Comparison between Endoscopic Treatment and Surgical Drainage of the Pancreatic Duct in Chronic Pancreatitis

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Background: Treatment of recurrent chronic obstructive pancreatitis is pancreatic duct decompression with endoscopic drainage (endoscopic pancreatic stenting [EPS] with extracorporeal shockwave lithotripsy [ESWL]) or surgical drainage. Despite the recent popularization of endoscopic drainage, treatment or stent removal is difficult in many patients. We compared the efficacy, safety, and medical cost of endoscopic and surgical treatments.
Patients and Methods: We retrospectively compared the treatment course and medical cost of hospitalization between 41 patients who had undergone pancreatic stenting between 2006 and 2010 (EPS group) and 10 patients who had undergone surgery for poor control of pancreatitis between 2001 and 2005 (surgical drainage group).
Results: No intergroup differences were observed in causes, symptoms, disease duration, smoking history, or endocrine and exocrine functions. The technical success rate was 100% in both groups, and pain had improved in all of the patients in both groups. The incidences of complications did not differ significantly, and the mortality rate was 0% in both groups. The rehospitalization rate was significantly higher in the EPS group (78%) than that in the surgical drainage group (20%; $P < 0.01$). This was considered attributable to rehospitalization for stent replacement. The effects to improve endocrine and exocrine functions were not different between the two groups before and after treatment, and the current condition was maintained in 80% or more of the patients. For the entire EPS group, the mean hospitalization period was 18 days and the mean medical cost of hospitalization was 2,133,330 yen. For the entire surgical drainage group, the mean hospitalization period was 23 days and the mean medical cost of hospitalization was 2,246,548 yen, thus indicating no significant differences between the two groups.
Conclusions: Although both endoscopic and surgical treatments achieved high symptom control and safety rates, re-hospitalization is required for stent replacement, which leads to poor cost-effectiveness, particularly in patients in whom stent removal is difficult. Endoscopic treatment for severe pancreatic duct stenosis will need to be advanced and evaluated in the future.

Key words: Chronic pancreatitis (CP), Endoscopic pancreatic stenting (EPS), cost-effectiveness

BACKGROUND

Recurrent chronic pancreatitis (CP) develops as a result of a pancreatic outflow disturbance associated, in most cases, with pancreatic duct stenosis or pancreatic calculi [1–3]. Therefore, it is reasonable, as a treatment of recurrent CP, to reduce intrapancreatic ductal pressure by removing pancreatic outflow disturbance. Surgical procedures such as pancreatectomy, pancreaticojejunostomy, and endoscopic pancreatic stenting (EPS) combined with extracorporeal shockwave lithotripsy (ESWL) are available for decompression of the pancreatic duct.

As EPS is a less-invasive, safe, and effective method, the use of this approach has spread rapidly. According to previous data, the success rates for EPS range from 72% to 100%, and this procedure achieves a symptom improvement rate of 65–87% [4–12]. If pain and pancreatic duct stenosis is improved, it is possible to remove the stent. Stent removal is the final goal; however, in some cases, it is difficult because of severe stenosis. Such patients require repeated replacement of pancreastic stents.

Cahen *et al*. conducted a randomized controlled trial (RCT) that compared surgical treatment with EPS in the treatment of recurrent CP and reported that surgical treatment was more effective [13, 14]. These prospective studies [13, 14] demonstrated the efficacy and safety of surgical drainage in the treatment of recurrent CP. However, the evaluation of endoscopic drainage may be underestimated.

We retrospectively compared the background, treatment processes, and costs of hospitalization with EPS and surgery for recurrent CP at our hospital.

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PATIENTS AND METHODS

Patients and indications for EPS and surgery

At our hospital, we had been treating recurrent CP primarily with surgical drainage until 2005 and with less-invasive endoscopic drainage after 2006. We could not perform endoscopic drainage until 2005. This study included 51 patients with recurrent CP, including 41 who underwent EPS between 2006 and 2010, and 10 who underwent surgical drainage between 2001 and 2005.

