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**ABOUT COVER**

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## Endoscopic retrograde cholangiopancreatography in the treatment of pancreaticopleural fistula in children

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## Abstract

### BACKGROUND

Pancreaticopleural fistula (PPF) is a rare disease, especially in children. Conservative treatment and surgery are traditional therapies, but surgery is invasive. The emergence of endoscopic retrograde cholangiopancreatography (ERCP) has provided a new noninvasive treatment for PPF and may become the first choice for children with PPF.

### AIM

To explore the treatment response to ERCP for PPF in children.

### METHODS

Seven children with PPF were hospitalized in the Gastroenterology Department of Beijing Children's Hospital from December 2007 to May 2019. Data on these seven patients' clinical characteristics, diagnosis, treatments, and outcomes were analyzed, and their treatment responses following surgery and ERCP were compared. The correlation between the length of hospital stay and conservative treatment was analyzed. Peer-reviewed articles written in English and Chinese published from January 2009 to December 2019 were obtained from various open data sources and reviewed.

### RESULTS

The seven patients comprised three boys and four girls with a mean age of  $6.57 \pm$

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3.26 years. The main symptoms were chest tightness and pain ( $n = 4$ ), intermittent fever ( $n = 3$ ), dyspnea ( $n = 3$ ), and abdominal pain ( $n = 1$ ), and all patients had bloody pleural effusion. All seven patients were diagnosed with PPF by magnetic resonance cholangiopancreatography, and all were initially treated conservatively for a mean of  $34.67 \pm 22.03$  d with a poor response. Among five patients who underwent ERCP, one required surgery because of intubation failure; thus, the success rate of ERCP was 80%. Two patients were successfully treated with surgery (100%). The postoperative hospital stay of the two patients treated by surgery was 20 and 30 d, respectively (mean of 25 d), and that of the four patients treated by ERCP ranged from 12 to 30 d (mean of  $19.25 \pm 8.85$  d). The recovery time after ERCP was short [time to oral feeding, 4-6 d (mean,  $5.33 \pm 1.15$  d); duration of closed thoracic drainage, 2-22 d (mean, 13.3 d)]. Analysis of previous cases of PPF published worldwide during the past decade showed that the treatment success rate of ERCP is not lower than that of surgery. There was no significant difference in the postoperative hospital stay between surgery ( $16 \pm 10.95$  d) and ERCP ( $18.7 \pm 6.88$  d,  $P > 0.05$ ). A positive linear correlation was found between the overall hospital stay and ERCP intervention time ( $R^2 = 0.9992$ ).

### CONCLUSION

ERCP is recommended as the first-choice treatment for PPF in children. ERCP should be performed as early as possible if conditions permit.

**Key Words:** Pancreaticopleural fistula; Childhood; Endoscopic retrograde cholangiopancreatography; Magnetic resonance cholangiopancreatography; Diagnostic; Treatment

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**Core Tip:** Data on the clinical characteristics, diagnosis, treatments, and outcomes of seven Chinese children with pancreaticopleural fistula (PPF) were analyzed and compared with those described in previous publications of children and adults with PPF worldwide. There was no significant difference in the postoperative hospital stays between surgical treatment ( $17.2 \pm 11.9$  d) and endoscopic retrograde cholangiopancreatography (ERCP) ( $20.75 \pm 5.78$  d). However, there was a positive linear correlation between the overall hospital stay and ERCP intervention time ( $R^2 = 0.9992$ ). Therefore, ERCP is recommended as the first-choice treatment of PPF in children. ERCP should be performed as early as possible if conditions permit.

