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A new biodegradable stent in bilio-pancreatic diseases: A prospective multi-center feasibility study

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ABSTRACT

Introduction

Biodegradable stents of various designs are reportedly used in pancreato-biliary conditions with promising results. Their major advantage is the avoidance of a repeat endoscopic procedure for stent removal thereby reducing overall cost along with ERCP associated adverse events. To evaluate the feasibility and safety of a new biodegradable stent in patients with pancreato-biliary diseases.

Methods

Prospective multicenter pilot study. All consecutive patients ≥18 years-old who underwent biliary or pancreatic stenting using the new biodegradable Archimedes stent were included. There were three biodegradation profiles. Technical and clinical success, feasibility and safety were assessed during a pre-established follow-up schedule.

Results

Fifty-three patients (mean age: 48.54±19.29, 66% male) having biliary (n=29, 54.7%%) or pancreatic (n=24, 45.3%) indications were included. The distribution of stents used according to degradation properties were as follows: fast (n=11, 20.8%), medium (n=16, 30.2%) and slow (n=26, 49.1%). The technical and clinical success were 100% and 77.8%. Thirty-five patients were followed for a median of 26 weeks (range: 4-56, 66%). There were 9 procedure-related adverse events (17%), all mild, including one uneventful stent-related event (external migration).

Conclusion

The biodegradable Archimedes stent placement is feasible and safe in pancreato-biliary diseases.

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INTRODUCTION

Biodegradable stents of various designs are reportedly used in pancreato-biliary conditions (chonic pancreatitis, benign biliary strictures, post-operative at pancreatic or biliary anastomosis) with promising results(1). The major advantage of biodegradable stent include avoidance of repeat endoscopic retrograde cholangiopancreatography (ERCP) or other endoscopic procedures for stent removal thereby reducing overall cost and ERCP related associated adverse events(2).

They are typically made from complex carbohydrate polymeric materials including polylactide or polyglycolide along with radio-opaque material embedded in stents for fluoroscopic visualization. e.g. BaSO4 (barium sulphate). They have variable shapes, designs and dissolution properties. While fast and medium biodegradation profiles are using polydioxanone and polyethylene glycol, slow is a co-polymer of polylactic acid, polytrimethylene carbonate and polycaprolactone. This material is degraded by natural physiologic hydrolysis into lactic acid and glycolic acid or glyoxylic acid. The end products are metabolized by physiological pathways.

Significant experience with biodegradable materials has been reported in different settings. In Gastroenterology, biodegradable stent were first reportedly used in patients with an esophageal stenosis with promising results (3). Among biliary applications, most of reports have been described in benign biliary strictures treated by a percutaneous approach (4, 5). A multicenter study of 159 patients with benign post-surgical biliary strictures showed a 100% technical success with 26.6% recurrent biliary obstruction rate (5). More recently publications inlcude short endoscopic case series on surgically altered anatomy (6, 7) or hybrid techniques (8). The recent pilot study from Anderloni et al (9) including 38 patients suggested that the biodegradation of the new biliary and pancreatic stents is reliable and in line with expected times. However, different stent designs, make of a variety of materials, and the feasibility on

endoscopic pancreato-biliary stenting remains unclear.

The aim of this study was to evaluate the feasibility and safety of a new biodegradable stent in patients with pancreatobiliary diseases.

METHODS AND PATIENTS

Design and Patients

In this prospective multicenter pilot study, consenting patients ≥ 18 years-old presenting with an indication for biliary or pancreatic stenting by ERCP between June 2015 and December 2018 were recruited. Relevant data such as demographic variables, underlying diagnosis and indication were noted. Liver function tests were performed considered at D1 and D7 in those with biliary indication.

For biliary strictures, patients with extra-hepatic strictures (at least 1cm distal to the hilum) were included. In pancreatic indications, both prophylactic and therapeutic stenting were included. The exclusion criteria were previous gastric surgery, pregnancy and life expectancy <1 month and failure to provide fully informed consent rendered the subject ineligible for the study.

A written informed consent was provided. The study was approved by the local Ethics Committee (UKM 1.5.3.5/FF-2014-324) according to the Declaration of Helsinki.