Since April 2006, at our hospital, EPS is indicated for (1) symptomatic or (2) asymptomatic patients in whom preservation of pancreatic function is required and (3) patients with alcoholic pancreatitis who are capable of abstaining from drinking. Surgical drainage is indicated for cases where EPS is difficult for severe stenosis of the pancreatic duct or is associated with duodenal stenosis as a comorbidity. There has been no surgical drainage since 2006, because all patients have been successfully treated with EPS.

Diagnosis of CP

Recurrent CP was diagnosed based on images obtained by using abdominal ultrasonography and endoscopic ultrasonography, computed tomography, magnetic resonance imaging, and endoscopic retrograde cholangiopancreatography (ERCP), in addition to biochemical data. Among all the patients, the imaging findings of pancreaticoduodenectomy met the definition of severe pancreatitis according to the Cambridge criteria [15].

Endoscopic therapy

Crossing the stenosis with a guidewire

ERCP was performed by using JF-240, JF-260V, or TJF-260V (Olympus Medical Systems Corp., Tokyo, Japan) under conscious sedation with diazepam and pethidine. We attempted to cross the stenotic lesion with a guidewire (Jagwire High-Performance Guidewire, Boston Scientific Corp., Natick MA, USA). Upon successfully crossing the stenosis, intraductal ultrasonography after the initial procedure, brushing cytological examination, pancreatic juice cytological examination, and biopsy were performed to exclude cancer. When crossing a stenotic lesion was difficult because of severe stenosis, the minor papilla approach was used.

Dilation of the stenosis

After crossing the stenotic sites, the stenotic lesions were dilated with a dilation catheter (6-, 7-, or 9-Fr Soehendra Biliary Dilation Catheter, Cook Medical, Bloomington, IN, USA) or a balloon dilatation catheter (6 mm in diameter and 2 cm in length; Hurricane RX Balloon Dilatation Catheter, Boston Scientific Corp.). In case of difficulty with dilation, a 5- or 7-Fr Soehendra Stent Retriever (Cook Medical) was used to dilate the stenotic lesions.

Pancreatic duct stenting

After dilation, a straight pancreatic stent (Geenen Pancreatic Stent Sets, Cook Medical) or S-shaped pancreatic stent (Olympus Medical Systems Corp.), which had a diameter of 5, 7, 8.5, or 10-Fr, had multiple side holes and was made of polyethylene, was implanted in the stenotic lesion.

ESWL

When the disease was attributable to pancreatolithiasis and calcification, ESWL was performed as needed. An electromagnetic lithotripter (Dornier Lithotripter S, Dornier MedTech, Wessling, Germany) was used for 25 patients. The stones were placed in the shockwave focus by using an X-ray focusing system. ESWL was performed as needed according to the size and number of stones, followed by endoscopic therapy.

Lithectomy

In the pancreatic duct, stones were removed with a basket catheter (FlowerBasket or TetraCatch, Olympus Medical Systems Corp.) or a balloon catheter (Offset Balloon Catheter, Zeon Medical Inc., Tokyo, Japan) during ERCP. In order to facilitate lithectomy, papillotomy was performed at the bile duct and pancreatic duct orifice.

Treatment protocol for EPS

Every 3 or 4 months, the stent was removed, and pancreatography was performed for assessment. In the patients with residual stenosis, another stent was implanted. A stent with a larger diameter was used if possible. Finally, the stent had to be removed within 1 year. We replaced the pancreatic stent during a mean hospitalization of 3 days.

Pancreatic function

We used the *N*-benzoyl-l-tyrosyl-*p*-aminobenzoic acid test to determine exocrine function before treatment. We considered pancreatic functioning diagnostant levels > 70% as indicative of normal exocrine function. In addition, we used the HbA1c level before treatment as a parameter of endocrine function. We considered HbA1c levels < 6.2% as indicative of normal endocrine function.

Medical expenses

Although there used to be no health insurance coverage for pancreatic stenting or ESWL in Japan, the costs of medical expenses for EPS or ESWL were revised in 2012. For the purpose of this study, we calculated all medical expenses based on revised costs of 2012.

