INTERNAL MEDICINE

□ ORIGINAL ARTICLE □

Risk Factors for Post-ERCP Pancreatitis in High Risk Patients Who Have Undergone Prophylactic Pancreatic Duct Stenting: A Multicenter Retrospective Study

Kei Ito[1], Naotaka Fujita[1], Atsushi Kanno[2], Hiroyuki Matsubayashi[3], Shinji Okaniwa[4], Kazunari Nakahara[5], Kazuya Suzuki[6] and Rhoichi Enohara[7]
Post-ERCP Pancreatitis Prevention by Pancreatic Duct Stenting Research Group (PEP Study Group), Japan

Abstract

Background and Aim Pancreatitis remains a serious complication after endoscopic retrograde cholangiopancreatography (ERCP). The efficacy of prophylactic pancreatic duct stent placement to prevent post-ERCP pancreatitis in patients at high risk has been established in several randomized controlled trials. The aim of this study was to investigate the frequency and risk factors of post-ERCP pancreatitis in patients who had undergone prophylactic pancreatic duct stenting.

Patients and Methods Between July 2002 and January 2010, ERCP-related procedures were performed in 9192 cases of pancreatobiliary diseases at seven institutions. Among them, 414 patients (246 men, 168 women; mean age, 68 yr; age range, 22-91 yr) at high risk of post-ERCP pancreatitis who had undergone prophylactic pancreatic duct stenting were included in this study. The stent used in the present study was a 5-Fr stent with a single duodenal pigtail, which is made of soft polyethylene and has no flange (Pit-stent: Cathex, Co., Ltd., Tokyo, Japan). The pancreatic duct stent was placed via the channel of the duodenoscope over a guidewire with the assistance of fluoroscopy at the end of the procedure. The frequency and risk factors of post-ERCP pancreatitis were investigated. Post-ERCP pancreatitis was defined based on the consensus criteria.

Results Therapeutic ERCP was performed in 52% of the patients. Indications for prophylactic pancreatic duct stenting were as follows: difficult cannulation of the bile duct, 192; pancreatic duct cytology/biopsy, 95; precut sphincterotomy, 40; pancreatic sphincterotomy, 29; female gender, 28; papillectomy, 25; sphincter of Oddi dysfunction, 12; history of pancreatitis, 10. Hyperamylasemia at 18-24 h after ERCP was observed in 64% (267 patients) of the patients. Pancreatitis occurred in 9.9% (41 patients: mild, 37; moderate, 2; severe, 2). Univariate analysis revealed intraductal papillary mucinous neoplasm (IPMN) of the pancreas to be the only significant risk factor for pancreatitis (OR 2.9, 95% CI 1.2, 7.1). Multivariate analysis also showed IPMN to be the only risk factor for pancreatitis (OR 3.1, 95% CI 1.2, 7.8). The mean diameter of the pancreatic head duct in patients with IPMN who developed post-ERCP pancreatitis was significantly smaller than that in those who did not develop pancreatitis (3.0 ± 1 mm vs 4.7 ± 2.6 mm, p=0.0037).

Conclusion Post-ERCP pancreatitis developed in 9.9% of the patients at high risk who had undergone prophylactic pancreatic duct stenting. Since the majority of cases of post-ERCP pancreatitis were mild, pancreatic duct stenting may contribute to lessening the severity of pancreatitis. The present results suggest that IPMN without a dilated pancreatic head duct is a possible risk factor for post-ERCP pancreatitis after prophylactic pancreatic duct stenting.

[1]Department of Gastroenterology, Sendai City Medical Center, Japan, [2]Department of Gastroenterology, Tohoku University Graduate School of Medicine, Japan, [3]Department of Endoscopy, Shizuoka Cancer Center, Japan, [4]Department of Gastroenterology, Iida Municipal Hospital, Japan, [5]Department of Gastroenterology and Hepatology, St. Marianna University Hospital, Japan, [6]Department of Gastroenterology, Kushiro City General Hospital, Japan and [7]Department of Gastroenterology, Osaka Police Hospital, Japan
Received for publication July 21, 2011; Accepted for publication September 5, 2011
Correspondence to Dr. Kei Ito, keiito@openhp.or.jp

Key words: endoscopic retrograde cholangiopancreatography, ERCP, pancreatitis, IPMN, pancreatic duct stenting

(Intern Med 50: 2927-2932, 2011)
(DOI: 10.2169/internalmedicine.50.6235)

Introduction

Pancreatitis remains the most common and serious complication of endoscopic retrograde cholangiopancreatography (ERCP). Patient-related factors such as female gender, suspected SOD, and previous pancreatitis, and procedure-related factors such as precut sphincterotomy, pancreatic duct injection of contrast, and biliary stenting have been reported to be risk factors for post-ERCP pancreatitis (1-7).