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## INTRODUCTION

Pancreaticopleural fistula (PPF) is a rare complication of chronic pancreatitis in both adults and children. In adults, PPF is often secondary to chronic alcoholic pancreatitis, accounting for about 0.4% of patients with pancreatitis<sup>[1]</sup> and 4.5% of patients with pancreatic pseudocysts<sup>[2]</sup>. The cause and incidence of PPF in children are still unclear. PPF can be diagnosed by laboratory examination and imaging examination. The traditional treatments are conservative treatment and surgery<sup>[3]</sup>. ERCP was a breakthrough in the diagnosis and treatment of biliopancreatic diseases when it was developed in 1968, replacing some of the traditional methods of examination and treatment of biliopancreatic diseases with endoscopy<sup>[4]</sup>. In 1993, Saeed *et al*<sup>[5]</sup> performed pancreatic stent implantation to cure adult PPF for the first time. ERCP has since been performed increasingly more often in the diagnosis and treatment of PPF in adults. However, the experience of ERCP in the treatment of PPF in children is limited. In the present study, the clinical data of children with PPF diagnosed in Beijing Children's

Hospital from December 2007 to May 2019 were retrospectively analyzed, and the children's therapeutic response to ERCP was explored by comparison with previous publications worldwide.

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## MATERIALS AND METHODS

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### **Objective**

To explore the treatment response to ERCP for PPF in children.

### **Setting, design, and sample size**

From December 2007 to May 2019, the clinical data of seven children with PPF in our department were retrospectively analyzed. The patients comprised three boys and four girls ranging in age from 2 to 10 years (mean age,  $6.57 \pm 3.26$  years). Their main symptoms were chest distress and pain ( $n = 3$ ), intermittent fever ( $n = 3$ ), dyspnea ( $n = 3$ ), and abdominal pain and distention ( $n = 4$ ). Five patients had massive pleural effusion, and two had moderate pleural effusion. Three patients had pleural effusion on the right side, one had effusion on the left, and three had effusion on both sides. One patient had a history of abdominal trauma, but no patients had a history of abdominal surgery.

### **Diagnostic criteria**

All seven patients were confirmed to have PPF by laboratory and imaging examinations. The laboratory examinations mainly included pancreatic and pleural effusion biochemical examinations. The imaging examinations mainly included B-ultrasound, enhanced computed tomography, magnetic resonance cholangiopancreatography, and ERCP.

### **Treatments**

All seven children initially received conservative treatment, including fasting, a somatostatin prescription to inhibit pancreatic secretion, anti-infection medication, and nutritional support. After conservative treatment, the body temperature normalized and pleural effusion disappeared in one patient, while a poor response was seen in six patients. Therefore, two patients were treated by surgery and five underwent ERCP, however, one of the five patients who underwent ERCP required surgery because of ERCP intubation failure.

### **Literature review**

Peer-reviewed English-language publications were retrieved from the PubMed database using the search term "[Pancreaticopleural Fistula] OR [PPF]," and Chinese publications were retrieved from the Wanfang and China National Knowledge Infrastructure databases using the search term "Pancreaticopleural Fistula." The time limit for the literature search was January 2009 to December 2019.

### **Statistical analysis**

SPSS 22.0 software (IBM Corp, Armonk, NY, United States) was used to analyze the correlation between the length of hospital stay and conservative treatment. Descriptive data are expressed as mean  $\pm$  standard deviation. The effects of surgical treatment and ERCP were compared by a *t*-test, and  $P < 0.05$  indicated a statistically significant difference.

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## RESULTS

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### **Diagnostic results**

All seven patients with pleural effusion had hemothorax. Four had a leukocyte count of  $> 500 \times 10^6/L$ , and five had a pleural effusion protein concentration of  $> 30 g/L$ . The concentration of amylase in the pleural fluid was substantially increased in all patients ( $> 1000 U/L$ ; reference,  $< 150 U/L$ ); five patients had a pleural fluid amylase concentration of 1000 to 50000 U/L, and two had a pleural fluid amylase concentration of  $> 50000 U/L$ . Table 1 shows that five of the seven patients had a high serum amylase concentration (mean,  $792.8 \pm 409.97 U/L$ ). The serum lipase concentration was increased in all seven children (mean,  $1826.1 \pm 1650.21 U/L$ ), and one patient had a

