Commentary

The freedom of choice

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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.

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Endoscopic stent placement is the current standard treatment for benign biliary strictures (BBS). There are two main treatment options: either the implantation of multiple plastic stents (MPS) or the implantation of self-expandable metal stents (SEMS) (1,2). Which of the two stent implantation strategies is the better choice remains a matter of interest. Other therapies such as balloon dilatation and bouginage that are still frequently used in clinical practice provide a modest additional benefit. The most common causes of BBS include stenosis due to chronic pancreatitis (CP) or postoperative after orthotopic liver transplantation (OLT) or cholecystectomy (CCY) (3). The combination of endoscopic dilatation with sequential placement of MPS over a 1-year period shows high efficacy in resolving BBS after OLT (80–90%) as well as in patients with CP (44–92%) (1,4). However, the procedure is demanding and an average number of 4–5 endoscopic retrograde cholangiopancreatography (ERCP) is needed and causes an increased rate of complications (5). Recent studies moved the use of fully covered self-expandable metal stents (FCSEMS) into focus. FCSEMS have a low occlusion rate and a larger diameter compared to PS, which may turn out to be beneficial in the long-term treatment of BBS (6,7). However, comparative studies demonstrating a longer patency of SEMS compared to MPS are not available. In a prospective nonrandomized clinical trial the effectiveness and safety of FCSEMS for the treatment of BBS has been shown (8). Randomized clinical studies comparing FCSEMS with MPS in BBS have not been conducted before. Coté *et al.* present an open-label, multi-centre, randomized clinical trial comparing FCSEMS with MPS in BBS (9). The study was conducted to reveal a non-inferiority of FCSEMS versus MPS.

One hundred and twelve patients (73 OLT patients, 35 CP patients, 4 CCY patients) with a symptomatic stricture of the common bile duct, located at least 2 cm below the hepatic confluence were randomized either to receive FCSEMS or MPS. Strictures had to be—in contrast to previous studies—less than 75% of the diameter of the unaffected bile duct with a minimum size of 6 mm and a maximum length of 8 mm. Diameter of FCSEMS was in addition adapted to the size of the surrounding bile duct to lower the migration rate. Successful stricture resolution was determined after a 12-month stent therapy and defined as a residual diameter of the stricture more than 75% of the duct above and below the stricture. With a resolution rate of 92.6% in the FCSEMS group against 85.4% in the MPS group (rate difference 7.2%; 95% CI, –3.0% to ∞; P<0.001), the noninferiority was proven. Furthermore, the number of ERCPs (2.14 *vs.* 3.24; P<0.001) and the time to resolve the stricture (181 *vs.* 225 days; P=0.006) was significant lower in the FCSEMS group compared to MPS group. Subgroup analysis confirmed these observations in patients after OLT and with CP without reaching statistical significance. However, the study was not adequately powered for this subgroup analysis. The deployment and removing of all MPS and FCSEMS were successful. The safety of removal FCSEMS after long term indwelling has previously been demonstrated in a study by Devière *et al.* (8). Migration of bile duct stents, known to be a major complication,

occurred approximately in 28% of the FCSEMS and 18% of the MPS patients. Nevertheless, a closer look at the data showed that in the FCSEMS group the majority of the cases with stent migration occurred after stricture resolution, which was in contrast to the MPS group. Other adverse events (post-ERCP pancreatitis, post procedure abdominal pain, secondary bile duct changes) were low. Interestingly the rate of cholangitis was generally low and not different in both groups. A 12-month follow up showed in both groups a low recurrence rate of the strictures (FCSEMS 14% *vs.* MPS 4.9%; P=0.18).

Dilatation previous to stent implantation was required more frequently with MPS compared to SEMS implantation. This indicates that the clinical success is not affected by dilatation as both treatment regimens were equivalent in outcome.

The randomized clinical trial by Coté *et al.* fills an important gap in the recent discussion about the optimal treatment in BBS. The data support the common hypothesis that FCSEMS are non-inferior to MPS for the first-line treatment of BBS. The resolution rates and complications are comparable to previous reports (1,4,8,10).

A direct translation of the results on FCSEMS, other than in this study investigated, is not possible. FCSEMS, although showing high similarities, present with distinct characteristics such as radial expansion force, material of cover, outer surface and many more that may influence clinical outcomes with special respect to dislocation rate and dilatation of a stenosis.

It deserves specific consideration that each entity of stenosis presents characteristics which affect the therapy and success. The main focus in the recent study emphasizes patients after OLT, what makes it difficult to generalize the results for other subgroups of patients with BBS. So, in contrast to patients with OLT, biliary strictures of patients with CP are characterized by the distal position of the stenosis, the stiff nature due to the dense periductal fibrosis/calcification and a high recurrence rate based on the chronic inflammation (11,12). All these factors need to be considered in the endoscopic approach. New data could document higher resolution rates by the use of FCSEMS (90–92.5%) with a lower trend of migration also in patients with CP (8,13).

Complicating, different study protocols make a direct comparison between the existing trials difficult what is a general problem in the recent debate. Knowledge about the adequate stent indwelling time, the role of sphincterotomy, balloon dilatation or preferred FCSEMS is missing so far.

Astonishingly many important questions on this particular clinical field still have to be evaluated in high quality studies.

In summary the trial by Coté *et al.* still leaves the question open which method to choose. However non-inferiority accompanied with less interventions needed and comparable complication rates are favourable arguments for an increased use of FCSEMS in future.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. Dumonceau JM, Tringali A, Blero D, et al. Biliary stenting: indications, choice of stents and results: European Society of Gastrointestinal Endoscopy (ESGE) clinical guideline. Endoscopy 2012;44:277-98.
2. ASGE Standards of Practice Committee, Chathadi KV, Chandrasekhara V, et al. The role of ERCP in benign diseases of the biliary tract. Gastrointest Endosc 2015;81:795-803.
3. Visrodia KH, Tabibian JH, Baron TH. Endoscopic management of benign biliary strictures. World J Gastrointest Endosc 2015;7:1003-13.
4. Costamagna G, Pandolfi M, Mutignani M, et al. Long-term results of endoscopic management of postoperative bile duct strictures with increasing numbers of stents. Gastrointest Endosc 2001;54:162-8.
5. Poley JW, Lekkerkerker MN, Metselaar HJ, et al. Clinical outcome of progressive stenting in patients with anastomotic strictures after orthotopic liver transplantation. Endoscopy 2013;45:567-70.
6. van Berkel AM, Cahen DL, van Westerloo DJ, et al. Self-expanding metal stents in benign biliary strictures due to chronic pancreatitis. Endoscopy 2004;36:381-4.
7. Kaffes AJ, Liu K. Fully covered self-expandable metal stents for treatment of benign biliary strictures. Gastrointest Endosc 2013;78:13-21.
8. 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.
9. 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.
10. 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.
11. Familiari P, Boškoski I, Bove V, et al. ERCP for biliary strictures associated with chronic pancreatitis. Gastrointest Endosc Clin N Am 2013;23:833-45.
12. 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.
13. Perri V, Boškoski I, Tringali A, et al. 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. Gastrointest Endosc 2012;75:1271-7.

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