Editorial

Endoscopic therapy for benign biliary strictures: evaluation of metal *vs.* plastic biliary stents

Joshua C. Obuch, Mihir S. Wagh

Interventional Endoscopy, Division of Gastroenterology, University of Colorado, Denver, CO, USA

Correspondence to: Mihir S. Wagh, MD, FACG, FASGE. Interventional Endoscopy, Division of Gastroenterology, University of Colorado, 1635 Aurora Court, F735, Aurora, CO 80045, USA. Email: mihir.wagh@ucdenver.edu.

Provenance: This is an invited Editorial commissioned by Editor-in-Chief Yilei Mao (Department of Liver Surgery, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing, China).

Comment on: Coté GA, Slivka A, Tarnasky P, *et al.* Effect of Covered Metallic Stents Compared With Plastic Stents on Benign Biliary Stricture Resolution: A Randomized Clinical Trial. JAMA 2016;315:1250-7.

Submitted Mar 02, 2017. Accepted for publication Apr 19, 2017.

doi: 10.21037/hbsn.2017.05.04

View this article at: http://dx.doi.org/10.21037/hbsn.2017.05.04

Biliary strictures arise from a myriad of malignant or benign etiologies. Most patients are initially asymptomatic, however consequences of obstruction and cholestasis are inevitable, necessitating biliary decompression for symptomatic relief. Methods for biliary decompression have changed dramatically in the last 40 years, from surgical bypass, like choledocho/hepatico-jejunostomy, to percutaneous transhepatic biliary drainage (PTBD), to endoscopic stenting via ERCP (1-3). Since their development in the 1980's, endoscopic biliary stents have been used to circumvent surgical and percutaneous routes of biliary decompression (4,5).

Plastic stents (PS) were initially used for biliary stricture management, being relatively inexpensive and effective with advantages of easy removability and exchange, with a major drawback being limited patency of typically less than 3 months related to occlusion from biliary sludge. In contrast, metal stents (uncovered, partially covered, and fully covered) developed later in the 1980s provided increased diameter (2–3 times the largest PS), translating to longer patency (median 9 months). This came with higher cost and lack of removability (regarding uncovered stents). Regardless, for distal malignant biliary strictures and life-expectancy greater than 6 months, uncovered metal stents became the standard of care, given equal technical success, efficacy, mortality/complication rate, and lower risk of recurrent obstruction compared to PS (6), translating to a more cost-effective approach for this patient population (7).

For benign biliary strictures (BBS), iatrogenic bile duct injury and chronic pancreatitis (CP) are the most common causes. PS have commonly been employed for these strictures, but require exchange/upsizing every 3–4 months with multiple stents needed for durable improvement (80–90% for postoperative strictures, 50–70% for CP strictures) (8).

Fully covered self-expanding metal stents (FCSEMS) have gained interest for BBS treatment as they have advantages of a narrow deployment system obviating the need for aggressive dilation before stent placement, and larger expansion diameter minimizing the risk of stent occlusion (9). FCSEMS have a full external or internal covering to prevent stent occlusion from reactive tissue hyperplasia/ingrowth thus contributing to improved patency and easier removability. A potential drawback is the rate of stent migration, as high as 40% depending on FCSEMS used and BBS etiology (10).

Placement of multiple PS with or without endoscopic dilatation is currently standard of care in BBS management, with most metal stents in BBS constituting off-label use in the USA. Thus FCSEMS are not traditionally used first line in BBS treatment, but this paradigm may be changing.

In 2014, a prospective multicenter study evaluated FCSEMS for BBS, with the majority of strictures from CP (33%), followed by anastomotic biliary strictures (AS)

(26%), with 50% of patients having PS prior to FCSEMS placement (11). Ninety-eight of the 133 patients had average stent removal at 3 months, with 77% showing resolution (gallstone-related disease: 91.6%, CP: 80.7%, AS: 61.2%). Resolution was more with stent duration over 3 months and lack of migration, with previous PS placement associated with decreased resolution. Stent migration occurred in 10.5% of cases, with AS having a 35.7% migration rate. Complications included stent migration (10.5%), pain requiring admission (6%), pancreatitis (2%), and stent occlusion (3%). There were no episodes of cholecystitis despite 10 patients having intact gallbladders and FCSEMS placement across the cystic duct.