Insufficient pancreatic duct drainage as a result of papillary edema after repetitive manipulation, one of the major mechanisms of post-ERCP pancreatitis, can be remediate by prophylactic pancreatic duct stenting. The usefulness of such stenting for the prevention of post-ERCP pancreatitis has been established by several randomized controlled trials (8-13). Tarnasky et al. (8) reported that pancreatic stent (5 or 7 Fr in diameter, 2 or 2.5 cm in length) placement reduced the incidence of post-ERCP pancreatitis from 26% to 7% in patients with pancreatic sphincter hypertension who had undergone biliary sphincterotomy. In a recent study by our group (13), pancreatic duct stent (5-Fr, 3-cm-long, single pigtail, no flanged) placement reduced the incidence of post-ERCP pancreatitis from 23% to 2.9% in patients who had undergone pancreatic duct guidewire placement for achieving selective biliary cannulation.

Although pancreatic duct stenting can reduce the incidence of post-ERCP pancreatitis in patients at high risk, it is impossible to completely prevent this particular complication even by stenting. The aim of the present study was to investigate the frequency and risk factors of post-ERCP pancreatitis in patients at high risk who had undergone prophylactic pancreatic duct stent placement.

Materials and Methods

Study population

Between July 2002 and January 2010, ERCP-related procedures were performed in 9192 cases of pancreatobiliary diseases at seven institutions (tertiary referral center, 5; university hospital, 2). Among them, 414 patients (246 men, 168 women; mean age, 68 yr; age range, 22-91 yr) at high risk of post-ERCP pancreatitis who had undergone prophylactic pancreatic duct stenting were included in this retrospective study. High risk factors of post-ERCP pancreatitis included female gender, a history of pancreatitis, difficult cannulation of the bile duct, pancreatic duct cytology/biopsy, precut sphincterotomy, pancreatic sphincterotomy, sphincter of Oddi dysfunction (SOD), and endoscopic papillectomy. Written informed consent was obtained from all patients. This study was approved by the Institutional Review Board of Sendai City Medical Center.

Pancreatic duct stenting and patient care after the procedure

The procedures were carried out with a side-viewing duodenoscope. The pancreatic duct stent used in this study was a 5-Fr, 3-cm-long stent with a single duodenal pigtail (Pitstent™: Cathex, Co., Ltd., Tokyo, Japan) (Fig. 1). It is made of soft polyethylene, does not have a flange, and has side-holes for avoiding blockage of side branches of the pancreas. The pancreatic duct stent was placed via the channel of the duodenoscope over a 0.025/0.035-inch guidewire with the assistance of fluoroscopy at the end of the procedure. In patients with a pancreatic duct stricture, stents were placed across the papilla, not the stricture. Abdominal radiographs were obtained to assess the stent position after deployment within seven days after the procedure. Endoscopic stent removal was performed if necessary.

Patients continued fasting after the procedure for a minimum of 18 hours with drip infusion of 2,000 mL and remained in the hospital for at least 24 hours. Except for one institution, patients received infusion of protease inhibitor (nafamostat mesilate, 20 mg/day, gabexate mesylate, 400-600 mg/day, or ulinastatin 50,000 U/day) for one or two days. Serum amylase levels were measured before the procedure and 18-24 hours after the procedure. Clinical records of symptoms (abdominal pain, nausea, etc.) and physical findings (abdominal tenderness) during the hospital stay were retrospectively reviewed.

Outcome measurements

The frequency and severity of post-ERCP pancreatitis, the frequency of hyperamylasemia, and the risk factors for post-ERCP pancreatitis were investigated. The mean amylase levels of the patients were not calculated because the normal upper limit of serum amylase level was different at each institution.