Procedure

ERCP was performed under conscious sedation or general anesthesia using a duodenoscope (TJF-180/190, Olympus, Tokyo, Japan). Antibiotics and rectal indomethacin were given before the procedure according to the local protocol. An endoscopic sphincterotomy was performed at the discretion of the endoscopist. The biodegradable stent was advanced under fluoroscopy over a 0.025/0.035-inch guidewire using a pushing catheter with the distal-end protruding into the duodenal lumen. The patient was managed according to local standard of care after the procedure.

Rectal indomethacin was administered in all study patients to prevent post-ERCP pancreatitis. Before final placement, the Archimedes stent was immersed in sterile saline for 60 seconds and then passed over a guidewire through the working channel of the duodenoscope.

Stent characteristics

The Archimedes biodegradable stent (amg International-GmbH, Winsen, Germany) has a gentle fluted-shaped curve. The cross-sectional profile shows two threads woven as a double helix two with a central lumen (**Figure 1**). The double helical design along the entire length of the stent allows dual drainage of fluid - through the center lumen of the stent ans also on the outside. The proximal end of the stent has a smooth tapering to allow for atraumatic insertion through the papilla. The distal end of the stent has a split flap to minimize migration. There are three available calibers (6, 8 and 10-French) and lengths range from 40mm up to 225mm. In this study, only 6 and 10-French diameter and at different lengths (4-12cm) were used.

Based on the degradation profile, the stents are classified as fast (12 days), medium (20 days), and slow (11 weeks). Degradation occurs through hydrolysis. Barium sulphate is embedded throughout the materials allowing for fluoroscopic visualization. The choice of stent was decided by the operator based on clinical characteristics (e.g. for post-ERCP pancreatitis prophylaxis fast degrading stent was placed).

Outcomes

The primary outcomes were technical success and safety of biodegradable stent placement at ERCP. Technical success was defined as completion of the initial ERCP and stent deployment. Safety was defined as occurrence of one or more adverse events, including migration, bleeding, perforation, post-ERCP pancreatitis and cholecystitis.

The secondary outcomes were to assess procedural performances and clinical success. Procedural performances were rated by the endoscopist using a prospective score of

technical variables such as: loadability (trackability over guide wire), pushability, flexibility, fluoroscopic visualization and deployment accuracy scored on a 4-points scale (1 - Excellent, 2 - Good, 3 - Fair, 4 - Poor), grouped in high (good/excellent) and low (poor/fair) scores. Clinical success was defined as when there was no requirement of a repeat pancreatic stenting within 3 months of placement. For biliary indication, it was defined as the >20% reduction of blood bilirubin levels within seven days of placement of stent.

Follow-up

Patients were monitored and clinically followed as scheduled in the outpatient clinic or by phone according to the biodegradation variant of the Archimedes stent (**Table 1**). They were followed up for 6 months with interval monitoring at 3 months to observe degradation of stents by serial abdominal radiograph at 3 and 6 months. Abdominal radiograph was done at 24 hours of the procedure to visualise the stent. Interim surveillance abdominal radiography was performed for the position and dissolution of the stent. If the stent was no visualised on abdominal radiograph on scheduled visit, then subsequent X-rays were abandoned to reduce risk from radiation.

Statistical analysis

Categorical variables were presented by percentages and compared using the χ^2-test. Non-normally distributed variables were analysed by the Mann-Whitney U-test. The data were presented as the mean (SD) or median (range), respectively. There was no sample size calculation as this is a pilot study. SPSS v.23 package (IBM, New York, US) was used.

RESULTS

Patients

Fifty-three patients (mean age: 48.5±19.3, 66% male) with biliary (n = 29, 54.7%%) and pancreatic (n = 24, 45.3%) indications were included. Most of indications were benign (n = 50, 94.3%). The indications were as follows: biliary stones/cholangitis (n = 26,

49.1%), chronic pancreatitis with pancreatic stones or pancreatic stricture (n = 23, 43.4%), malignant biliary strictures (n = 2), benign biliary strictures (n = 1), prophylactic pancreatic stent (n = 1).

Biodegradable stenting

The technical success was 100%. Almost half of patients (n = 25, 47.2%) had previous stenting. The median procedure time was 18 minutes (range: 6-60). Prior sphincterotomy was present in 29 cases (54.7%) and was less common in patients with biliary indications (40.6%) compared to pancreatic indications (76.2%) (p=0.01).

