

# World Journal of *Gastroenterology*

*World J Gastroenterol* 2018 January 21; 24(3): 315-444



### MINIREVIEWS

- 315 Use of direct-acting antiviral agents in hepatitis C virus-infected liver transplant candidates  
*Gadiparthi C, Cholankeril G, Perumpail BJ, Yoo ER, Satapathy SK, Nair S, Ahmed A*

### ORIGINAL ARTICLE

#### Basic Study

- 323 circRNA\_0046366 inhibits hepatocellular steatosis by normalization of PPAR signaling  
*Guo XY, Sun F, Chen JN, Wang YQ, Pan Q, Fan JG*
- 338 Effect of *Lactobacillus rhamnosus* GG supernatant on serotonin transporter expression in rats with post-infectious irritable bowel syndrome  
*Cao YN, Feng LJ, Liu YY, Jiang K, Zhang MJ, Gu YX, Wang BM, Gao J, Wang ZL, Wang YM*
- 351 Epidermal growth factor receptor-targeted immune magnetic liposomes capture circulating colorectal tumor cells efficiently  
*Kuai JH, Wang Q, Zhang AJ, Zhang JY, Chen ZF, Wu KK, Hu XZ*
- 360 Hypoxia preconditioning protects Ca<sup>2+</sup>-ATPase activation of intestinal mucosal cells against R/I injury in a rat liver transplantation model  
*Ji ZP, Li YX, Shi BX, Zhuang ZN, Yang JY, Guo S, Xu XZ, Xu KS, Li HL*

#### Case Control Study

- 371 Multi-parameter gene expression profiling of peripheral blood for early detection of hepatocellular carcinoma  
*Xie H, Xue YQ, Liu P, Zhang PJ, Tian ST, Yang Z, Guo Z, Wang HM*

#### Retrospective Study

- 379 Clinical advantages of single port laparoscopic hepatectomy  
*Han JH, You YK, Choi HJ, Hong TH, Kim DG*
- 387 Autoimmune liver disease-related autoantibodies in patients with biliary atresia  
*Pang SY, Dai YM, Zhang RZ, Chen YH, Peng XF, Fu J, Chen ZR, Liu YF, Yang LY, Wen Z, Yu JK, Liu HY*

#### Observational Study

- 397 *Helicobacter pylori* and corpus gastric pathology are associated with lower serum ghrelin  
*Manero P, Matus GS, Corti RE, Cabanne AM, Zerbetto de Palma GG, Marchesi Olid L, Piskorz MM, Zubillaga MB, Janjetic MA, Goldman CG*

- 408 Metal stents placement for refractory pancreatic duct stricture in children

*Jeong IS, Lee SH, Oh SH, Park DH, Kim KM*

**Prospective Study**

- 415 Optimization of hepatobiliary phase delay time of Gd-EOB-DTPA-enhanced magnetic resonance imaging for identification of hepatocellular carcinoma in patients with cirrhosis of different degrees of severity

*Wu JW, Yu YC, Qu XL, Zhang Y, Gao H*

**SYSTEMATIC REVIEWS**

- 424 Epidemiology of inflammatory bowel disease in racial and ethnic migrant groups

*Misra R, Faiz O, Munkholm P, Burisch J, Arebi N*

**CASE REPORT**

- 438 Beneficial long term effect of a phosphodiesterase-5-inhibitor in cirrhotic portal hypertension: A case report with 8 years follow-up

*Deibert P, Lazaro A, Stankovic Z, Schaffner D, Rössle M, Kreisel W*

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## Observational Study

**Metal stents placement for refractory pancreatic duct stricture in children**

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**Abstract****AIM**

To evaluate the use of fully covered self-expandable metal stents (FCSEMSs) for pancreatic duct strictures in children with chronic pancreatitis.

