Fully covered self-expandable metal stents in biliary strictures caused by chronic pancreatitis not responding to plastic stenting: a prospective study with 2 years of follow-up

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Parenchymal fibrosis in chronic pancreatitis (CP) may induce stricturing of the common bile duct. The prevalence of CP-related benign biliary stricture (BBS) ranges between 3% and 46%.[1] A durable drainage is needed if the stricture results in persistent increase in liver function test (LFT) results, jaundice, and cholangitis.[2] If left untreated, symptomatic BBS can lead to secondary biliary cirrhosis.[3]

Biliodigestive anastomosis (hepaticojejunostomy) is the treatment of choice for persistent CP-related BBS.[1,4] However, surgery may be difficult because of local complications of CP, mainly portal hypertension, and limited by other comorbidities or patient refusal.

Endoscopic biliary stenting may be an alternative to surgery, being minimally invasive and having a lower short-term complication rate and a shorter hospital stay.[5-8] Furthermore, endoscopic biliary drainage does not preclude subsequent surgery when necessary.[9] Endoscopic treatment of BBS includes the placement of plastic stents or self-expandable metal stents (SEMSs). Long-term results of the placement of plastic stents are disappointing.[10-13]

Biliary SEMSs are uncovered or partially covered (PC) with a plastic coating. More recently, fully covered (FC) SEMSs have been developed and, being removable, are proposed also for benign indications. Uncovered and PC biliary SEMSs may clog because of tissue ingrowth through the uncovered meshes.[14,15] Removable FC SEMSs are an attractive option for CP-related BBS, but limited data are available.

We conducted a prospective, single-center trial to investigate the durability of CP-related BBS resolution after temporary insertion of FCSEMSs with unflared ends (UEs) and flared ends (FEs).

METHODS

Inclusion criteria were (1) age 18 years of age and older, (2) symptomatic common bile duct strictures secondary to CP (leading to anicteric cholestasis, cholangitis, or jaundice) that persisted 3 months or more after placement of a single 10F plastic stent, and (3) patients who were unfit for surgery (cavernous transformation of the portal vein or significant comorbidities) or patient refusal of surgery. Exclusion criteria were (1) BBS secondary to compression from a pancreatic pseudocyst, (2) patients with associated pancreatic neoplasia, or (3) ongoing alcohol abuse (ethanol consumption >80 g/day).

Between January 2007 and September 2009, 17 patients (mean age 52 years, 16 men) were enrolled. The primary endpoint was the resolution rate of CP-related BBS after temporary insertion of FCSEMSs. Secondary endpoints were (1) SEMS removability, (2) normalization of LFT results during stenting period and during long-term follow-up, and (3) SEMS-related complications.

Nitinol FCSEMSs 10 mm in diameter (Niti-S; TaeWoong Medical Co, Gyeonggi-do, Korea) were used. The inner part of the stent is covered by silicone at both ends (3 cm) and by polytetrafluoroethylene (PTFE) in the central part. The FCSEMSs were available with UEs for easier removal or with 14-mm FEs. The enrollment started with UE-SEMSs, which migrated more than expected; therefore, FE-SEMS were used in the second part of the study.

Stent removal was planned after 6 months (T0). Follow-up was done at 6-month intervals (LFT and telephone interview) for 24 months. Follow-up was stopped in case of cholangitis or symptomatic stricture recurrence.

The study was approved by the local ethics committee, and written informed consent was obtained from all pa-

Abbreviations: BBS, benign biliary stricture CP, chronic pancreatitis; FC, fully covered; FE, flared end; LFT, liver function test; PC, partially covered; PTFE, polytetrafluoroethylene; SEMS, self-expandable metal stent; UE, unflared end.

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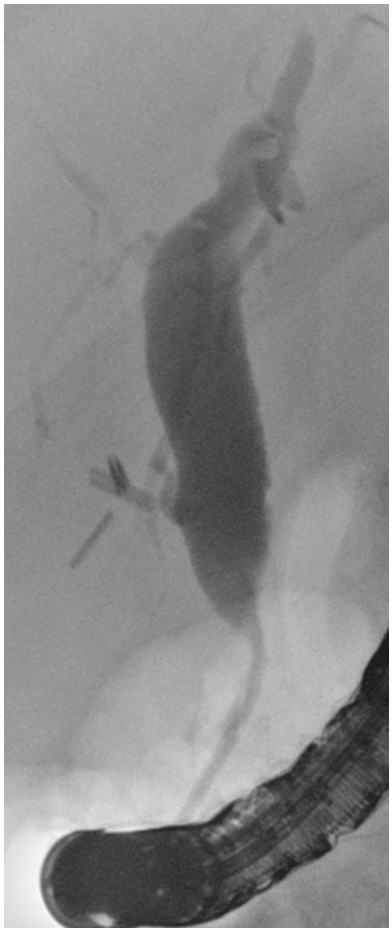

