et al. and Fölsch et al. reported 23% and 20% of patients from the conservative group, respectively, received rescue ERCP within 4 weeks from randomization, although the number of patients with predicted mild disease is not exactly specified. Remarkably, Fan et al. reported that 9 (15.6%) out of 58 patients with predicted mild disease from the conservative group received emergency ERCP with a median of 48 hours after admission. Among the 40 patients with predicted severe disease from the conservative group, 18 (45.0%) received emergency ERCP, with a median of 60 hours after admission. Because early ductal decompression
is a mandatory part of the treatment of acute cholangitis, it is critical to perform ERCP as early as possible, if it can be performed relatively safely. Procedure-related complications, such as bleeding or perforation, were not reported to be increased by almost all of the relevant studies. However, further injury by manipulations of ERCP itself is still a matter of concern. The exact mechanism by which ERCP insults the pancreas is not fully understood. However, a decrease in the flow of pancreatic juice due to papillary edema caused during manipulations is believed to be one of the most important causes. The papilla of a patient with ABP in whom ERCP is going to be performed is obstructed by a gallstone, in which point in time, the flow of pancreatic juice has already been disturbed. In such an unfavorable circumstance, even the very successful extraction of the stone with the finest manipulations always leaves a chance that might bring about further swelling of the papilla, which would surely impose an unfavorable influence on ABP even after stone removal. We assumed that this can be overcome by temporary pancreatic stenting, which has been proven for preventing PEP.

There is still much to be elucidated about the use of a pancreatic stent in patients with acute pancreatitis, unlike patients with chronic pancreatitis in whom pancreatic stenting is most commonly used. Madácsy et al., in a case series, described the use of rescue pancreatic stenting to prevent the evolution of severe PEP. Fejes et al. reported that temporary pancreatic stenting can serve as a good bridging procedure in 27 patients with severe ABP in whom biliary EST was unsuccessful. However, the number patients in the study was small, and the lack of a control group limited the full understanding of the consequences of failed stenting.

In our study, it is admitted that patients in the no PS group might have a smaller and more tortuous pancreatic duct, making the stent insertion more difficult. Moreover, we cannot deny the possibility that a worse outcome in the no PS group resulted due to the failed attempts, as Freeman et al. suggested. To minimize possible insults, however, we limited the number of attempts for recannulation of the pancreatic duct to less than 5 times. More importantly, the development of overall complication of ‘unfavorable’ no PS group was not increased compared with the previous series. The complication rates of the early ERCP group of the prospective randomized trials were 10/59 (17%) by Neoptolemos et al., 17/97 (18%) by Fan et al., and 58/126 (46%) by Fölsch et al. This implies that our new strategy, in which early ERCP is performed for all patients with ABP having radiologically-proven CBD stones regardless of severity, can be helpful if pancreatic stent can be inserted successfully after ERCP, as expected for most of them, with minimal harm even in failed cases. This is supported by our data, as no patient experienced paradoxical elevation of serum amylase and lipase after ERCP. By our strategy, unnecessary prolongation of hospital stays and increased medical costs, which are unavoidable in ‘the wait-and-see principle’, can be evaded.

Ideally, a study in which patients were randomized into either the PS group or the no PS group would have been a better comparison. However, such an approach can be achieved only after knowing the feasibility of pancreatic stenting in patients with ABP. We firmly believe that our study is a good cornerstone for future studies.

In conclusion, temporary pancreatic stenting after early ERCP for patients with ABP appears to be safe since there was no increase in the occurrence of complications even in the failed cases. However, if successful, local complications are significantly reduced.

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