A similar multinational prospective observational study (10) analyzed FCSEMS in 187 patients with various BBS. Most strictures were due to CP (68%), then post-LT (22%) and post-cholecystectomy (CCY) (10%), with 74% of patients having PS before FCSEMS placement. Eighty percent of CP patients had stricture resolution, followed by 72% of CCY patients and 68% of LT patients, with stent migration reducing resolution rates (56% *vs.* 85%, P<0.001). Sixty-two adverse events occurred in 51 patients, with cholangitis/fever in over 40%. Cholecystitis was reported in 7% of CP patients with gallbladder *in situ* and cystic duct occlusion by the stent *vs.* 0% without cystic duct occlusion, but was not statistically significant (P=0.074).

One of the first randomized trials to compare PS to SEMS in patients with BBS addressed CP induced BBS (12). The reported stricture resolution rate was 88% (95% CI 69–92%) in the PS group and 91% (95% CI 71–99%) (P=1.00) in the CSEMS group, with insignificant differences in adverse event rates (AER). The authors concluded that 6-month treatment with six 10-Fr PS or one 10-mm CSEMS safely produced good long-term relief of CP induced BBS.

Attempts have been made to assess the heterogeneous observational data on various stents for BBS. A 2014 meta-analysis of 25 articles included 946 patients (9). To assess outcomes, three groups were created: CP, LT, and other strictures (OS). There was equal success between CSEMS and PS regarding technical deployment and removal, with CSEMS having significantly shorter indwell times (4.5 *vs.* 11 months) and fewer ERCP sessions (median 1.5 *vs.* 3.9), with no difference in early complications, but late complications occurred more often in the PS group (4.6% *vs.* 14%). The CP group AER was 3% *vs.* 67% for CSEMS and PS respectively, driven mostly by stent clogging. Patients with CP strictures trended towards better patency in the CSEMS group *vs.* PS group after 1 month (77% *vs.* 33%, P=0.06), with no significant difference in the OLT or OS group. While this meta-analysis suggested better success with equivalent complication rates for CSEMS compared to PS for CP induced BBS, no difference was noted among other etiologies. Unfortunately, the heterogeneity of studies and lack of RCTs made firm conclusions from this meta-analysis difficult.

In March 2016, Coté and colleagues conducted the first multicenter, prospective, RCT to better assess the use of PS versus FCSEMS in BBS management (13), with the hypothesis that FCSEMS would be non-inferior to multiple PS for first-line endoscopic treatment of BBS. Patients had BBS with jaundice or cholangitis, and at least 25% diameter narrowing compared to unaffected portions of the extrahepatic biliary duct. Ducts smaller than 6 mm and patients where FCSEMS placement would jail off intact gallbladders were excluded, and stratified randomization by etiology and site accounted for the varying difficulty of BBS. For PS patients, ERCPs were repeated every 3–4 months with complete stent removal followed by dilation and upsizing if a stricture persisted. Dilation pre-stent deployment was performed as needed for FCSEMS patients, with repeat ERCPs with re-stenting as needed at 6-month intervals. Treatment failure was defined as persistent stricture after 12 months of endoscopic therapy, a major adverse event, or two minor adverse events. Patients achieving resolution within 12 months had additional 12 months of follow-up for recurrence assessment. The authors' calculations of non-inferiority margins of –15% and assumption of 90% stricture resolution with a modified intention to treat approach and sensitivity analysis of worst case scenario minimized biasing conclusions that would favor FCSEMS.

BBS composition included 65.2% LT, 31.3% CP, and a small percentage comprising other postoperative strictures (3.6%). Resolution occurred in 85.4% of PS patients and 92.6% of FCSEMS patients with comparable rates noted after sensitivity analysis, thus rejecting the null hypothesis that FCSEMS are inferior to PS for BBS. Additionally, the FCSEMS group achieved stricture resolution quicker and averaged 1 less ERCP than the PS group, with statistically similar rates of recurrence (14% FCSEMS *vs.* 5% PS, P=0.15) and AER between the two groups. However,

FCSEMS migration occurred more frequently in patients with LT AS.

While Coté's study is the first multicenter prospective RCT to address FCSEMS in the management of BBS, there are some limitations. One exclusion criteria was avoiding patients with gallbladder *in situ* in which cystic duct occlusion with the FCSEMS may occur. Prior studies regarding malignant biliary strictures have shown cholecystitis rates ranging from 4% to 25%, with increased risk when tumor involves the cystic duct (14,15). For CSEMS in BBS, cholecystitis rates have ranged 0–7% (10,11) but have not shown to be statistically different from PS rates. Additionally, accurately locating the cystic duct takeoff on 2-Dimensional fluoroscopy is challenging, making exclusion of this patient group tricky. Nonetheless, there were no reports of cholecystitis in this study.