Study items

The present situation of pancreatic duct drainage in our hospital was retrospectively examined by comparing the EPS and surgical drainage groups. The parameters studied included patient characteristics, outcomes after therapy, complications, follow-up results, and medical expense.

As more than one procedure was performed in the EPS group, the frequency of complications was calculated as the frequency of complications resulting from all procedures during follow-up, and not as the frequency of complications resulting from a single procedure.

Statistical analysis

Results are expressed as the mean ± standard devia-

Table 1 Demographic and clinical characteristics of patients

	EPS (N = 41)	Surgery (N = 10)	P value
· Age (Mean ± SD) (years)	59 ± 14 (34–80)	49 ± 16 (31–82)	0.07
· Male (sex)	35 (85%)	5 (50%)	0.03
· Cause of pancreatitis:			
Alcohol	35 (85%)	8 (80%)	0.43
Pancreatic divism	3 (7%)	0 (0%)	
Surgery	1 (3%)	1 (10%)	
Idiopathic causes	2 (5%)	1 (10%)	
· Pain: no. of patients (%)	37 (90%)	9 (90%)	0.75
· Duration of symptoms (Mean ± SD) (months)	13 ± 11	18 ± 17	0.45
· Number of smokers	34 (83%)	8 (80%)	0.56
· Exocrine function;			
PFD < 70% no. (%)	13/21 (62%)	6/8 (75%)	0.65
· Endocrine function;			
HbA1c > 6.2% no. (%)	21/41 (51%)	6/10 (60%)	0.54

tion or as a percentage of the total number of patients. A chi-squared analysis or the two-tailed Fisher's exact test of independence was used to compare differences between the two groups. $P < 0.05$ was considered to be statistically significant. All analyses were performed by using statistical software (Stat View Ver.5.0, SAS Institute, Cary, NC, United States).

RESULTS

EPS group

This group included 41 patients with recurrent CP, who underwent EPS from April 2006 and were observed for 1 year or longer (35 men [85%] and 6 women [15%]; mean ± standard deviation age, 59 ± 14 years; age range, 34–80 years). The causes of recurrent CP were alcohol consumption in 35 patients (85%), pancreatic divisum in 3 patients (7%), postoperative anastomotic stenosis in 1 patient (3%), and idiopathic in 2 patients (5%; Table 1).

Surgical drainage group

This group comprised 10 patients with recurrent CP who underwent surgical drainage from April 2001 and were observed for 1 year or longer (5 men [50%] and 5 women [50%]; mean ± standard deviation age, 49 ± 16 years; age range, 31–82 years). The causes of recurrent CP were alcohol consumption in 8 patients (80%), postoperative anastomotic stenosis in 1 patient (10%), and idiopathic in 1 patient (10%; Table 1). For surgical drainage, pylorus preserving pancreatoduodenectomy was performed in 6 patients; distal pancreatectomy, in 2 patients; and the Beger's procedure, in 2 patients.

Background characteristics

Comparing the surgical drainage group with the EPS group, the patients tended to be younger ($P = 0.07$) and the ratio of females to males was significantly higher ($P = 0.03$; Table 1). The cause of pancreatitis was alcohol consumption in more than 80% of the patients in both groups, without significant differences between the EPS and surgical drainage groups. The rate of symptomatic patients was 90% in the EPS and surgical drainage groups, and the symptom durations were 13 ± 11 and 18 ± 17 months, respectively, without significant differences between the groups. The proportions of smokers in the EPS and surgical drainage groups were 83% and 80%, respectively, without significant differences between the groups. As for pancreatic exocrine and endocrine functions, no significant differences were observed between the groups.

Success rate of the procedure

Both EPS and surgical drainage were successful in all patients (100%). Therefore, none of the patients had conversion to surgery from EPS. No significant differences were observed between the EPS and surgical drainage groups (Table 2).

Outcomes after therapy

Pain relief with reduction in the doses of analgesics was achieved in all of the 37 patients (100%) in the EPS group who experienced pain. In the surgical drainage group, pain relief with reduction in the doses of analgesics was also achieved in all of the patients. No significant differences were observed between the EPS and surgical drainage groups (Table 2).