The 6-French and 10-French were used in 23 (43.4%) and 30 cases (56.6%) respectively. In biliary stenting, all except two patients, had 10-French stents. The stent length was 12cm (n = 8, 15.1%), 10cm (n = 32, 60.4%), 8cm (n = 10, 18.9%), 6cm (n = 2, 3.8%) and 4cm (n = 1, 1.9%). In pancreatic stenting, a 6-French size was used in all patients (6cm, n = 1; 8cm, n=1, 10cm, n = 22).

The biodegradable profile was fast (n = 11, 20.8%), medium (n=16, 30.2%) and slow (n = 26, 49.1%). Most fast-degradation stents (n = 10/11, 90.9%) were used for ensuring biliary clearance as follows: biliary stones (n = 5), cholangitis (n = 3), benign biliary strictures (n = 2).

There were 9 adverse events (17%), that included mild sphincterotomy related bleeding (n=4, 7.5%), post-ERCP pancreatitis (n = 2, 3.8%), ascending cholangitis (n = 1, 1.9%) and acute cholecystitis (n = 1, 1.9%). There was one device-related event (n = 1, 1.9%) - stent migration of a biliary 6-French stent in a patient with prior sphincterotomy not associated with recurrent biliary obstruction. 10-French stents were placed in all cases of post sphincterotomy bleeding.

Procedural performances

The feasibility analysis is shown in **Table 2**. At ERCP, higher flexibility of stent was more frequent with 6-French stents compared to the 10-French stents (100% vs. 83.3%, p =

0.04). The fluoroscopic visualization was not statistically different between 6-French and 10-French stents (high in 87% vs. 93.3%, p = 0.642) **(Figure 2)**. There were no statistical differences observed regarding stent length and feasibility outcomes.

Follow-up

Thirty-five patients were followed a median of 26 weeks (range: 4-56, 66%) and the stent degradation was confirmed within expected follow-up times. Fourteen cases were lost to follow-up (26.4%) and four patients prematurely exited the study due to death from other reasons (7.5%). Overall, there was a clinical success rate of 77.8% in biliary cases and 100% in pancreatic cases. All patients with chronic pancreatitis remained asymptomatic following pancreatic stenting during the six month follow-up.

DISCUSSION

The present prospective pilot study includes the largest series to date of patients who underwent biodegradable Archimedes endoscopic stenting, concluding a 100% technical success. Flexibility scored higher with 6-French stents. There was only one stent-related complication.

Biodegradable biliary and pancreatic stents can be handled similarly to plastic stents. The major advantage of such stent is avoidance of a second ERCP to retrieve the stent (9) along with the cost-benefit and lesser strain on heaith care system apart from psychological reassurance to the patient. In our study, the majority of patients had a benign biliary or pancreatic indication. Compared to plastic stents, the 10-French Archimedes stents are deployed using a guidewire and a pushing catheter without a stablising internal catheter. This mechanism could have decreased the flexibility or pushability compared to 6-Fr variant.

The overall adverse events were mild and were within acceptable range. Most were attributed to the several steps of ERCP procedure, rather the stent. Although stent delayed migration may be difficult to differentiate from an unexpected faster

biodegradation, in our study, we performed a sequential radiological monitoring and the migration rate was very low (1.9%), probably related to the new design of this device.

The present feasibility study achieved high technical success and procedural performances in a a heterogeneous group of patients who underwent ERCP stenting with different stent profiles, sizes and lehgts. Altough there was a relatively high lost to follow-up, these good technical outcomes in this large multicentric cohort, support the safety and feasibility of the device. Further prospective studies with a specific focus on clinical outcomes and total cost of care versus the current standard of care in more selected settings seems necessary.