The most common type of BBS is post CCY, however the majority of patients in this study were LT and CP patients. Lastly, a cost analysis would have assisted in adopting one strategy over the other given the large cost difference between PS and FCSEMS.

While the study was not powered to detect differences in safety, recurrence, or ERCPs needed, the results are intriguing. The authors plan an economic evaluation of PS versus FCSEMS in BBS, the results of which will certainly shed more light on the role of FCSEMS as the initial choice for BBS. Until then, findings from this trial suggest FCSEMS can lead to similar rates of stricture resolution compared to serial plastic stenting for BBS, with fewer endoscopic procedures.

Acknowledgements

None.

Footnote

Conflicts of Interest: Mihir S. Wagh is a consultant for Boston Scientific and Medtronic.

References

1. Srinivasan I, Kahaleh M. Biliary stents in the millennium. Adv Ther 2011;28:960-72.
2. Sicklick JK, Camp MS, Lillemoe KD, et al. Surgical management of bile duct injuries sustained during laparoscopic cholecystectomy: perioperative results in 200 patients. Ann Surg 2005;241:786-92; discussion 793-5.
3. Lillemoe KD, Melton GB, Cameron JL, et al. Postoperative bile duct strictures: management and outcome in the 1990s. Ann Surg 2000;232:430-41.
4. Soehendra N, Reynders-Frederix V. Palliative bile duct drainage - a new endoscopic method of introducing a transpapillary drain. Endoscopy 1980;12:8-11.
5. Walta DC, Fausel CS, Brant B. Endoscopic biliary stents and obstructive jaundice. Am J Surg 1987;153:444-7.
6. Moss AC, Morris E, Leyden J, et al. Do the benefits of metal stents justify the costs? A systematic review and meta-analysis of trials comparing endoscopic stents for malignant biliary obstruction. Eur J Gastroenterol Hepatol 2007;19:1119-24.
7. Chen VK, Arguedas MR, Baron TH. Expandable metal biliary stents before pancreaticoduodenectomy for pancreatic cancer: a Monte-Carlo decision analysis. Clin Gastroenterol Hepatol 2005;3:1229-37.
8. Costamagna G, Tringali A, Mutignani M, et al. Endotherapy of postoperative biliary strictures with multiple stents: results after more than 10 years of follow-up. Gastrointest Endosc 2010;72:551-7.
9. Siiki A, Helminen M, Sand J, et al. Covered self-expanding metal stents may be preferable to plastic stents in the treatment of chronic pancreatitis-related biliary strictures: a systematic review comparing 2 methods of stent therapy in benign biliary strictures. J Clin Gastroenterol 2014;48:635-43.
10. Devière J, Nageshwar Reddy D, Püspök A, et al. Successful management of benign biliary strictures with fully covered self-expanding metal stents. Gastroenterology 2014;147:385-95; quiz e15.
11. Kahaleh M, Brijbassie A, Sethi A, et al. Multicenter trial evaluating the use of covered self-expanding metal stents in benign biliary strictures: time to revisit our therapeutic options? J Clin Gastroenterol 2013;47:695-9.
12. Haapamäki C, Kylänpää L, Udd M, et al. Randomized multicenter study of multiple plastic stents vs. covered self-expandable metallic stent in the treatment of biliary stricture in chronic pancreatitis. Endoscopy 2015;47:605-10.
13. Coté GA, Slivka A, Tarnasky P, et al. Effect of Covered Metallic Stents Compared With Plastic Stents on Benign Biliary Stricture Resolution: A Randomized Clinical Trial. JAMA 2016;315:1250-7.

14. Nakai Y, Isayama H, Kawakubo K, et al. Metallic stent with high axial force as a risk factor for cholecystitis in distal malignant biliary obstruction. J Gastroenterol Hepatol 2014;29:1557-62.
15. Shimizu S, Naitoh I, Nakazawa T, et al. Predictive factors for pancreatitis and cholecystitis in endoscopic covered metal stenting for distal malignant biliary obstruction. J Gastroenterol Hepatol 2013;28:68-72.

Cite this article as: Obuch JC, Wagh MS. Endoscopic therapy for benign biliary strictures: evaluation of metal *vs.* plastic biliary stents. HepatoBiliary Surg Nutr 2017;6(4):268-271. doi: 10.21037/hbsn.2017.05.04

