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

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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 biliary 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 cholecystitis/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 OL T 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.

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**Footnote**

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**References**