A diagnosis of post-ERCP pancreatitis was made based on the presence of abdominal pain at 18-24 hours after the procedure and an increase in serum amylase level greater than three times the upper normal limit. The severity of pancreatitis was classified according to the modified consensus criteria (14) as mild if prolongation of the planned hospitalization was within 1-3 days, moderate for hospitalizations 4-

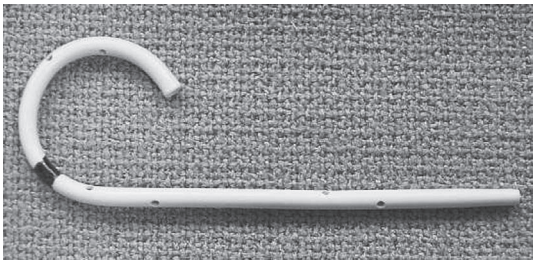

Figure 1. Pancreatic duct stent (Pit-stent™: Cathex, Co., Ltd., Tokyo, Japan).

Table 1. Characteristics of the Patients

No. of patients	414
Mean age (range), yrs	68 (21-91)
Age<60	95 (23%)
Male/female	246:168
History of pancreatitis	55 (13%)
History of post-ERCP pancreatitis	4 (1%)
Therapeutic ERCP	215 (52%)
Pancreatic duct opacification	414 (100%)
Biliary sphincterotomy	106 (26%)
Pancreatic sphincterotomy	33 (8%)
Intraductal ultrasonography of the bile duct	73 (18%)
Intraductal ultrasonography of the pancreatic duct	40 (10%)
Biliary stent placement	98 (24%)
Papillary balloon dilatation	6 (1%)
Cytology of pancreatic juice	93 (22%)
Biopsy of the pancreatic duct	26 (6%)
Papillectomy, cancer/adenoma	25, 8/17 (6%)
Difficult bile duct cannulation	192 (46%)
Failed bile duct cannulation	34 (8%)

ERCP, endoscopic retrograde cholangiopancreatography

10 days long, and severe for hospital stays of more than 10 days, as well as development of hemorrhagic pancreatitis, phlegmon, or pseudocyst. Other complications such as bleeding, perforation, and cholangitis were also defined according to the consensus criteria (14).

Statistical analysis

Fisher's exact probability test, Student's *t*-test, and the Mann-Whitney U test were used for statistical analyses where appropriate. As for risk factors for post-ERCP pancreatitis, variables found to be possibly significant [p <0.5 and odds ratio (OR) >1] by univariate analysis were chosen for entry into a multiple logistic regression. A P value less than 0.05 was regarded as significant. Statistical analysis was performed with StatMate III (ATMS Co. Ltd., Tokyo, Japan) and StatView Ver.5.0 (SAS Institute, Cary, NC, USA).

Results

Post-ERCP pancreatitis and hyperamylasemia

Characteristics and diagnosis of the patients are shown in Tables 1 and 2, respectively. Therapeutic ERCP was performed in 52% (215 patients) of the patients. Indications for

Table 2. Diagnosis of the Patients

Choledocholithiasis	82 (20%)
Gallbladder carcinoma	9 (2%)
Cholecystolithiasis	32 (8%)
Cholangiocarcinoma	31 (7%)
Sphincter of Oddi dysfunction	12 (3%)
Pancreatic cancer	77 (19%)
Ampullary neoplasm, cancer/adenoma	61, 21/40 (15%)
IPMN of the pancreas	32 (8%)
Chronic pancreatitis	43 (10%)
Autoimmune pancreatitis	9 (2%)
PSC	6 (1%)

IPMN, intraductal papillary mucinous neoplasm; PSC, primary sclerosing cholangitis

Table 3. Post-ERCP Pancreatitis and Hyperamylasemia after PD Stenting

Post-ERCP pancreatitis	41/414 (9.9%)
mild	37 (8.9%)
moderate	2 (0.5%)
severe	2 (0.5%)
Hyperamylasemia	267/414 (64%)

PD, pancreatic duct; ERCP, endoscopic retrograde cholangiopancreatography

prophylactic pancreatic duct stenting were as follows: difficult cannulation of the bile duct, 192; pancreatic duct cytology/biopsy, 95; precut sphincterotomy, 40; pancreatic sphincterotomy, 29; female gender, 28; endoscopic papillectomy, 25; sphincter of Oddi dysfunction, 12; history of pancreatitis, 10.