**Table 1** Laboratory findings in patients with pancreaticopleural fistula

Patients	Appearance of pleural effusion	Leukocyte count of pleural fluid ( $\times 10^6$ L)	Pleural effusion protein (g/L)	Pleural amylase (U/L)	Serum amylase (U/L)	Blood lipase (U/L)	Ascites amylase (U/L)
1	Bloody	300	40.0	6625	1026	3912.9	13053.0
2	Bloody	560	34.0	10477	423	1051	-
3	Bloody	3600	40	3178	409	950	-
4	Bloody	1700	17.4	50465	284-654	355.4	-
5	Bloody	800	45	1584	110	4470	-
6	Bloody	1200	27.6	65000	1368	1312.2	-
7	Bloody	6	46.7	25549	738	731.2	-

large amount of ascites with an amylase concentration of 13053 U/L. **Table 2** shows that all seven patients had negative results of acid-fast staining and bacterial culture of the pleural effusion, and no tumor cells were found in the pathological examination. All seven patients were diagnosed with PPF by magnetic resonance cholangio-pancreatography. Pulmonary imaging showed a large amount of pleural effusion in all children; the effusion was present on the right side in three children, on the left side in one, and on both sides in three.

#### **Treatments and outcomes**

All seven patients with PPF were initially treated with conservative therapy for 10 to 60 d (mean,  $34.67 \pm 22.03$  d). Six of them had a recurrent fever and continuous pleural effusion following the conservative treatment. Therefore, five patients underwent ERCP, and one of these patients was transferred to surgery after ERCP intubation failed. The remaining four children who underwent ERCP recovered well without a recurrent fever after the procedure. Their body temperature normalized within 2 to 4 d, and they began to eat within 4 to 6 d. Pump infusion of a somatostatin was continued for 4 to 20 d, and the amylase concentration recovered to normal in 4 to 23 d. The patients underwent 2 to 22 d of closed thoracic drainage; the one child who underwent drainage for 22 d required prolonged drainage because of obstruction of the ERCP tent by small stones. The hospitalization stay after ERCP ranged from 12 to 30 d among these four patients (mean,  $18 \pm 10.39$  d) (**Table 3**).

#### **Association between overall hospital stay and duration of conservative treatment**

SPSS software was used to fit the overall hospital stay and duration of conservative treatment, and a positive linear correlation was obtained ( $R^2 = 0.9992$ ) (**Figure 1**).

#### **Literature review**

Articles describing clinical operations for PPF published worldwide during the past decade were reviewed and summarized (**Table 4**)<sup>[6-40]</sup>. In total, 37 case reports were found among 35 non-duplicated publications. The 37 patients comprised 25 adults and 12 children. Among seven patients who received conservative treatment, one died of a poor response. Thirteen patients received surgical treatment, and among the 17 patients who received ERCP treatment, three were converted to surgical treatment because of a poor response to ERCP. The duration of conservative treatment ranged from 7 to 60 d (mean,  $30.76 \pm 17.4$  d). The postoperative hospital stay of patients who underwent surgical treatment ranged from 5 to 30 d (mean,  $16 \pm 10.95$  d), and the postoperative hospital stay of patients who underwent ERCP ranged from 12 to 30 d (mean,  $18.7 \pm 6.88$  d). There was no significant difference in the postoperative hospital stay between the two groups ( $P > 0.05$ ).

## **DISCUSSION**

#### **Treatment status of PPF worldwide**

PPF is a rare complication of chronic pancreatitis. The main symptoms of PPF are chest pain, tachypnea, and dyspnea, and the condition is difficult to diagnose. In 1976, Cameron *et al*<sup>[41]</sup> considered PPF to be caused by entry of pancreatic secretions into the

