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ORIGINAL ARTICLE

양성 담도협착에서 완전 피막형 금속 스텐트 삽입의 효과

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Temporary Placement of Fully Covered Self-expandable Metal Stents in Benign Biliary Strictures

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Background/Aims: Benign biliary strictures (BBSs) have been endoscopically managed with plastic stent placement. However, data regarding fully covered self-expandable metal stents (FCSEMSs) in BBS patients remain scarce in Korea.
Methods: Forty-one patients (21 men, 65.9%) with BBSs underwent FCSEMS placement between February 2007 and July 2010 in Asan Medical Center. Efficacy and safety were evaluated retrospectively. Patients were considered to have resolution if they showed evidence of stricture resolution on cholangiography and if an inflated retrieval balloon easily passed through the strictures at FCSEMS removal.
Results: The mean FCSEMS placement time was 3.2 (1.9-6.2) months. Patients were followed for a mean of 10.2 (1.0-32.0) months after FCSEMS removal. The BBS resolution rate was confirmed in 38 of 41 (92.7%) patients who underwent FCSEMS removal. After FCSEMS removal, 6 of 38 (15.8%) patients experienced symptomatic recurrent stricture and repeat stenting was performed. When a breakdown by etiology of stricture was performed, 14 of 15 (93.3%) patients with chronic pancreatitis, 17 of 19 (89.5%) with gall stone-related disease, 4 of 4 (100%) with surgical procedures, and 2 of 2 (100%) with BBSs of other etiology had resolution at FCSEMS removal. Complications related to stent therapy occurred in 12 (29%) patients, including post-ERCP pancreatitis (n=4), proximal migration (n=3), distal migration (n=3), and occlusion (n=2).
Conclusions: Temporary FCSEMS placement in BBS patients offers a potential alternative to plastic stenting. However, because of the significant complications and modest resolution rates, the potential benefits and risks should be evaluated in further investigations. **(Korean J Gastroenterol 2013;62:49-54)**

Key Words: Bile duct disease; Stent

INTRODUCTION

Benign biliary strictures (BBSs) occur as the result of a variety of etiologies, such as chronic pancreatitis, anastomotic strictures from liver transplantation, inflammatory conditions (i.e., primary sclerosing cholangitis), and choledocholithiasis.[1] Biliary strictures may lead to pain, jaundice, cholangitis, and secondary biliary cirrhosis.[2] Because of the serious and irreversible nature of some of these complications, prompt treatment of these strictures is essential.

Two options for the management of BBSs are available: endoscopic stricture dilatation (consisting of repeated balloon dilatation or temporary insertion of a plastic stent) and surgical biliary drainage (mainly Roux-en-Y hepaticojejunostomy).

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Although balloon dilatation alone has been shown to be inferior,[3] debate exists regarding whether endoscopic stent placement is equivalent to surgery. Although surgery has the theoretical advantage of being definitive,[4] endoscopic stent placement has gained acceptance as an initial treatment because of its simplicity and low morbidity and mortality.

Metal biliary stents provide longer periods of patency than plastic stents in patients with malignant obstructive jaundice.[5] In cases of BBSs, potential benefits have also been attributed to the use of metal stents,[6] although current data favor the use of plastic stents in BBS patients.[7-11]

Uncovered metal stents have been placed in refractory BBS patients.[12-14] However, their long-term efficacy has been limited owing to their lack of long-term patency.[12,14] Their placement has been associated with epithelial hyperplasia and embedding the stent in the bile duct, thus making their removal extremely difficult.[14] Fully covered metal stents have been shown to remain patent longer than uncovered metal stents[15,16] and have the added advantage of being removable by endoscopy in the event of malfunction.[17-19] Therefore, we evaluated the efficacy and complications of fully covered self-expandable metal stents (FCSEMSs) in BBS patients.

SUBJECTS AND METHODS

1. Subjects

Endoscopy databases were retrospectively reviewed to identify eligible patients. Eligible subjects included all consecutive patients above the age of 18 years who had an FCSEMS placed and removed endoscopically for benign indications between February 2007 and July 2010 in Asan Medical Center. The patients' characteristics, including age, sex, indication for stent placement, and any complications were noted and reviewed.