**METHODS**

Eight patients with refractory benign dominant stricture of the main pancreatic duct (MPD) were enrolled through chart reviews between December 2014 and June 2017 in a single center. Endoscopic retrograde cholangiopancreatography (ERCP) with placement of a 6-mm FCSEMS with dual flaps was performed. Endoscopic removal of FCSEMSs was performed with a snare or rat-tooth forceps. All procedures were performed by a pediatric gastroenterologist. For the assessment of outcomes, technical and clinical success, adverse events, and stent patency were evaluated retrospectively.

## RESULTS

The placement and removal of the FCSEMSs were successful in all 8 patients. Five patients were boys and 3 were girls. The median age at initial FCSEMS placement was 12 years (range, 5-18 years). The diameters of all the inserted stents were 6 mm, and the lengths were 4-7 cm. The median indwelling time was 6 mo (range, 3-10 mo). No pancreatic sepsis, pancreatitis, cholestasis, or mortality occurred. There was no proximal and distal migration. All subjects showed a patent stent. On follow-up ERCP, the mean diameter of the stricture improved from 1.1 mm to 2.8 mm ( $P < 0.05$ ), whereas that of upstream dilation improved from 8.4 mm to 6.3 mm ( $P < 0.05$ ).

## CONCLUSION

This initial experience showed that temporary FCSEMS placement is feasible and safe for the management of refractory benign MPD stricture in children.

**Key words:** Chronic pancreatitis; Pancreatic duct; Self-expandable metal stent; Child; Endoscopic retrograde cholangiopancreatography

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**Core tip:** This study reports the initial experience with the use of fully covered self-expandable metal stents (FCSEMSs) for recurrent benign pancreatic duct strictures in children. We indwelled 6-mm FCSEMSs with dual flaps in the pancreatic duct of pediatric patients for 6 mo. The placement and removal of the FCSEMSs were technically and clinically successful. There were no adverse events or stent obstruction. The findings support the applicability of FCSEMSs to the pediatric population.

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## INTRODUCTION

Plastic stents (PSs) or metal stents have been widely used for the management of biliary and pancreatic duct strictures in endoscopic interventions<sup>[1]</sup>. The fully covered self-expandable metal stent (FCSEMS) was designed to compensate for the defects of PSs and uncovered self-expandable metal stents (SEMSs). The SEMS has the advantages of longer patency and resolution of main pancreatic duct (MPD) strictures because its lumen diameter is larger than that of the PS<sup>[2,3]</sup>. Meanwhile, the FCSEMS has been shown to improve tissue embedding by wrapping around the

frame of the uncovered SEMS<sup>[4]</sup>.

As SEMSs were initially used for malignant biliary obstruction<sup>[5]</sup>, FCSEMSs have been widely used for the management of biliary and pancreatic duct strictures in adults<sup>[6]</sup>. FCSEMSs have proven to be a particularly useful intervention for malignant biliary obstruction<sup>[7,8]</sup>, and their use in the management of benign biliary strictures has been expanding steadily<sup>[9]</sup>. In recent studies, FCSEMSs were increasingly used for the management of MPD strictures refractory to PS placement in adults<sup>[10]</sup>.

In general, studies on the application of stents in pediatric patients are lacking. However, most pediatric studies of endoscopic retrograde cholangiopancreatography (ERCP), including our previous study, investigated the use of PSs; therefore, stenting is an important indication in pediatric ERCP<sup>[11-13]</sup>. One pediatric study showed that PS placement was effective for reducing the recurrence of pancreatitis<sup>[14]</sup>.

For these reasons, FCSEMSs may be useful even in pediatric populations. In this study, we evaluated the feasibility, safety, and therapeutic effect of FCSEMSs for the management of benign MPD strictures in pediatric patients with chronic pancreatitis (CP).