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FIGURE LEGENDS

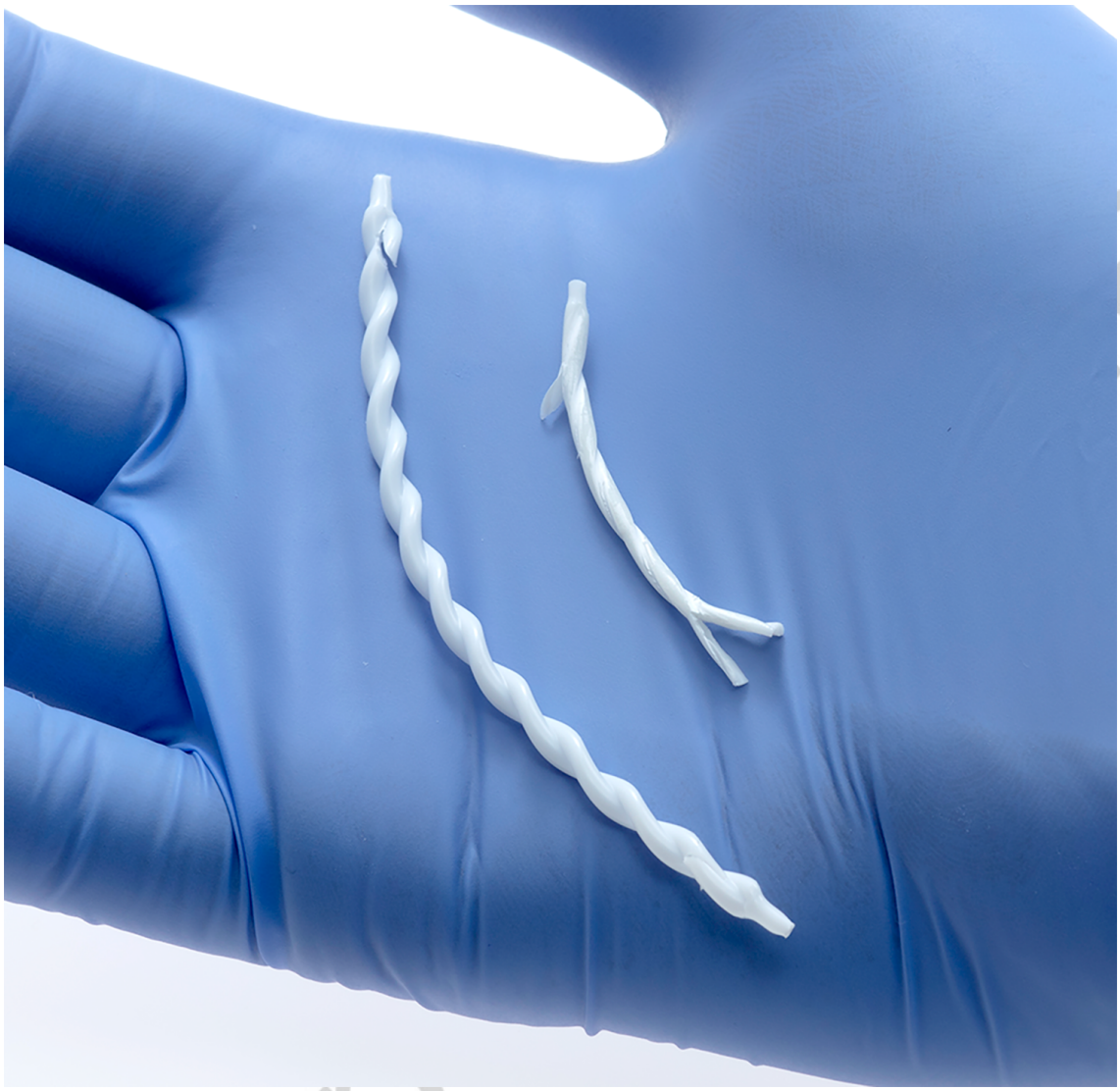

Figure 1: A 10-French (left) and 6-French (right) biodegradable stents. They have a curved form and comprise a fluted-shaped, cross-sectional profile which contains two channels. This helical design allows an external drainage. Both models have internal and external flaps.