2. Methods

FCSEMSs were placed as first-line treatment in patients at first diagnosis of BBS, or as second-line treatment in patients at treatment failure on biliary sphincterotomy with or without previous single or double plastic stents (10F or double 10F). The stent investigated was a flexible commercially available nitinol FCSEMS (Wallstent, Boston Scientific Co., Natick, MA, USA; Bonastent, Standard Sci Tech, Seoul, Korea; Niti-S Com VI fully covered biliary stent, Taewoong Medical, Gimpo, Korea; Hanaro, M.I Tech, Pyeongtaek, Korea). Stricture resolution was determined by assessing any or all of the following: 1, the absence of waist with an appropriately inflated dilatation balloon catheter; 2, reduction of proximal duct size on cholangiography and improvement of liver function tests; 3, the ability to pass a retrieval balloon through the stricture. and 4, drainage of contrast injected proximal of the stricture. Between two and six months (mean 3.2 months) after FCSEMS placement, stent removal was performed with a side-viewing duodenoscope and stents were removed using snare or rat-tooth forceps, depending on the position of the stent and preference of the investigator. In most cases, the stents were pulled into and though the endoscope channel without difficulty. During the follow-up period, patients were seen in the outpatient clinic at 1-month intervals. At each visit, a plain abdominal radiograph was obtained to monitor stent position, and liver function tests and serum pancreatic enzyme tests were performed. Recurrence was defied as anormalies in liver function tests and the need for repeat stent placement after initial stricture resolution.

Complications related to FCSEMSs and the procedure were analyzed separately.

The study was approved by the institutional review board of Asan Medical Center, Seoul, Korea (No. 2010-107).

3. Statistical analysis

The primary study endpoint was biliary stricture resolution after FCSEMS removal. Variables were analyzed with Student's t-test or Mann-Whitney U-test according to the continuous data with normal or non-normal distributions. Differences in categorical variables were analyzed by chi square test and Fisher exact tests. Multivariate logistic regression analysis of the potential predictive factors of stricture resolution (e.g., age, sex, previous treatments, length of FCSEMS, length of stricture, placement time, and etiology) was performed. The level of significance was set at $p < 0.05$ for all statistical analyses. All analyses were done with IBM SPSS Statistics for Windows, version 20.0 (IBM Co., Armonk, NY, USA).

RESULTS

A total of 41 patients underwent endoscopic FCSEMS in-

Table 1. Patient Characteristics and Indications for FCSEMS Placement

Characteristic	Data
Patient (n)	41 (100)
Sex (male/female)	24/14 (65.9/34.1)
Mean age (yr)	55 (21-79)
Etiology of BBSs	
Gall stone-related disease	19 (46.3)
Chronic pancreatitis	15 (36.6)
Postsurgical complication	4 (9.8)
PSC	1 (2.4)
Other	2 (4.9)
FCSEMS length (mm)	
40	13 (31.7)
50	19 (46.3)
60	6 (14.6)
70/80/90	1/1/1 (2.4/2.4/2.4)
Stent time (mo)	3.2 (1.9-6.2)
Follow-up period after stent removal (mo)	10.2 (1.0-32.0)
First-line treatment	17 (41.5)
Second-line treatment	24 (58.5)
Previous cholecystectomy	19 (46.3)

Values are presented as n (%) or median (range).
FCSEMS, fully covered self-expandable metal stents; BBS, benign biliary stricture; PSC, primary sclerosing cholangitis.