## MATERIALS AND METHODS

### Patients

This was a retrospective study of data collected through medical chart reviews between December 2014 and June 2017 at Asan Medical Center Children's Hospital in Seoul, South Korea. Eight patients with CP and benign dominant MPD stricture refractory to PS placement were enrolled (Table 1). Patients with MPD dilatation due to a malignant cause or trauma were excluded. Five patients were boys and 3 were girls. Their median age was 12 years (range, 5-18 years). The patients in this study had pancreatic divisum and/or gene mutations. The genetic mutations were *PRSS1* p.Gly208Ala, *PRSS1* p.Arg122His, *SPINK1* p.Asn34Ser, *SPINK1* p.ThrT53Ilefs\*41, *SPINK1* IVS3(+2)T>C, and *CFTR* p.Gln1352His. The strictures were located at the pancreatic head in 5 patients, at the pancreatic neck in 2 patients, and at the pancreatic body in 1 patient. The subjects had a history of previous PS trials after endoscopic sphincterotomy. The median number of days and total duration of PS placement were 2 d (range, 1-7 d) and 57 d (range, 1-431 d), respectively. The stricture was verified using imaging methods [ultrasonography, computed tomography, endoscopic retrograde pancreatography (ERP), or magnetic resonance cholangiography]. A dominant stricture was defined when the contrast medium on the ERP film was not washed out and the upstream MPD dilation was  $\geq 6$  mm in diameter<sup>[15]</sup>.

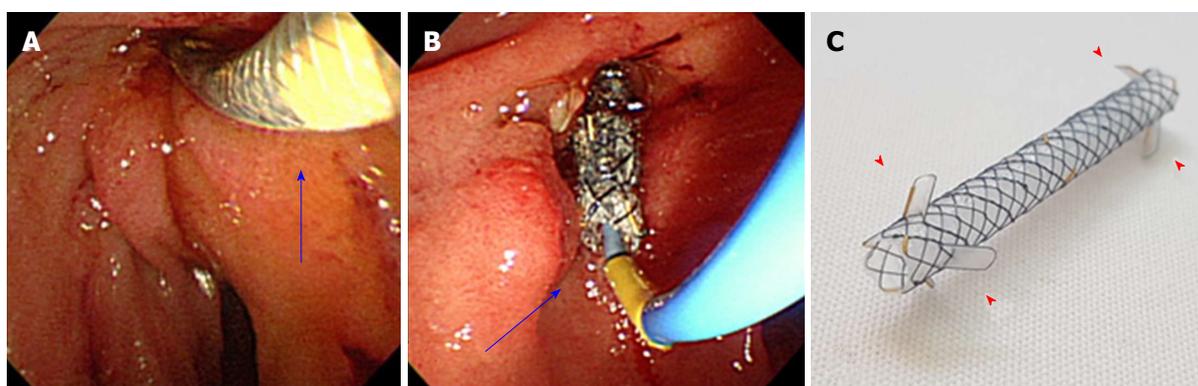
### Procedure

The first session of placement and removal of FCSEMS

**Table 1** Baseline characteristics of the 8 patients with refractory benign dominant main pancreatic duct strictures treated with a fully covered self-expandable metal stent

Case no.	Sex	Anatomical abnormality	Genetic mutation	No. of previous plastic <sup>1</sup> stent placements	Placement time for each plastic stent (d), median (range)	Age at first insertion of a FCSEMS (yr)	Location of the stricture	Diameter and length of the stent (mm/cm)
1	F	Pancreas divisum	<i>PRSS1</i>	2	25.5 (19-32)	17	Head	6/4
2	M	-	<i>SPINK1</i>	7	42.0 (4-93)	12	Head	6/5
3	M	Incomplete pancreas divisum	-	4	126.5 (63-431)	10	Head	6/6
4	M	Pancreas divisum	<i>CFTR</i>	3	57.0 (1-109)	12	Body	6/7
5	F	-	<i>PRSS1</i>	1	46.0	18	Neck	6/7
6	M	-	<i>PRSS1</i>	2	58 (24-92)	5	Head	6/4
7	F	-	<i>SPINK1</i>	1	87	9	Head	6/4
8	M	-	<i>SPINK1</i>	1	29	16	Neck	6/7

<sup>1</sup>Single and multiple stents were used in our study. FCSEMS: Fully covered self-expandable metal stent.



