A prospective, randomized study of the patency period of the plastic antireflux biliary stent: an interim analysis

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Background: There is as yet no ideal design of a plastic biliary stent with the longest patency period.

Objective: To study the safety and effective patency period of a new plastic antireflux biliary stent in the clinical setting.

Design: We conducted a prospective, randomized trial to compare the patency of 2 similar plastic biliary stents, one of which has an antiduodenobiliary reflux property.

Setting: The study was conducted at 2 separate tertiary centers in 2 countries.

Patients: Patients with inoperable distal malignant biliary obstruction were recruited.

Interventions: One of the 2 types of plastic stents under study was randomly chosen and inserted in the common bile duct of the study subjects. The subjects were followed until the end of study or occlusion occurrence.

Main Outcome Measurements: Our primary endpoint was the time to stent occlusion in days, with stent-related adverse events and all-cause mortality the secondary endpoints.

Results: A total of 16 subjects were recruited for the study; 7 were allocated to group A (ordinary Tannenbaum stent) and 9 to group B (antireflux biliary stent). Five of 7 subjects (71%) in group B had stent occlusion within 8 days, and the primary end point was reached in all 7 subjects within 30 days, whereas the primary endpoint was not reached within 30 days in any of the subjects in group A. Our data showed a significantly shorter stent patency period in group B compared with group A ($P < .003$).

Limitations: Small sample size.

Conclusion: Routine use of antireflux plastic biliary stents in the palliative management of malignant biliary obstructions cannot be recommended at present. (Clinical trial registration number: NCT01142921.) (Gastrointest Endosc 2016;83:387-93.)

Malignant biliary obstruction is a condition commonly seen in Asians.[1,2] Because many of these tumors are discovered at a late stage, curative treatment may not be feasible.[1,3] Palliative endoscopic stent placement across the obstruction remains a viable option for the majority of patients.[4,5]

The main issue with stent placement in the biliary system is the relatively short period of stent patency. Although this problem is somewhat addressed by the use of longer lasting self-expandable metal stents,[4] many Asian patients still choose plastic stents over the metal stents because of the cost. There have been reports of

Abbreviations: ARBS, antireflux biliary stent; OTS, ordinary Tannenbaum stent.

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modifications made to plastic biliary stents, including changes in stent design and stent material and the use of prophylactic antibiotics or ursodeoxycholic acid in an attempt to prolong the stent patency, but none has shown conclusive benefits.[6-9] Although the actual mechanisms of plastic stent occlusion remain largely unknown, one plausible explanation is duodenobiliary reflux, which deposits plant fibers that facilitate the formation of a bacteria biofilm within the stent lumen, thereby hastening the stent occlusion process.[10] The study by Dua et al[11] demonstrated promising results with the use of plastic stents with an antireflux property. Stents inserted proximally and completely into the bile duct above the sphincter, thereby preserving the barrier function of the sphincter, have also been reported anecdotally to yield good patency.[12]

We postulated that Fusion Marathon stent, the new plastic antireflux biliary stent (ARBS) from Cook Medical (Bloomington, Ind) with a collapsible polytetrafluoroethylene antireflux sleeve at the duodenal end will effectively prevent reflux of duodenal contents into the biliary system, thereby conferring a longer period of patency compared with ordinary plastic biliary stents in patients with malignant biliary strictures.

MATERIAL AND METHODS

Plastic stents

To allow a better comparison between the 2 groups, 2 commercially available 10F plastic stents made of the same material with almost identical design (Tannenbaum design) (Cook Medical) were selected. The difference is the additional soft antireflux sleeve attached to the duodenal end of 1 stent (ARBS), which prevents the backflow of duodenal contents into the biliary system in a retrograde manner. Both the ordinary Tannenbaum stent (OTS) stent and the ARBS do not have any side holes near the stent ends, so that the bile and duodenal contents can only flow across the stent through a single opening at each end. The length ranges from 5 cm to 9 cm for both stent types, and we allowed the endoscopists to determine the ideal length for each study subject during stent deployment.

Patient selection

Consecutive patients with malignant extrahepatic biliary obstruction distal to the hilum were invited to participate in the study. Included were extrahepatic cholangiocarcinoma, pancreatic cancer, gallbladder cancer, periampullary tumors, and metastatic cancer with extrahepatic biliary obstruction. Patients with a resectable tumor, biliary stricture involving the hilum or proximal biliary segments, or previous sphincterotomy were excluded. Patients with a life expectancy of less than 3 months (American Society of Anesthesiologists grade 4 and higher) were also excluded from the study.

Study design

We conducted a prospective, randomized, double-blind comparative trial at 2 tertiary centers in 2 countries: The Prince of Wales Hospital, Shatin, Hong Kong SAR, People's Republic of China and Tan Tock Seng Hospital, Republic of Singapore. The study protocol was reviewed and approved by the institutional review board at each institution before the recruitment started sequentially. The recruitment process was started at the Hong Kong center before registration with ClinicalTrials.gov (NCT01142921, June 8, 2010). Consecutive patients of at least 18 years of age (at least 21 years of age in Singapore) who presented with suspected malignant distal biliary strictures and satisfied the criteria were invited to participate in the study after providing the necessary informed consent. Baseline demographic data, liver function test results, and other concurrent comorbidities were recorded. Patients were randomized to group A (receiving the OTS) or group B (receiving the ARBS). The randomization process involved placing group allocation tags generated randomly by a computer program into serially numbered sealed envelopes in a box. After cholangiographic confirmation of a distal biliary stricture during ERCP, the endoscopists would select the envelope next in line in a sequential manner to determine the group allocation, without disclosing the information to the patients. Depending on the location and length of the strictures, a single 10F plastic stent of the most suitable length was inserted by using a standard endoscopic technique for both groups without any sphincterotomy. The time to deep cannulation and time to stent deployment were recorded to reflect on the level of difficulty in bile duct cannulation and stent deployment processes, respectively. Antibiotics were given to patients only to treat clinical infections and not prophylactically. The use of nonsteroidal anti-inflammatory drugs was prohibited before ERCP.

The subjects were followed up 1 week after stent insertion if clinically stable, followed by a monthly assessment of their clinical status and liver function. Unless subjects dropped out of the study, all subjects were followed until stent occlusion occurred or up to a period of 6 months. The assessments were done by physicians blinded to the group allocation process. Stent occlusion was defined as clinical cholangitis or worsening serum bilirubin level and/or serum alkaline phosphatase, together with endoscopic confirmation of stent occlusion during subsequent ERCP. The primary endpoint was the time to stent occlusion in days starting from stent insertion until stent exchange. Secondary endpoints were adverse events related to the stent placement process and all-cause mortality during the follow-up period until stent occlusion occurred.

Statistical analysis

Sample size was estimated by using the PASS software program (NCSS Statistical Software, Kaysville), and data