Table 2. Results from Use of FCSMS to Treat BBS

Overall rate	Stricture resolution	Recurrence	Migration
Etiologies	38/41 (92.7)	6/38 (15.8)	6/41 (14.6)
Gall stone-related disease	17/19 (89.5)	2/17 (11.8)	4/19 (21.8)
Chronic pancreatitis	14/15 (93.3)	2/14 (14.3)	0/15 (0)
Postsurgical complication	4/4 (100)	2/4 (50.0)	1/4 (2.4)
PSC	1/1 (100)	0 (0)	1/1 (100)
Other etiology	2/2 (100)	0 (0)	0 (0)
Previous treatments			
No	16/17 (94.1)	1/16 (6.3)	2/17(11.8)
Yes	22/24 (91.7)	5/22 (22.7)	4/24 (16.7)
Length of stricture (cm)			
1.0	1/2 (50.0)	0 (0)	0/2 (0)
1.5	7/7 (100)	2/7 (28.6)	1/7 (14.3)
2.0	15/16 (93.8)	1/15 (6.7)	1/16 (6.3)
2.5	7/8 (87.5)	1/7 (14.3)	2/8 (25.0)
3.0	4/4 (100)	1/4 (25.0)	2/4 (50.0)
3.5	4/4 (100)	1/4 (25.0)	0/4 (0)
Length of FCSEMS (cm)			
4	11/13 (84.6)	3/11 (27.3)	1/13 (7.7)
5	19/19 (100)	0 (0)	3/19 (15.8)
6	5/6 (83.3)	1/5 (20.0)	1/6 (16.7)
7/8/9	3/3 (100)	2/3 (66.6)	1/3 (33.3)

Values are presented as n (%).
FCSEMS, fully covered self-expandable metal stents; BBS, benign biliary stricture; PSC, primary sclerosing cholangitis.

sertion at Asan Medical Center. Table 1 summarizes the indications for FCSEMS placement and patient characteristics. The mean time of FCSEMS placement was 3.2±1.3 months (range, 1.9-6.2 months). Patients were followed for a mean of 10.2±8.2 months (range, 1.0-32 months) after FCSEMS removal. Seventeen patients (41.5%) presented for first-line treatment. Among 24 second-line treatment patients, all patients had previously had plastic stent placement with or without endoscopic sphicterotomy, the mean number of stent had been 3.96 (range, 3-6). Stricture resolution after FCSEMS placement was confirmed in 38 of 41 (92.7%) patients. When a breakdown by etiology of stricture was performed, 17 of 19 (89.5%) patients had gall stone-related disease, 4 of 4 (100%) had postsurgical complications, 14 of 15 (93.3%) had chronic pancreatitis, 1 of 1 (100%) had the primary sclerosing cholangitis (PSC), and 2 of 2 (100%) had other etiologies (Table 2).

The recurrence rate after FCSEMS removal was as follows: gallstone-related disease, 12 of 17 (11.8%); postsurgical complications, 2 of 4 (50%); chronic pancreatitis, 2 of 14 (14.3%); PSC, 0 of 1 0%; and other etiology 0 of 2 (0%) (Table 2). There was no significant difference in stricture resolution and recurrence rate between FCSEMS placement as first-line treatment or second-line treatment (p=0.370). Complications related to FCSEMS placement (14.6%) included post-ERCP pancreatitis (n=4, defined as severe by consensus criteria) and pain (n=2). Post-removal complications included pain (n=1, 2.4%) only. The FCSEMS migration rate was 14.6% (6/41). No difference in terms of migration was observed between FCSEMS placement as first-line treatment or second-line treatments (p=1.000). Three patients had FCSEMS duodenal migration with resolution of the stricture. Two of 3 patients with proximal biliary migration had resolution of the stricture. Two patients developed stent occlusion during follow-up period (Table 3).

None of the variables (gender, age, etiologies of BBS, length of stricture, length of FCSEMS) were associated with the stricture resolution, recurrence and migration. Logistic regression analysis failed to identify any factor that was predictive of stricture resolution (e.g., age, sex, previous treatments, length of FCSEMS, length of stricture, placement time, and etiology).