**Figure 1** The fully covered self-expandable metal stent with 3 flaps at both ends used in this study (Hanarostent Biliary dual flap; M.I. Tech, Seoul, South Korea). A and B: The border between the gray and yellow points, shown by the blue arrows, marks the end of the stent. C: Small red arrow heads indicate the flaps.

was performed by an adult and pediatric gastroenterologist. Thereafter, all procedures were performed by a pediatric gastroenterologist. ERP was performed using either an adult duodenoscope (JF; Olympus Optical, Tokyo, Japan) or a therapeutic duodenoscope (TJF, Olympus Optical, Tokyo, Japan). Commercially available 6-mm FCSEMSs (Hanarostent Biliary dual flap; M.I. Tech, Seoul, South Korea) that consisted of nitinol material with a silicone covering membrane were used (Figure 1). After the endoscopic sphincterotomy, which had been described elsewhere, dilatation of the stricture was performed with a Soehendra stent retriever (Wilson Cook Medical, Winston-Salem, NC, United States) and/or a Hurricane dilator balloon (Boston Scientific, Natick, MA, United States) prior to stent placement. The insertion length of the stent was determined such that at least 1 cm of ampulla and normal area at the end of the stenosis were each covered. Repositioning was carried out until the stent was fully inflated and placed in the targeted location. On the basis of previous studies in adults<sup>[16]</sup>, stent removal was planned with rat-tooth forceps at 6 mo after placement, unless adverse events or episodes of pancreatitis had occurred. Informed consent was obtained from the parents of the patients, after the risks and benefits of the procedure and alternative treatments were explained. The study

protocol was approved by the institutional review board of Asan Medical Center (2017-0210).

### Measurement of outcome

Feasibility was evaluated in terms of technical success, migration, and patency. Technical success was determined in accordance with the success of stent placement and removal. Successful stenting was attained when the stent passed through the stricture and the mesh spread easily, followed by a flow of pancreatic juice or washing fluid into the lumen of the stent. Successful removal was attained when the entire stent was removed without ductal leakage during contrast medium injection. Stent patency was assessed *via* visual inspection when the FCSEMS was removed. Efficacy was evaluated according to the improvements of the stricture and reduction of pancreatic pain and pancreatitis. Stricture improvement was evaluated by measuring the diameter of the stricture and the upstream dilation of the MPD as shown on pancreatography after the removal of the first metal stent. Safety was evaluated based on the occurrence of adverse events such as pancreatitis, cholestasis, bowel perforation, sepsis, or mortality. Blood pressure, heart rate, body temperature, laboratory tests (complete blood count and C-reactive protein, total bilirubin, direct bilirubin, amylase, and lipase levels), and abdominal

**Table 2** Resolution of pancreatic duct strictures after the first placement of a fully covered self-expandable metal stent

Case no.	Duration of stenting (mo)	Diameter of the stricture (cm)		Diameter of the dilated segment <sup>1</sup> (cm)	
		Pre	Post	Pre	Post
1	3	0.8	3.0	6.5	4.9
2	10	1.5	2.0	12.1	8.7
3	6	1.2	3.4	11.3	7.1
4	6	0.9	3.4	8.1	6.4
5	6	1.0	4.4	7.1	5.0
6	6	0.9	0.9	6.0	5.2
7	6	1.6	2.1	9.4	6.1
8	6	0.8	3.0	7.0	7.0
mean ± SD	6 <sup>2</sup>	1.1 ± 0.3	2.8 ± 0.9	8.4 ± 2.5	6.3 ± 1.6
P value	NA		0.017		0.018

<sup>1</sup>The diameter was measured at the dilated segment upstream of the pancreatic duct stricture; <sup>2</sup>Expressed as a median value. NA: Not applicable.

radiographs were conducted at 3 d and 14-21 d after FCSEMS placement to evaluate for short-term adverse events.