Hyperamylasemia at 18-24 h after ERCP was observed in 64% (267 patients) of the patients. Pancreatitis occurred in 9.9% (41 patients: mild, 37; moderate, 2; severe, 2) (Table 3). No procedure-related deaths occurred in any of the patients. The cases of mild pancreatitis accounted for 90% of post-ERCP pancreatitis cases. Of 384 patients who received prophylactic infusion of a protease inhibitor, post-ERCP pancreatitis occurred in 9.9%. On the other hand, of the 30 patients who did not receive such a drug, the frequency of pancreatitis was 10%. Of 113 patients who underwent pancreatic guidewire placement for achieving biliary cannulation, post-ERCP pancreatitis occurred in 8.0% (9 patients: 8, mild; 1, severe). Of the 26 patients who had undergone biliary stenting without biliary sphincterotomy, post-ERCP pancreatitis occurred in 4% (1, mild). Of the 77 patients with pancreatic cancer, biliary drainage was performed in 17 patients, and post-ERCP pancreatitis occurred in 6% (1, mild). Two patients who developed moderate post-ERCP pancreatitis. One patient (76-year-old man) with bile duct stones underwent precut sphincterotomy due to difficult biliary cannulation. Moderate pancreatitis occurred due to the occlusion of the placed pancreatic duct stent the day after the procedure. The stent was endoscopically removed two days after the procedure. The other patient (23-year-old woman) with bile duct stones underwent endoscopic sphincterotomy. Duodenal perforation occurred, which was followed by the development of moderate pancreatitis. These two patients were improved with conservative therapy. Two

Table 4. Risk Factors for Post-ERCP Pancreatitis after PD Stenting Regarding Patient Characteristics (Univariate Analysis)

	Pancreatitis (+) (n = 41)	Pancreatitis (-) (n = 373)	p	OR (95% C.I.)
Age<60	7	88	0.46	0.67 (0.29, 1.6)
Female gender	18	150	0.77	1.2 (0.61, 2,2)
History of pancreatitis	6	49	0.98	1.1 (0.45, 2.8)
History of PEP	1	3	0.86	3.1 (0.31, 30)
Therapeutic ERCP	18	197	0.36	0.70 (0.37, 1.3)
Pancreatic duct opacification	41	373	-	-
Biliary sphincterotomy	5	101	0.060	0.37 (0.14, 0.98)
Pancreatic sphincterotomy	5	28	0.45	1.7 (0.62, 4.7)
Intraductal ultrasonography	12	95	0.73	1.2 (0.59, 2.5)
Biliary stent placement	7	91	0.39	0.64 (0.27, 1.5)
Papillary balloon dilatation	0	6	0.90	1
Cytology of pancreatic juice	11	82	0.61	1.3 (0.63, 2.7)
Biopsy of the pancreatic duct	0	26	0.16	1
Papillectomy	1	24	0.50	0.36 (0.048, 2.8)
Difficult cannulation	17	175	0.62	0.80 (0.42, 1.5)
Failed cannulation	2	32	0.60	0.55 (0.13, 2.4)

PD, pancreatic duct; RR, relative risk; C. I., confidence interval; ERCP, endoscopic retrograde cholangiopancreatography

Table 5. Risk Factors for Post-ERCP Pancreatitis after PD Stenting Regarding Diagnoses (Univariate Analysis)

	Pancreatitis (+) (n = 41)	Pancreatitis (-) (n = 373)	p	OR (95% C.I.)
Choledocholithiasis	5	77	0.28	0.53 (0.2, 1.4)
Gallbladder carcinoma	0	9	0.66	0
Cholecystolithiasis	4	28	0.84	1.3 (0.44, 4.0)
Cholangiocarcinoma	4	27	0.79	1.4 (0.46, 4.2)
Sphincter of Oddi dysfunction	3	9	0.19	3.2 (0.83, 12)
Pancreatic cancer	6	71	0.63	0.73 (0.30, 1.8)
Ampullary cancer/adenoma	6	55	0.83	0.99 (0.40, 2.5)
IPMN of the pancreas	7	25	0.040	2.9 (1.2, 7.1)
Chronic pancreatitis	5	38	0.90	1.2 (0.45, 3.3)
Autoimmune pancreatitis	0	9	0.66	0
PSC	1	5	0.90	1.8 (0.21, 16)