Table 3. Complications Related to the Procedure and Stent

Complication	n (%)
Placement complication	6 (14.6)
Post-ERCP pancreatitis	4 (9.8)
Pain	2 (4.9)
Removal complication	2 (2.4)
Pain	2 (2.4)
Stent complication	8 (19.6)
Proximal migration	3 (7.3)
Distal migration	3 (7.3)
Occlusion	2 (4.9)

DISCUSSION

Of the nonsurgical approaches to BBS treatment, plastic stents have become the most widely used in most tertiary care centers. However, durable stricture resolution usually requires multiple endoscopic sessions, with the placement of larger diameter stents, and often, increasing numbers of stents during each session.[20,21] Short-term patency of plastic stents has led some centers to consider metal stent placement.[12-14] However, uncovered metal stents are associated with epithelial hyperplasia, leading to chronic inflammation of the bile duct and occlusion.[22,23] Recently, covered metal stents have been introduced to overcome these limitations, as their covering membrane is designed to prevent both tissue ingrowth and embedding of the stent into the biliary wall.[24] Using temporary placement of partially covered metal stents, Kahaleh et al.[25] demonstrated a success rate of 90% in a series of 79 patients. However, their use has been limited by epithelial hyperplasia at the uncovered portions and difficulty in removal.[24-26] As a result, fully covered metal stents have emerged as a promising therapeutic option for the treatment of BBSs and have largely replaced their partially covered counterparts. Cahen et al.[20] published a case series of 6 patients with common bile duct stricture resulting from chronic pancreatitis who were treated with fully covered metal stents (Hanaro). The stent was removed successfully in 4 of the 6 patients with a 66% resolution rate. Another study reported an 81% success rate in patients with post orthotopic liver transplantation (OLT) removal of a fully covered metal stent (Niti-S Com VI fully covered biliary stent).[27]

Placement of FCSEMS (Niti-S Com VI fully covered biliary stent) for treatment of BBS was reported in 51 patients who had failed conventional treatments as plastic stenting, radiologic intervention, or combined rendezvous approaches. The FCSEMSs were removed after 3 months and stricture resolution was confirmed. The stricture resolution after a median follow-up time of 15.9 months was noted in 92.2% (47/51) and 4 patients showed stricture recurrence within 18 months after stent removal.[28]

In this study of the treatment of BBSs, we found acceptable rates of stricture resolution after stent removal and reported relatively high rates of resolution compared with prior studies.

However, the overall rate of post stenting pancreatitis in this study was higher than that in previous studies.[25,29] The frequency of post stenting pancreatitis in this study might be related to the endoscopic retrograde cholangiopancreatography itself, and there were some plausible factors, including occlusion of the pancreatic orifice due to the covering membrane of the FCSEMS and high radial forces exerted by stent expansion.[30] The ideal radial force of the FCSEMS to prevent post ERCP pancreatitis without sacrificing patency may need to be evaluated.

The occurrence of stent migration of FCSEMSs has been reported to range from 4% to 38% in BBS patients.[24,27,30,31] Our migration rate was 14.6%. Distal stent migration may lead to inadequate dilatation of the stricture and a decrease in treatment efficacy. To date, FCSEMSs with anchoring fins or flared ends have become available to prevent stent migration. FCSEMSs with flared ends were designed to facilitate stent removability and prevent stent migration simultaneously.[20,31,32] Park et al.[32] reported a lack of migration of FCSEMSs with anchoring fins comparing to that of FCSEMSs with flared ends (0% *vs.* 33%), and all FCSEMSs with anchoring fins were removed without complication. However, a long-term study with this device in BBS patients is warranted. The US Food and Drug Administration has not approved the utilization of both types of stents for benign disease to date.

There are several limitations to this study. The number of patients observed in this study was relatively small, and we did not compare our methods to conventional endoscopic methods (plastic stent and/or balloon dilatation). Short-term follow-up after stent removal did not evaluate the long-term efficacy for BBS treatment. As this was a retrospective review, we could not employ a clear definition of BBS and could not exclude the possibility of diagnostic error, because the study relied on fluoroscopic and radiologic findings for BBSs and did not confirm pathologic findings. However, no patients

were diagnosed with malignant disease during the follow-up period.

In conclusion, the results of the present study in BBS patients are promising but need to be confirmed in further prospective studies with more rigid and better-defined entry criteria. Because BBSs are a heterogeneous group of variable pathogeneses, the clinical responses and adverse effects of FCSEMSs may differ. The potential risks of temporary FCSEMS placement should be evaluated in further investigations.

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