### Statistical analyses

The Wilcoxon signed-rank test was used to compare changes in the diameter of the pancreatic duct between pre- and post-FCSEMS measurements. The IBM SPSS Statistics ver. 23.0 (IBM Co., Armonk, NY, United States) software was used for statistical analysis, and the stenting duration and patency are expressed as median values and ranges. *P* values < 0.05 were considered statistically significant.

## RESULTS

### Evaluation of feasibility

In all 8 patients, the placement of the FCSEMS with dual flaps was technically successful. The diameters of all inserted stents were 6 mm, and the lengths were 4-7 cm. The stents were successfully removed in all patients. The median indwelling time of stenting was 6 mo (range, 3-10 mo; Table 2). One patient had the stent removed 4 mo later than the planned time of removal because of personal reasons. However, stent embedding and occlusion did not develop (Figure 2). The patency of the stent lumen in the 8 patients with an FCSEMS had been maintained upon assessment at the time of stent removal. No stent migrations were observed.

### Evaluation of efficacy

Recurrent pancreatitis and pancreatic pain did not develop in 4 patients during FCSEMS placement. In 1 patient, pain developed 3 mo after stenting, resulting in an early removal that revealed remnant stones blocking the distal MPD, although the lumen of the FCSEMS was patent. Following the removal of the stone and reinsertion of the stent, the pain disappeared and statistically significant improvements in stricture and upstream dilation were observed. The mean stricture diameter was 1.1 ± 0.3 cm before stenting and 2.8 ± 0.9 cm after stenting (*P* < 0.05).

The diameter of the upstream dilatation showed improvement from 8.4 ± 2.5 cm to 6.3 ± 1.6 cm after stenting (*P* < 0.05).

### Safety

No adverse events such as pancreatitis, cholestasis, sepsis, bowel perforation, or mortality occurred during FCSEMS placement (Table 3).

## DISCUSSION

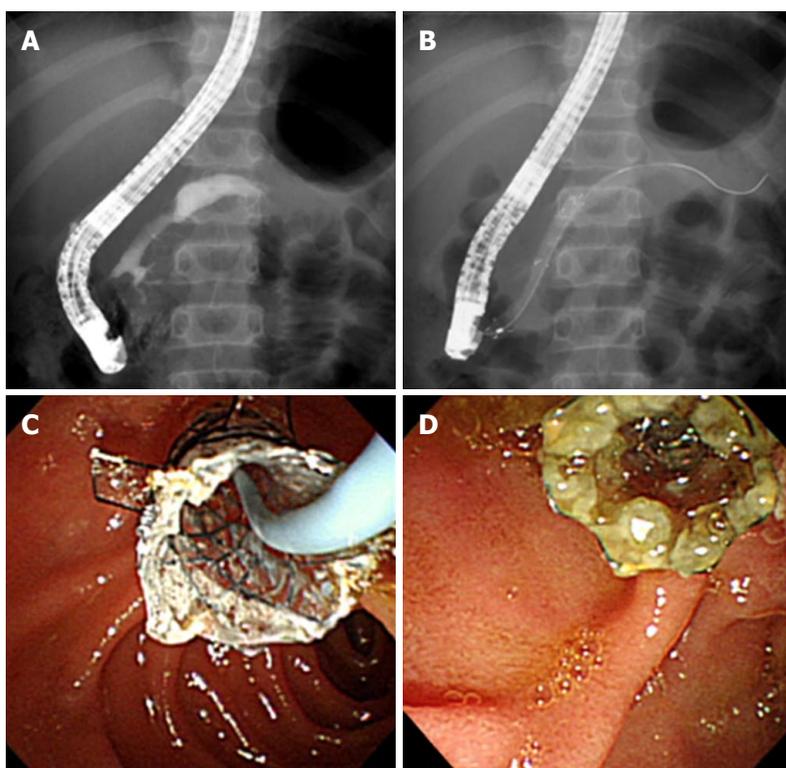
We, herein, report the first case series of the use of FCSEMSs in pediatric patients with CP and MPD strictures refractory to PS placement. Despite the small sample size and lack of long-term follow-up, this preliminary study presents evidence of the feasibility of the use of FCSEMS even in children, with technical and functional success. The disadvantages of PSs include migration and occlusion by sludge, resulting in necessary replacement at around 3 mo<sup>[17]</sup>. In a previous study, FCSEMSs in the management of MPD stricture showed efficacy and safety at 6-mo intervals in adults<sup>[16]</sup>. We suggest that our short-term outcomes are similar to the results for adults in terms of the improvement of strictures and the safety of the procedure<sup>[17]</sup>. Uncovered SEMSs are associated with tissue ingrowth through the stent mesh, which makes their removal difficult<sup>[18]</sup>. Tissue hyperplasia was reported in 23% of patients with partially covered stents<sup>[19]</sup>. When the stent was pulled using rat-tooth forceps at the scheduled removal time, the stent moved easily out of the pancreatic duct without resistance.