**Table 2 Clinical symptoms, treatments, and outcomes of seven children with pancreaticopleural fistula**

Patients	1	2	3	4	5	6	7
Age (yr)	8	10	3	2	5	8	10
Gender	Male	Female	Male	Male	Female	Female	Female
Symptom	Fatigue, poor appetite, intermittent fever, abdominal distention	Intermittent chest tightness and upper abdominal pain	Chronic pancreatitis, recurrent abdominal pain	Wheezing, shortness of breath, repeated bloody pleural effusion	Abdominal pain for half a year, fever and chest tightness	Intermittent chest tightness and dyspnea for more than 20 d	Chest pain with dyspnea
Etiology	Suspected trauma and pseudocyst	Dilatation and calculus of pancreatic duct	Congenital pancreatic duct dysplasia and pseudocyst	Pseudocyst and dilatation of pancreatic duct	Pseudocyst and dilatation of pancreatic duct	Dilatation and calculus of pancreatic duct	Pancreatic duct stone, pseudocyst, dilatation of pancreatic duct
Diagnosis	laboratory examination, B ultrasound, MRCP	laboratory examination, MRCP	laboratory examination, enhanced CT, MRC, ERCP	laboratory examination, CT, B ultrasound, MRCP	laboratory examination, CT, B ultrasound, MRCP	laboratory examination, CT, MRCP, ERCP	laboratory examination, CT, B ultrasound, MRCP
Location of pleural effusion	Right	Bilateral	Bilateral	Left	Right	Bilateral	Right
Amylase in pleural effusion (U/L)	6625	10477	3178	50465	1584	65000	25549
Conservative treatment time (d)	10	21	60	24	19	20	10
ERCP treatment	Yes (Surgical treatment after ERCP failure)	No (Operation)	Yes	Yes	No (Operation)	Yes	Yes
Serum amylase concentration before operation (U/L)	889.4	153	367	429	93.0	292	283
Serum amylase concentration after operation (U/L)	102		267	315		105	110
Time for amylase to return to normal (Days after operation)			23	10		9	4
Lipase concentration before operation/ERCP (U/L)	567	1051		355.4	115	106	731.2
Lipase concentration after operation/ERCP (U/L)						51.7	62.4
Stop somatostatin pump maintenance time (days after operation)			19	5		3	4
Postoperative recovery time of eating (days after operation)	3	3	6	6		4	15
Times of fever treated	1	3	5	3	4		Normal temperature

conservatively						
Chest closed drainage time (days after operation)	-	-	16	-	-	-
Postoperative hospital stay (d)	20	30	30	12	12	23
Total length of stay (d)	30	52	90	36	32	33

CT: Computed tomography; ERCP: Endoscopic retrograde cholangiopancreatography; MRCP: Magnetic resonance cholangiopancreatography.

body cavity rather than the duodenum. In the present study, PPF originated from a ruptured main pancreatic duct or leaking pseudocyst. If the front of the pancreatic duct is damaged, extrapancreatic secretions will leak into the abdominal cavity, resulting in pancreatic ascites; if the duct is damaged at the rear, extrapancreatic secretions will leak into the mediastinum through the posterior peritoneum *via* the aorta or esophageal hiatus; and if the secretion penetrates the pleura, it will cause fluid accumulation (with or without bleeding) in one or both thoracic cavities<sup>[41-44]</sup>. In adults, PPF is usually secondary to chronic alcoholic pancreatitis. However, the cause is unclear in children.

PPF can be treated by conservative therapy with medication, surgery, or endoscopic technology<sup>[9,44]</sup>. In previous research, 31% to 65% of adult patients with PPF fully responded to octreotide combined with total parenteral nutrition treatment and usually took 2 to 3 wk to recover<sup>[6,45]</sup>. However, because of the repeated occurrence of pleural effusion in children, a closed thoracic drainage tube should be placed. During conservative treatment, children may develop malnutrition, catheter infection, septicemia, and other complications that are difficult to treat<sup>[46]</sup>. Children who undergo failed conservative treatment need further surgical and endoscopic treatment. Surgery is one of the main treatment methods for PPF. The purpose of surgical treatment is to connect the pancreaticojejunal channel to drain fully the pancreatic juice. The most common surgical treatment is pancreatojejunostomy. Frey's operation can be performed when a pancreatic head mass compresses the pancreatic duct and biliary tract; this procedure involves pancreatectomy and longitudinal pancreatojejunostomy<sup>[47]</sup>. Placement of an ERCP stent is a new nonsurgical treatment for PPF. An ERCP stent can open the proximal end of the pancreatic duct, smoothly drain the pancreatic juice, allow the pancreatic juice to flow to the duodenum with low resistance, and close the fistula that is abnormally connecting the pancreatic duct and pleura<sup>[29]</sup>.