Figure 1. Cholangiography in a patient with benign biliary stricture caused by chronic pancreatitis and calcifications of the head of the pancreas, without flow of the contrast medium into the duodenum.

tients. The study was registered in ClinicalTrials.gov (NCT01457092).

Stent placement and removal

SEMSs were placed by using the standard technique, after plastic stent removal (Figs. 1 and 2). To avoid cholecystitis in patients with a gallbladder in situ,[16,17] the insertion of the cystic duct into the common bile duct was identified during fluoroscopy. It was possible to avoid closure of the cystic duct in all patients with a gallbladder in situ by placing the proximal end of the stent just below its orifice.

Stent removal was performed by using rat-tooth forceps (Fig. 3A). In case of stricture resolution, a nasobiliary drain was left in place for 24 to 48 hours (Fig. 4). If at planned removal, the stent was not visible on the plain radiograph (complete distal migration) and the patient was asymptomatic with normal LFT results, no ERCP was performed and the patient was followed.

Definitions

Clinical success was defined as disappearance of the stricture after stent removal or spontaneous distal migration without the need for any retreatment during the 24-month follow-up period. Stricture recurrence during follow-up was defined as onset of jaundice, cholangitis, and abnormal LFT results together with cholangiographic evidence of BBS. SEMS-related cholangitis was defined as the onset of cholangitis during the stenting period.

Statistical analysis

Descriptive continuous variables in the 2 groups were analyzed. Differences in categorical variables were analyzed by the 2-tailed Fisher exact test. $P < .05$ was considered statistically significant. Statistical analysis was performed with SPSS version 13.0 for Windows (SPSS Inc, Chicago, Ill).

RESULTS

Seventeen patients (mean age 52 years, 16 men) met the inclusion criteria and were enrolled in the study. Three were unfit for surgery because of cavernous transformation of the portal vein, and 14 were given the alternative of hepaticojejunostomy, but refused (Table 1). All of the patients had been previously treated with a single 10F plastic biliary stent (mean 2.18 stent exchanges per patient, range 1-6).

UE-SEMSs were placed in the first 7 patients and FE-SEMSs in the latter 10 patients. Stent deployment was successful in all of the patients, without procedure-related complications. Nine patients had a gallbladder in situ with stones in 2. Cholecystitis developed in none of the patients.

The migration rate was 100% for UE-SEMSs and 40% for FE-SEMSs (Table 2). SEMS removal was successful in all 6 patients with the stent still correctly in place and in all of the patients with intrabiliary migrated UE-SEMSs. No patient had incomplete distal stent migration. In all of the removed stents, the PTFE covering was intact (Fig. 3).

Stricture resolution at the 6-month scheduled stent removal (or asymptomatic distal migration) was observed in 12 patients (70.6%) (Table 1). At 12 months of follow-up, persistent asymptomatic BBS resolution with normalization of LFT results was 43% and 80% for UE-SEMS and FE-SEMS, respectively (Fig. 5). After 24 months, 8 of 15 patients (53%) had normal LFT results (Table 1, Fig. 5). Stent-related cholangitis caused by proximal and distal migration (Table 2) was more frequently observed in patients with UE-SEMSs and shorter stents (40 mm and 50 mm in length), and proximal migration was observed only in patients with UE-SEMSs (Fig. 6).

At the 6-month scheduled stent removal, among the 12 patients with stricture resolution, 7 (58%) had pancreatic head calcifications, whereas among the 5 patients without stricture resolution, 4 had pancreatic head calcifications (80%) ($P = .39$).

Among the 12 patients with stricture resolution (at the 6-month scheduled stent removal), 4 had a pancreatic duct plastic stent (33%), whereas among the 5 patients without stricture resolution, a pancreatic plastic stent had been placed in 4 (80%) ($P = .11$). Three patients had cholangitis