Initially, the introduction of FCSEMSs solved the tissue ingrowth issue but led to greater stent migration, with an incidence as high as 41%<sup>[20]</sup>. To overcome this challenge, fins and flaps have been incorporated into these devices<sup>[8,21]</sup>. During our procedure with a dual-flapped FCSEMS, we did not encounter any bleeding, ulcers, or migration problems. In terms of bioavailability, the nitinol materials and silicone membranes of the FCSEMSs applied in the present study series have been used safely in a previous study on the drainage of walled-off necrosis in children<sup>[22]</sup>.

**Table 3** Feasibility and safety of the placement of a fully covered self-expandable metal stent based on the occurrence of adverse events

Case no.	Stent migration	Stent patency	Pancreatitis	Cholestasis	Bowel perforation	Sepsis	Mortality
1	N	Y	N	N	N	N	N
2	N	Y	N	N	N	N	N
3	N	Y	N	N	N	N	N
4	N	Y	N	N	N	N	N
5	N	Y	N	N	N	N	N
6	N	Y	N	N	N	N	N
7	N	Y	N	N	N	N	N
8	N	Y	N	N	N	N	N

N: No; Y: Yes.



**Figure 2** Endoscopic retrograde pancreatography images for case 3. A: Pancreatography image showing a pancreatic duct stricture in the pancreatic neck before the insertion of the fully covered self-expandable metal stent (FCSEMS). B and C: An FCSEMS with flaps placed through the narrow pancreatic duct. D: The stent lumen showing patency at 6 mo after FCSEMS placement.

The major cause of CP in pediatric patients is hereditary pancreatitis rather than gallstones and alcoholism<sup>[23,24]</sup>. Furthermore, because the pancreas reserve of pediatric patients may worsen over time, considering total pancreatectomy with autologous islet transplantation (TP-IAT) may be much more important in children<sup>[25]</sup>. Surgery can result in a reduction of chronic pain through TP-IAT, which was shown to have a more protective effect against negative developments such as postoperative diabetes in preadolescence<sup>[26]</sup>. However, insulin dependency was still present in approximately 40% of postoperative patients<sup>[27]</sup>. Surgical burdens including morbidity, gastric motility dysfunction, and endocrine and exocrine replacement may also occur<sup>[28,29]</sup>. Given that the cause of CP differs between adults and children, adult guidelines for treating this

condition as well as surgical recommendations cannot be automatically applied to pediatric cases. Therefore, until these problems are definitively resolved, endoscopic rather than surgical treatment should be considered in children.

In conclusion, this study showed that the use of FCSEMSs is feasible and safe and may be effective for the management of children with refractory benign MPD strictures. A future long-term investigation with a greater number of patients is warranted.