In the present study, we summarized 37 cases of PPF treatment published in the past decade (25 adults and 12 children). The proportions of adults and children who received conservative treatment, surgical treatment, and ERCP treatment were 16.67% and 25%, 50% and 41.7%, and 42.7% and 33.3%, respectively. However, conservative treatment produced a limited response. One of seven patients who received conservative treatment died, and the success rate was only 16.67%. Surgery was

Table 3 Comparison of therapeutic effect of endoscopic retrograde cholangiopancreatography vs conservative treatment

Patients	Conservative treatment time (d)	Recovery time of indexes after ERCP (d)				Serum amylase concentration (U/L)		Hospital stay after different treatment (d)		Total length of stay (d)
		Postoperative discharge	Somatostatin pump maintenance	Recovery time of eating	Blood amylase recovery	2 d before operation	2 d after operation	Operation	ERCP	
1 <sup>2</sup>	10							20		30
2 <sup>2</sup>	21							31		52
5 <sup>2</sup>	19	-								
3 <sup>3</sup>	60	30	19	6	23	367	292		30	90
4 <sup>3</sup>	24	12	5	6	10	267	249		12	36
6 <sup>3</sup>	20	12	3	4	9	429	283		12	32
7 <sup>1,3</sup>	10	23	4	15	4	315	110-		23	33
Average (ERCP)	34.67 ± 22.03	18 ± 10.39	9 ± 8.72	5.33 ± 1.15	14 ± 7.81	344.5 ± 69.58	233.5 ± 84.39	25.5 ± 7.78	18 ± 10.39	-

<sup>1</sup>The second day after endoscopic retrograde cholangiopancreatography (ERCP) stent placement, the patient had poor drainage of the pancreatic stent outflow tract because of stone blockage. This made it difficult to control the secondary infection, and the hospitalization time was prolonged. This patient was not included in the statistical analysis.

<sup>2</sup>Surgical treatment.

<sup>3</sup>ERCP treatment. ERCP: Endoscopic retrograde cholangiopancreatography.

historically the most frequently used treatment but was invasive. With the development of minimally invasive ERCP in recent years, ERCP is now being increasingly used in the treatment of patients with PPF, especially children.

### Optimal PPF treatment method

PPF is a rare disease, and no systematic study has been performed to determine the best treatment; therefore, no consensus has been reached regarding the optimal therapy. Conservative treatment has a low success rate and is associated with many complications, and patients often need secondary surgery or endoscopic treatment. Both surgery and endoscopic treatment can effectively treat PPF. However, no systematic study has been performed to compare the efficacy of the two treatments. We herein performed a preliminary comparison of surgery and endoscopic treatment of PPF by summarizing the treatment results and prognosis of seven children treated in our hospital and both adults and children described in previous publications worldwide. The first case of PPF cured by surgery was reported in 1960<sup>[48]</sup>. The first adult with PPF cured by ERCP was reported by Saeed *et al*<sup>[9]</sup> in 1993. Current research data show that more adults and children with PPF choose ERCP treatment.

All seven patients with PPF in this study initially received conservative treatment, but the responses were poor. Among the five patients who received ERCP treatment, one was converted to surgery because of incubation failure; the treatment success rate was thus 80%. Two patients underwent surgery (one was lost to follow-up after transfer to another hospital), and both recovered. The mean postoperative hospital stay for the two patients who underwent surgery and the four patients who underwent ERCP was 25 d and 19.25 d, respectively. The preliminary conclusion was that the recovery time was shorter after ERCP than after surgical treatment. However, because of the small number of cases, the hospital stay of the two treatment methods could not be statistically analyzed. The present study also showed that patients with PPF who undergo ERCP require a very short time until they start to eat, discontinue somatostatin pump maintenance, return to a normal amylase concentration, and discontinue closed thoracic drainage.