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ENFERMEDADES DIGESTIVAS
The Spanish Journal of Gastroenterology

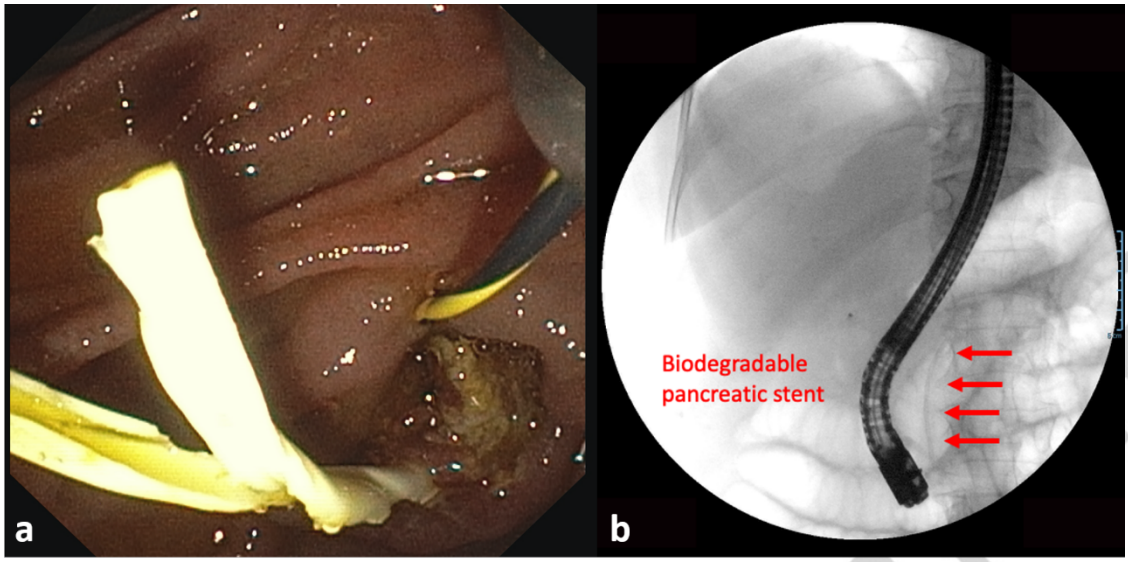

Figure 2: Endoscopic (a) and radiological images (b) of a patient who underwent biodegradable pancreatic stenting (arrows) using a 6-French Archimedes stent.

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The Spanish Journal of Gastroenterology

TABLES

Table 1. Follow-up strategy in patients who underwent a biliary or pancreatic Archimedes stenting depending on the degradation profile.

	Day			Month				
Stent profile	**1**	**7**	**14**	**1**	**3**	**6**	**9**	**12**
Fast	X	X	X	X	X			
Medium	X			X	X	X		
Slow	X			X	X	X	X	X

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Table 2: **Procedural performances of the new biodegradable Archimedes stent for biliary and pancreatic indications using a predesigned 4-points score (1-excellent, 2-good, 3-fair, 4-poor) grouped in high (1-2) or low (3-4).**

	Loadability	**Pushability**	**Flexibility**	**Fluoroscopic visualization**	**Deployment accuracy**
Overall (score)	Excellent (n=43, 81.1%) Good (n=9, 17%) Fair (0) Poor (n=1, 1.9%)	Excellent (n=45, 84.9%) Good (n=4, 7.5%) Fair (n=2, 3.8%) Poor (n=2, 3.8%)	Excellent (n=32, 60.4%) Good (n=16, 30.2%) Fair (n=3, 5.7%) Poor (n=2, 3.8%)	Excellent (n=30, 56.6%) Good (n=18, 34%) Fair (n=5, 9.4%) Poor (0)	Excellent (n=41, 77.4%) Good (n=10, 18.9%) Fair (n=2, 3.8%) Poor (0)
Overall (median, range)	1 (1-4)	1 (1-4)	1 (1-4)	1 (1-3)	1 (1-3)
Biliary indications	High (n=28, 96.6%) Low (n=1, 3.4%)	High (n=25, 86.2%) Low (n=4, 13.8%)	High (n=24, 82.8%) Low (n=5, 17.2%)	High (n=27, 93.1%) Low (n=2, 6.9%)	High (n 27, 93.1%) Low (n=2, 6.9%)
Pancreatic indications*	High (n=24, 100%) Low (0)	High (n=24, 100%) Low (0)	High (n=24, 100%) Low (0)	High (n=21, 87.5%) Low (n=3, 12.5%)	High (n=24, 100%) Low (0)

* There were only 6-French stents used for a pancreatic indication.

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