Complications, reoperation, and death

We examined 273 procedures, including 153 PD stenting procedures, in the EPS group. The early complications were ERCP-induced pancreatitis in 7 patients (17.1%, all mild in severity), and hemorrhage, basket impaction, and rupture of PD in 1 patient each (2.4%). Late complications were pancreatic ductitis in 3 patients (7.3%), stent displacement in 2 (4.9%), PD stent migration in 4 (9.8%, retrieved in all of the patients), bile duct stent migration in 2 (4.9%, retrieved in all of the patients), and tear during removal of the PD stent in 4 (9.8%, retrieved in 3 patients). Most cases were relieved immediately with conservative treatment or endoscopic treatment. Eleven patients (27%) in the EPS group had the above-mentioned complications, whereas 2 patients (20%) in the surgical drainage group had pancreatic fistula as a complication. Most cases in both the groups were relieved with conservative treatment. None of the patients in the surgical drainage group underwent reoperation. No differences were observed between the EPS and surgical drainage groups (Table 2). No deaths occurred in both the groups.

Re-admission

The readmission rates in the EPS and surgical

Table 2 Outcomes of EPS and Surgical Treatment

	EPS (N = 41)	Surgery (N = 10)	P value
· Pain relief	37/37(100%)	9/9 (100%)	0.75
· Conversion to surgery	0 (0%)	NA	1
· Technical success	41 (100%)	10 (100%)	
· Complications	11 (27%)	2 (20%)	0.54
· Re-operation	NA	0 (0%)	
· Death	0 (0%)	0 (0%)	1
· Re-admission	32 (78%)	2 (20%)	< 0.01
· Exocrine function;			0.55
Preserved	34 (83%)	8 (80%)	
Worsened	4 (10%)	1 (10%)	
Improved	3 (7%)	1 (10%)	
· Endocrine function;			0.54
Preserved	36 (89%)	8 (80%)	
Worsened	4 (10%)	1 (10%)	
Improved	1 (1%)	1 (10%)	
· Hospital stay; Median (range) (days)	18 (3–62)	23 (14–85)	0.38
· Cost of hospitalization (Mean ± SD) (Yen)	2,133,330 ± 1,343,519	2,246,548 ± 870,258	0.58

Table 3 Outcomes of EPS

	Stent removal group 25 patients (61%)	Stent retention group 16 patients (39%)	P value
· Treatment duration; Median(range) (days)	516 (93–1438)	1396 (436–2534)	0.02
· Number of EPS exchanges (Mea ± SD)	3.7 ± 2.4	9.2 ± 5.0	< 0.01
· Number of ESWL (Mean ± SD)	1.6 ± 2.1	3.2 ± 2.8	0.06
· Cost of hospitalization, (Mean ± SD) (Yen)	1,350,130 ± 697,292	3,357,080 ± 1,176,189	< 0.01

drainage groups were 78% and 20%, respectively. Re-admission was for stent exchange in the EPS group and for inappetence in the surgical drainage group. The re-admission rate was significantly higher in the EPS group than that in the surgical drainage group ($P < 0.01$; Tables 2).

Clinical course after EPS

Of 41 patients with stent placement, 25 (61%) had stenosis improvement during follow-up and could undergo stenosis removal, and 16 (39%) had no stenosis improvement and continued undergo stent replacement. In the comparison between the removal and continuous exchange groups, the mean treatment periods were 516 and 1396 days, respectively; the mean frequencies of stent replacement were 2.7 and 8.2 times, respectively; and the mean numbers of ESWL procedures were 1.6 and 3.2, respectively, with the removal group showing significantly smaller values for all parameters ($P = 0.02$, $P < 0.01$, and $P = 0.04$, respectively, Table 3). In addition, the hospitalization cost was significantly lower in the removal group ($P < 0.01$).

Pancreatic function

In both the EPS and surgical drainage groups, pancreatic exocrine and endocrine functions persisted in less than 90% of the cases and got worse in 10% of the cases. No significant differences were observed between the EPS and surgical drainage groups (Table 2).