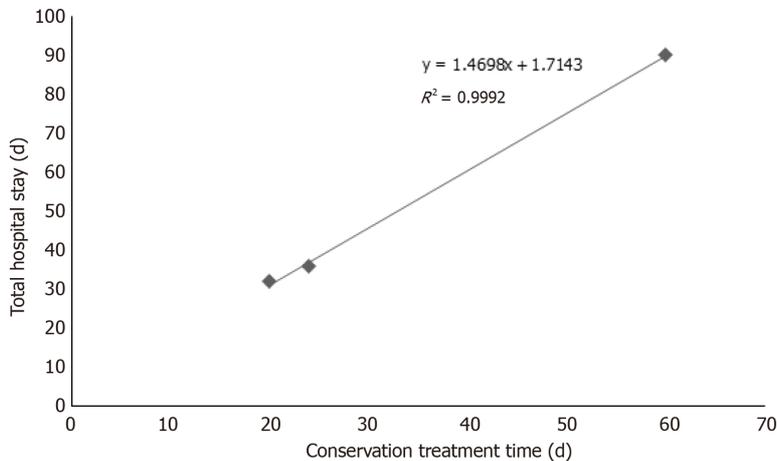
Because children very rarely develop PPF, the present study summarized the clinical outcome data for both adults and children with PPF worldwide during the past decade for a comprehensive analysis. The mean postoperative hospital stay of patients treated with surgery and ERCP was 16 ± 10.95 d and 18.7 ± 6.88 d, respectively ( $P > 0.05$ ). There was no significant difference in the postoperative hospital stay between the two treatment methods, and the curative effect of the two

Table 4 Worldwide cases of pancreaticopleural fistula published in the most recent 10 years

Publication years	Gender/age (yr)	Diagnosis	Treatments	Conservative treatment time (d)	Postoperative hospital stays (d)	
					Operation	ERCP
Adult						
2009 <sup>[6]</sup>	F/52	CT/MRCP	Conservative/ERCP	14		7
2009 <sup>[6]</sup>	M/46	MRCP	Conservative/ERCP	27		14
2010 <sup>[7]</sup>	F/44	CT	Conservative/operation		5	
2012 <sup>[8]</sup>	M/64	B ultrasound/ERCP	Conservative/ERCP			
2012 <sup>[9]</sup>	F/52	CT	Conservative/operation			
2012 <sup>[10]</sup>	M/58	CT/ERCP	Conservative/operation	42		
2013 <sup>[11]</sup>	F/47	CT	Conservative			
2013 <sup>[12]</sup>	M/59	CT/ERCP	Conservative	56		
2013 <sup>[13]</sup>	F/58	CT/MRI	Conservative/ERCP	7		12
2016 <sup>[14]</sup>	F/65	CT/MRCP	Conservative/operation		21	
2014 <sup>[15]</sup>	F/50	CT/MRCP	Conservative/ERCP/operation			
2014 <sup>[16]</sup>	M/49	CT/MRCP/MRI	Conservative/operation			
2015 <sup>[17]</sup>	M/43	CT/ERCP	Conservative/operation	35	10	
2015 <sup>[18]</sup>	M/43	CT/MRCP	Conservative/ERCP/operation	28		
2016 <sup>[19]</sup>	M/58	CT	Conservative/ERCP			
2016 <sup>[20]</sup>	M/51	CT/ERCP/MRI	ERCP	21		
2016 <sup>[21]</sup>	F/51	CT/MRCP	Conservative/operation	28	5	
2016 <sup>[22]</sup>	F/63	CT/MRCP	Conservative/operation		30	
2016 <sup>[23]</sup>	M/78	CT	Conservative			
2017 <sup>[24]</sup>	M/44	MRCP	Conservative/ERCP			
2017 <sup>[25]</sup>	M/52	CT/MRCP	Conservative			
2018 <sup>[26]</sup>	M/49	CT/MRCP/ERCP	Conservative/ERCP			
2019 <sup>[27]</sup>	M/52	Operation	Conservative/ERCP			21
2019 <sup>[28]</sup>	M/35	CT	Conservative/ERCP	14		20
2019 <sup>[29]</sup>	M/65	CT/MRCP/ERCP	Conservative/operation			
Children						
2009 <sup>[30]</sup>	M/4	CT/MRCP	Conservative/ERCP	60		30
2013 <sup>[31]</sup>	F/5	CT	Conservative	50		
2013 <sup>[32]</sup>	M/15	CT/MRI	Conservative/ERCP			28
2014 <sup>[33]</sup>	M/2.5	B ultrasound/CT	Conservative/operation	26	11	
2014 <sup>[34]</sup>	M/8	CT	Conservative	60		
2014 <sup>[34]</sup>	M/2	CT	Conservative			
2016 <sup>[35]</sup>	M/2	CT	operation			
2018 <sup>[36]</sup>	F/8	CT/MRCP	Conservative/ERCP	17		19
2018 <sup>[37]</sup>	F/14	CT/MRCP	Conservative/operation		30	
2019 <sup>[38]</sup>	M/3	CT/MRCP	Conservative/ERCP			18
2019 <sup>[39]</sup>	F/8	CT/MRCP	Conservative/ERCP	8		18