PD, pancreatic duct; IPMN, intraductal papillary mucinous neoplasm; PSC, primary sclerosing cholangitis; OR, odds ratio; C. I., confidence interval

patients who developed severe post-ERCP pancreatitis. In one patient (64-year-old woman) with sphincter of Oddi dysfunction, endoscopic sphincterotomy was attempted. Pancreatic guidewire placement for achieving biliary cannulation was performed due to the difficulty in biliary cannulation. The guidewire inserted into the pancreatic duct penetrated the pancreatic duct at the pancreatic tail. She complained of abdominal pain several hours later. The day after the procedure, CT demonstrated fluid collection surrounding the pancreatic tail. A pseudocyst was formed four days afterward. In the other patient (60-year-old man) under suspicion of primary sclerosing cholangitis, biliary cannulation was difficult. Although pancreatic guidewire placement was attempted, the guidewire was repeatedly inserted into side branches due to a tortuous main pancreatic duct. Abdominal pain was documented the day after the procedure, and CT showed a swollen pancreas and a fluid collection surrounding the pancreatic head. These two patients showed clinical improvement after intensive care without the need for surgical treatment.

Risk factors for post-ERCP pancreatitis after pancreatic duct stenting

Univariate analysis revealed intraductal papillary mucinous neoplasm (IPMN) of the pancreas to be the only significant risk factor for pancreatitis (OR 2.9, 95% confidence interval (CI) 1.2, 7.1) (Table 4 and 5). Multivariate analysis showed the same result (OR 3.1, 95% CI 1.2, 7.8) (Table 6).

Thirty-two patients with IPMN of the pancreas underwent prophylactic pancreatic duct stenting in this study. Twenty-three patients were diagnosed as branch duct type, seven as main duct type, and two as combined type. Mild post-ERCP pancreatitis occurred in seven of the patients with IPMN. Of these seven patients, six patients had branch-duct IPMN and one patinet had main-duct IPMN. The mean size of the main pancreatic duct of the patients with IPMN who developed mild pancreatitis was significantly smaller than that of the patients with IPMN who did not suffer from pancreatitis (4.1 ± 2.5 mm vs 6.6 ± 4.6 mm, p=0.03). The mean diameter of the main duct at the pancreatic head in the patients with IPMN who developed post-ERCP pancreatitis was sig-

Table 6. Risk Factors for Post-ERCP Pancreatitis after PD Stenting (Multivariate Analysis)

	p	OR (95% C.I.)
Pancreatic sphincterotomy	0.44	1.5 (0.52, 4.5)
IPMN of the pancreas	0.015	3.1 (1.2, 7.8)
Sphincter of Oddi dysfunction	0.12	3.1 (0.76, 13)

PD, pancreatic duct; IPMN, intraductal papillary mucinous neoplasm; OR, odds ratio; C. I., confidence interval

nificantly smaller than that of the patients with IPMN who did not suffer from pancreatitis (3 ± 1 mm vs 4.7 ± 2.6 mm, p=0.0037). Of 24 male and 8 female patients with IPMN, post-ERCP pancreatitis occurred in 5 and 2 patients, respectively. There was no significant difference of post-ERCP pancreatitis between male and female patients (21% vs 25%, p=0.78).

Discussion

Although prophylactic pancreatic duct stenting can reduce the incidence of post-ERCP pancreatitis in patients at high risk (8-13), it is impossible to completely prevent it. Therefore, endoscopists who perform ERCP should always be aware of the possible occurrence of this particular complication after the procedure. Many researchers have reported risk factors for post-ERCP pancreatitis in patients who underwent ERCP procedures (1-7). However, risk factors for post-ERCP pancreatitis in patients at high risk who have undergone prophylactic pancreatic duct stenting have not been clarified. Thus this multicenter retrospective case-series study was conducted to investigate the frequency and the risk factors of post-ERCP pancreatitis in such patients.

Post-ERCP pancreatitis developed in 9.9% of the patients in our study. Since all patients had risk factors of post-ERCP pancreatitis, this relatively high incidence is acceptable. The majority of the patients who developed post-ERCP pancreatitis were classified as mild pancreatitis. The frequency of moderate/severe pancreatitis was 10% of the patients with post-ERCP pancreatitis. Freeman et al (1) reported that post-ERCP pancreatitis occurred in 6.7% of 1,963 ERCP procedures. Among them, moderate/severe pancreatitis accounted for 47%. In a recent large case series study by Cotton et al (5), post-ERCP pancreatitis occurred in 2.6% of 11,497 ERCP procedures. The incidence of moderate/severe pancreatitis was 25% of the patients with post-ERCP pancreatitis. The frequency of moderate/severe pancreatitis in our study was obviously lower than those of these previously reported studies. Therefore, it is inferred that pancreatic duct stenting may contribute to lessening the severity of post-ERCP pancreatitis. The severity of post-ERCP pancreatitis is important for the determination of adequate treatment and prediction of patient prognosis. Further comparative trials for assessment of the efficacy of pancreatic duct stenting are awaited.