### ARTICLE HIGHLIGHTS

#### Research background

Plastic stents (PSs) or metal stents have been widely used for the management of biliary and pancreatic duct strictures in endoscopic interventions. The fully

covered self-expandable metal stent (FCSEMS) was designed to compensate for the defects of PSs and uncovered self-expandable metal stents (SEMSs). FCSEMSs have been widely used for the management of biliary and pancreatic duct strictures in adults. In general, studies on the application of stents in pediatric patients are lacking. This study reported our experience with using FCSEMS as part of the treatment for benign main pancreatic duct (MPD) strictures in pediatric patients with chronic pancreatitis (CP).

### Research motivation

The major cause of CP in pediatric patients is hereditary pancreatitis rather than gallstones and alcoholism, unlike in adults. Pediatric patients experience mental and physical repetitive pain from complications of MPD stricture during their long life. Stenting is an important indication in pediatric ERCP. In a previous study, the use of FCSEMSs in the management of MPD stricture showed efficacy and safety at 6-mo intervals in adults. We report that our short-term outcomes in children are similar to the results obtained for adults, in terms of the improvement of strictures and the safety of the procedure.

### Research objectives

This study evaluated the feasibility, safety, and therapeutic effect of FCSEMSs for the management of benign MPD strictures in pediatric patients with CP.

### Research methods

This was a retrospective study of data collected through medical chart reviews between December 2014 and June 2017 at Asan Medical Center Children's Hospital in Seoul, Korea. Eight patients with CP and benign dominant MPD stricture refractory to PS placement were enrolled. A dominant stricture was defined when the contrast medium on the endoscopic retrograde pancreatography film was not washed out and the upstream MPD dilation was  $\geq 6$  mm in diameter. Feasibility was evaluated based on technical success, migration, and patency. Technical success was determined in accordance with the success of stent placement and removal. Stricture improvement was evaluated by measuring the diameter of the stricture and the upstream dilation of the MPD. Safety was evaluated based on the occurrence of adverse events at 3 d and 14-21 d after FCSEMS placement. The Wilcoxon signed-rank test was used to compare changes in the diameter of the pancreatic duct between pre- and post-FCSEMS measurements. The IBM SPSS Statistics ver. 23.0 software was used for statistical analysis, and the stenting duration and patency are expressed as median values and ranges.

### Research results

In all 8 patients, the placement of the 6-mm FCSEMS with dual flaps was technically successful. The median indwelling time of stenting was 6 mo (range, 3-10 mo). Stent embedding and occlusion did not develop. The patency of the stent lumen in the 8 patients with an FCSEMS had been maintained upon assessment at the time of stent removal. No stent migrations, adverse events, and mortalities were observed. After the removal of the stone and insertion of the stent, the pain disappeared and statistically significant improvements in stricture and upstream dilation were observed. The mean stricture diameter was  $1.1 \pm 0.3$  cm before stenting and  $2.8 \pm 0.9$  cm after stenting ( $P < 0.05$ ). The diameter of the upstream dilatation showed improvement from  $8.4 \pm 2.5$  cm to  $6.3 \pm 1.6$  cm after stenting ( $P < 0.05$ ). A future study with a larger sample size could clarify the usefulness of FCSEMS in children with benign MPD dilatation.

### Research conclusions

This is the first study to investigate the efficacy and safety of the placement of the 6-mm FCSEMS with dual flaps in children. Despite the technical success and satisfactory clinical outcomes in these 8 children, the present study had certain limitations, including its retrospective design, relatively small sample size, and short follow-up period. In this study, we report our experience with using FCSEMS as part of the management of benign MPD strictures in pediatric patients with CP, providing valuable information about useful treatment for such patients. FCSEMS placement is an effective and safe management strategy for MPD strictures in pediatric patients with CP.

### Research perspectives

We report the first case series of the use of FCSEMSs in the pediatric

population with CP and MPD strictures refractory to PS placement. Despite the small sample size and lack of long-term follow-up, this preliminary study presents evidence of the feasibility of using FCSEMS even in children, with technical and functional success. A future long-term investigation with a greater number of patients is warranted.

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