2019 <sup>[40]</sup>	M/14	CT	Conservative/operation	30		
AVG				30.76 ± 17.4	16 ± 10.95	18.7 ± 6.88
P value					P > 0.05	

CT: Computed tomography; ERCP: Endoscopic retrograde cholangiopancreatography; MRCP: Magnetic resonance cholangiopancreatography; MRI: Magnetic resonance imaging.



**Figure 1** The correlation between endoscopic retrograde cholangiopancreatography intervention time and total hospital stay. The linear equation is not a model prediction but only a correlation analysis.

methods was equivalent. The success rate of ERCP treatment (80%) was slightly lower than that of surgical treatment (100%), which may have been due to the small number of patients. In some studies, the duration of using ERCP to cure PPF was 4 to 12 wk with different success rates. The success rates reported by Khan *et al*<sup>[49]</sup>, Pai *et al*<sup>[50]</sup>, and Varadarajulu *et al*<sup>[51]</sup> were 100%, 96.4%, and 50.0% (the low success rate was due to stent placement failure or failure to pass through the pancreatic duct rupture site), respectively, similar to the surgery success rate (94%) reported by King *et al*<sup>[7]</sup>. These findings indicate that the success rate of ERCP treatment is not lower than that of surgical treatment. Our data are consistent with the findings of most previous studies; statistical analysis was impossible because of the limited sample size. The results of the literature review of studies published in the past decade indicated that the average recovery time following ERCP was slightly longer than that following surgery. This result might have been related to either variations in techniques between surgery and ERCP or limited information from the publications reviewed. The literature describes multiple surgical procedures (including distal pancreatectomy with splenectomy, pancreatic duct anastomosis with an intestinal loop, pancreaticoduodenectomy, cystogastrostomy, and cystojejunostomy)<sup>[14]</sup>, which are traumatizing and associated with many complications such as leakage, intra-abdominal infections, and fistula recurrence<sup>[7]</sup>. No further analysis was performed because of the limited number of cases reported. In addition, the results showed that the standard deviation of the ERCP group was smaller, suggesting that the ERCP group had less invasive treatment, a shorter postoperative recovery time, and a lower incidence of complications (infection, bleeding, destruction of pancreatic duct anatomy, repeated fluid accumulation, and pancreatitis). All four patients treated with ERCP reportedly had a good prognosis with no complications. The standard deviation of the postoperative recovery time in the surgery group was larger, indicating that the postoperative recovery time in the surgery group had greater variation and higher uncertainty. In summary, we believe that ERCP can reduce the hospitalization time and should be the preferred treatment for PPF in children.