In the present study, all four patients with moderate/severe post-ERCP pancreatitis had obvious causes of this condition other than insufficient pancreatic duct drainage, except for one patient who developed pancreatitis due to the occlusion of the placed pancreatic duct stent. Injury of the pancreatic parenchyma by a guidewire was associated with severe pancreatitis. Although guidewire insertion into the pancreatic duct should be carefully attempted, it is sometimes difficult, especially in patients with a tortuous main pancreatic duct. Further development progress of the technique for successful pancreatic duct stenting is necessary.

The present study identified IPMN of the pancreas to be the only risk factor for post-ERCP pancreatitis. Subgroup analyses of the cases of IPMN revealed a non-dilated duct at the pancreatic head to be associated with the development of post-ERCP pancreatitis. Although the mean maximun size of the pancreatic duct was also significantly different between patients with pancreatitis and those without in our study, the size of the pancreatic head duct was more important regarding the occurrence of pancreatitis. This can be explained by the fact that a small caliber stent may possibly be occluded by mucin, which has a higher viscosity than normal pancreatic juice. Harada et al (15) reported a retrospective case-controlled study on prophylactic pancreatic duct stenting in patients with IPMN. In their study, the frequency of post-ERCP pancreatitis in the stent group was higher than that in the non-stent group, although the difference was not significant (13% vs 5%, p=0.21). The size of the pancreatic head duct was not documented in their study. They suggested that pancreatic duct stenting is possibly detrimental in male patients or in patients with a non-dilated main pancreatic duct. In the present study, there was no significant difference in the incidence of post-ERCP pancreatitis between male and female patients. Pharmacological drugs such as somatostatin, which can reduce pancreatic juice secretion, may be effective for the prevention of post-ERCP pancreatitis in place of pancreatic duct stenting for IPMN without dilation of a pancreatic head duct. In patients with a dilated main pancreatic duct, the prophylactic effect of pancreatic duct stenting remains unclear. Since such cases have a patulous orifice of the papilla of Vater due to copious mucin secretion, it is expected that insufficient pancreatic duct drainage as a result of papillary edema is not the main mechanism of post-ERCP pancreatitis. Further adequate studies regarding the prevention of post-ERCP pancreatitis in patients with IPMN are necessary.

Several factors which are generally recognized as risk factors for pancreatitis after ERCP procedures, such as female gender, pancreatic sphincterotomy, difficult biliary cannulation, etc., were not found to be risk factors for pancreatitis in our study. This may suggest that indications for pancreatic duct stenting in our study were appropriate and that pancreatic duct stenting can prevent post-ERCP pancreatitis in such cases.

Therapeutic ERCP was performed in 52% of the patients in the present study. In spite of the recent trend of the decrease of the number of diagnostic ERCPs, this high ratio of diagnostic ERCP was due to a high proportion of patients

with pancreatic diseases such as pancreatic cancer and IPMN, which necessitated diagnostic procedures such as pancreatic juice cytology, pancreatic duct biopsy, and intraductal ultrasonography.

The present study had some limitations. First, the routine administration of protease inhibitor which is widely used by Japanese endoscopists might have influenced the frequency of post-ERCP pancreatitis. There was, however, no significant difference of the frequency of post-ERCP pancreatitis between patients who received such a drug and those who did not. Second, cases of unsuccessful stenting were not included in this study because our study was a retrospective one. Unsuccessful pancreatic duct stenting may be associated with the development of post-ERCP pancreatitis. Prospective assessment of the incidence of post-ERCP pancreatitis in such cases is necessary. Third, comparison of patients with and without prophylactic pancreatic duct stenting was not performed. Although IPMN was found to be a risk factor for post-ERCP pancreatitis after prophylactic pancreatic duct stenting in our study, IPMN is not generally recognized as having a high risk of pancreatitis. Further investigations regarding the indications for pancreatic duct stenting in patients with IPMN after the procedure are necessary. Fourth, data regarding several potential risk factors such as the number of cannulation attempts and pancreatogram extent could not be collected because it was a retrospective study. Fifth, only one risk factor was found by both univariate and multivariate analyses in our retrospective study, analysis of the frequency of post-ERCP pancreatitis between patients with one single risk factor and those with multiple risk factors was not possible. Despite these limitations, the findings of our study can contribute to the determination of appropriate indications for prophylactic pancreatic duct stenting.