Medical expenses

The mean hospitalization periods in the EPS and surgery groups were 18 and 23 days, respectively; and the mean hospitalization cost was 21,33,330 and 22,46,548 yen, respectively, indicating no significant differences (Table 2).

DISCUSSION

Treatment of recurrent symptomatic chronic obstructive pancreatitis includes endoscopic drainage, which has become popular in recent years, and surgical drainage. Only few articles have discussed which treatment is superior [13, 14]. These reports suggest that surgery is more effective than endoscopic procedure based on long-term results. Based on these long-term results, surgery performed as the initial treatment was superior to endoscopic treatment using ESWL and pancreatic stent placement, in terms of not only pain relief but also the frequency of retreatment and medical expenses. Other benefits of surgery include the need for fewer procedures. A single surgery achieves permanent pain relief, whereas endoscopic treatment requires more than one procedure. Endoscopic treatment was converted to surgery in nearly half of the patients because of poor efficacy. The results of another prospective analysis of CP showed that surgery is more beneficial in terms of the hospitalization period, quality of life, and medical expenses [16].

In the present study, both EPS and surgery were safe and effective. Endoscopic treatment in combina-

tion with ESWL resulted in pain relief effects in all of the patients, achieving high patient satisfaction. With regard to pancreatic function preservation, both exocrine and endocrine functions were preserved in many cases. The possibility of pancreatic exocrine and endocrine function preservation is also suggested, but long-term evaluation may be necessary.

Endoscopic treatment is considered less invasive than surgery. However, stent removal was not clinically possible in some EPS cases, because of the presence of severe stenosis and stones. Such cases required repeated stent replacement, increasing the cost of hospitalization. In this study, 61% of the patients showed improvement in pancreatic duct stenosis and underwent stent removal, and the stents were repeatedly replaced in the remaining patients. Multiple stent replacement increased the complication rate and resulted in a significantly increased re-hospitalization rate, as compared to the surgical drainage group.

Endoscopic treatment is not problematic in all respects. Patients with stent placement may undergo pancreatic duct evaluation every 3 to 4 months, and the stents may be removed in those who show improvement in pancreatic duct stenosis. The problem lies in patients in whom stent removal is difficult. With stent placement, these patients have no symptoms and show preserved pancreatic function. However, as the number of hospitalizations and ERCP procedures naturally increase in these patients, the complication rate also increases, which inevitably incurs higher medical expenses. If patients can undergo stent removal within 1 year, endoscopic treatment is comparably effective and safe as surgery but costs less, making it more beneficial than surgery. However, surgery is clearly more beneficial for patients in whom stent removal is difficult.

Is it difficult to overcome problems with stent removal? We have managed pancreatic duct stenosis by using balloon dilatation, dilatation using a dilatation catheter, and stent diameter enlargement. Furthermore, multiple stent placement and metallic stent placement have also been reported [17-19]. If stent stenosis is improved, stent removal may be possible, overcoming the disadvantageous conditions as compared with surgery.

However, it may not be expedient to continue with endoscopic treatment. It is important to adequately examine patients and determine whether endoscopic treatment or surgery should be chosen. Endoscopic treatment is a good indication for a single pancreatic stone or non-severe pancreatic duct stenosis. A short disease duration has been reported to be a predictor of long-term pain relief after endoscopic treatment [20]. Thus, endoscopic treatment may be a good indication for mild or asymptomatic patients.

In conclusion, this is not an RCT; however, it but showed that endoscopic treatment is as safe and effective as surgical treatment. When a patient with severe stenosis undergoes endoscopic treatment, continuous stent placement in the pancreatic duct will be required, incurring medical costs for repeated hospitalizations and making the burden on patients inevitable. Endoscopic treatment for severe pancreatic duct stenosis will need to be advanced and evaluated in the future. As it is not realistic to perform surgery in all patients, we suggest that a clear index is needed to be established at this stage regarding whether endoscopic or surgical treatment should be selected.

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