Aswani *et al*<sup>[3]</sup> also reported that after ERCP, patients can quickly transition to the oral feeding stage and have a short recovery time, which reduces the hospital stay and mortality rate compared with a traditional operation. Therefore, existing research suggests that ERCP should be the first choice for patients with PPF who have a poor response to conservative treatment, and only after failure of conservative treatment and ERCP treatment should surgical treatment be considered. Because of the limited

number of patients in the present study, further prospective studies are needed to compare the cost-effectiveness and long-term results of ERCP and surgery.

### **Best operation time for ERCP**

Patients with PPF initially receive conservative treatment and will choose surgery or ERCP treatment if their condition does not fully respond. We recommend ERCP as the first-choice treatment. Pleural effusion readily recurs after conservative treatment, potentially resulting in malnutrition, catheter infection, septicemia, and other complications. A longer duration of conservative treatment is associated with a greater risk for the patient. The present study investigated the relationship between the duration of conservative treatment and the overall hospital stay. The fitting analysis of the conservative treatment time and the total length of stay of three patients who received ERCP showed a positive linear correlation and suggested that a shorter conservative treatment time is associated with earlier performance of ERCP and a shorter overall hospital stay. Although conservative treatment has a certain response rate for PPF, the rate is very low, and the treatment cycle is long. Some researchers have proposed that conservative treatment should only be used as the initial stage of PPF treatment to stabilize the condition and should not be used as the treatment plan for PPF<sup>[7,52]</sup>. For patients with PPF, the duration of conservative treatment should be reduced, and ERCP treatment should be carried out as early as possible.

## **CONCLUSION**

In conclusion, the success rate of ERCP for patients with PPF was similar to that of surgical treatment, and the prognosis was not worse than that of surgical treatment. Compared with traditional surgery, ERCP does not require laparotomy, is a simple operation, induces less trauma and fewer complications, and promotes rapid fast recovery. Thus, it is very suitable for children and advanced-age patients who cannot tolerate surgery or have poor health conditions. Earlier performance of ERCP promotes faster recovery and a shorter total length of stay. Therefore, ERCP is recommended as the first-choice treatment for PPF in children. ERCP should be performed as early as possible if conditions permit during conservative treatment. Because PPF is a rare disease and it is difficult to obtain data on clinical cases, the present study included only seven patients, one of whom was lost to follow-up after discharge. Thus, we were unable to perform a scientific and systematic comparative analysis on the curative effect of surgery and ERCP. The conclusions of this study still need to be validated.

## **ARTICLE HIGHLIGHTS**

### **Research background**

Pancreaticopleural fistula (PPF) can be diagnosed by laboratory examination and imaging examination. The traditional treatments are conservative treatment and surgery. Endoscopic retrograde cholangiopancreatography (ERCP) has since been performed increasingly more often in the diagnosis and treatment of PPF in adults. However, the experience of ERCP in the treatment of PPF in children is limited.

### **Research motivation**

In the present study, the clinical data of children with PPF diagnosed in Beijing Children's Hospital were retrospectively analyzed, and the children's therapeutic response to ERCP was explored by comparison with previous publications worldwide.

### **Research objectives**

This study is aimed to explore the treatment response to ERCP for PPF in children.

### **Research methods**

Data on the clinical characteristics, diagnosis, treatments, and outcomes of seven Chinese children with PPF were analyzed and compared with those described in previous publications of children and adults with PPF worldwide.

### Research results

There was no significant difference in the postoperative hospital stays between surgical treatment and ERCP. However, there was a positive linear correlation between the overall hospital stay and ERCP intervention time.

### Research conclusions

ERCP is recommended as the first-choice treatment of PPF in children. ERCP should be performed as early as possible if conditions permit.

### Research perspectives

Because PPF is a rare disease and it is difficult to obtain data on clinical cases, the present study included only seven patients, one of whom was lost to follow-up after discharge. Thus, we were unable to perform a scientific and systematic comparative analysis on the curative effect of surgery and ERCP. The conclusions of this study still need to be validated.

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