In conclusion, prophylactic pancreatic duct stenting may contribute to lessening the severity of pancreatitis. IPMN of the pancreas without a dilated pancreatic head duct is a possible risk factor for post-ERCP pancreatitis after prophylactic pancreatic duct stenting.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We would like to express our deepest gratitude to Prof. Tooru Shimosegawa, Division of Gastroenterology, Tohoku University Graduate School of Medicine, for his insightful comments and suggestions.

References

1. Freeman ML, DiSario JA, Nelson DB, et al. Risk factors for post-ERCP pancreatitis: a prospective, multicenter study. Gastrointest Endosc **54**: 425-434, 2001.
2. Masci E, Toti A, Mariani A, et al. Complications of diagnostic and therapeutic ERCP: a prospective multicenter study. Am J Gastroenterol **96**: 417-423, 2001.
3. Vandervoort J, Soetikno RM, Tham TC, et al. Risk factors for complications after performance of ERCP. Gastrointest Endosc **56**: 652-656, 2002.
4. Cheng CL, Sherman S, Watkins JL, et al. Risk factors for post-ERCP pancreatitis: a prospective multicenter study. Am J Gastroenterol **101**: 139-147, 2006.
5. Cotton PB, Garrow DA, Gallagher J, Romagnuolo J. Risk factors for complications after ERCP: a multivariate analysis of 11,497 procedures over 12 years. Gastrointest Endosc **70**: 80-88, 2009.
6. Matsubayashi H, Fukutomi A, Kanemoto H, et al. Risk of pancreatitis after endoscopic retrograde cholangiopancreatography and endoscopic biliary drainage. HPB (Oxford) **11**: 222-228, 2009.
7. Wilcox CM, Phadnis M, Varadarajulu S. Biliary stent placement is associated with post-ERCP pancreatitis. Gastrointest Endosc **72**: 546-550, 2010.
8. Tarnasky PR, Palesch YY, Cunningham JT, Mauldin PD, Cotton PB, Hawes RH. Pancreatic stenting prevents pancreatitis after biliary sphincterotomy in patients with sphincter of Oddi dysfunction. Gastroenterology **115**: 1518-1524, 1998.
9. Fazel A, Quadri A, Catalano MF, Meyerson SM, Geenen JE. Does a pancreatic duct stent prevent post-ERCP pancreatitis? A prospective randomized study. Gastrointest Endosc **57**: 291-294, 2003.
10. Harewood GC, Ponchron NL, Gostout CJ. Prospective, randomized, controlled trial of prophylactic pancreatic stent placement for endoscopic snare excision of the duodenal ampulla. Gastrointest Endosc **62**: 367-370, 2005.
11. Tsuchiya T, Itoi T, Sofuni A, et al. Temporary pancreatic stent to prevent post endoscopic retrograde cholangiopancreatography pancreatitis: a preliminary, single-center, randomized controlled trial. J Hepatobiliary Pancreat Surg **14**: 302-307, 2007.
12. Sofuni A, Maguchi H, Itoi T, et al. Prophylaxis of post-endoscopic retrograde cholangiopancreatography pancreatitis by an endoscopic pancreatic spontaneous dislodgement stent. Clin Gastroenterol Hepatol **5**: 1339-1346, 2007.
13. Ito K, Fujita N, Noda Y, et al. Can pancreatic duct stenting prevent post-ERCP pancreatitis in patients who undergo pancreatic duct guidewire placement for achieving selective biliary cannulation? A prospective randomized controlled trial. J Gastroenterol **45**: 1183-1191, 2010.
14. Cotton PB, Lehman G, Vennes J, et al. Endoscopic sphincterotomy complications and their management: An attempt at consensus. Gastrointest Endosc **37**: 383-393, 1991.
15. Harada R, Kawamoto H, Fukatsu H, et al. Nonprevention of post-endoscopic retrograde cholangiopancreatographic pancreatitis by pancreatic stent after aspiration of pure pancreatic juice in patients with intraductal papillary mucinous neoplasms of the pancreas. Pancreas **39**: 340-344, 2010.