



## No flare(s), no problem: treating recalcitrant pancreatic duct strictures with short fully covered metal stents

Pain, the hallmark symptom of chronic pancreatitis, remains difficult to treat, particularly given the unclear mechanism of pain in this disease.<sup>1</sup> Pain likely results from an interplay between pancreatic ductal and parenchymal hypertension in combination with neural remodeling and sensitization, making it particularly challenging to identify which patients will respond to which treatments.<sup>2</sup>

The first-line treatment for painful chronic pancreatitis typically includes analgesics, and in the United States, this frequently entails opiate therapy. In addition to contributing to the growing epidemic of opiate use in the United States, treatment with opiates is associated with higher rates of hospitalization in patients with chronic pancreatitis, further emphasizing the need for effective nonfoliate treatments for this disease.<sup>3</sup>

Operating on the basis of improving pancreatic duct obstruction and hypertension, pancreatic endotherapy offers a potential treatment option for morphologic adverse events of chronic pancreatitis, such as pancreatic duct strictures and stones, in addition to pancreatic fluid collections. From this standpoint, endoscopic dilation and stent placement represents a primary treatment modality for symptomatic main duct strictures associated with upstream ductal dilatation.<sup>4</sup> Stent placement can be performed with 1 or multiple plastic stents, with removal/exchange at intervals determined by the endoscopist. Although stent placement has been shown to be effective in improving short-term and long-term pain, a subset of patients will experience recalcitrant pancreatic duct strictures that simply do not respond to conventional plastic stents.<sup>4</sup> Within this context, several groups have evaluated the use of fully covered self-expanding metal stents as a salvage maneuver for these strictures.<sup>5-7</sup> Although currently available metal stents are designed for biliary indications, limited case series have found high success rates for pancreatic strictures but with the important caveat that randomized studies have not been performed for refractory pancreatic duct strictures.

In this issue of *Gastrointestinal Endoscopy*, Lee et al<sup>8</sup> examine the use of a novel nonflared, short, fully covered metal stent (Bon stent M, Standard Sci Tec Inc,

Seoul, South Korea) in a single-center prospective trial including 25 Korean patients with painful chronic pancreatitis and ductal strictures in the head or body that did not respond to treatment with a single plastic stent. Designed to address adverse events related to fully covered metal stents in the pancreatic duct, this stent (8-mm or 10-mm diameter) has rounded margins with no flares at the 2 ends of the stent in an attempt to reduce the risk for the development of de novo stent-induced strictures, which can occur at rates over 25% with metal stents in the pancreas.<sup>5</sup> Furthermore, to reduce the risk of migration, the stent has a central saddle-shaped portion 1 to 3 cm

As for the risk of blocking or “jailing” the side branches of the pancreatic duct, this remains a concern with fully covered metal stents; however, recent studies examining these stents in the pancreatic duct have reported low rates of postprocedure pancreatitis or pancreatic sepsis, which begs the question of what role side branch occlusion plays in pain pathogenesis.

long that is designed to be placed directly across the stricture. Available in lengths of 3 to 7 cm, the stent is short and can be placed intraductally because it contains a lasso system at the distal end of the stent that allows for easy removal. All stents were successfully placed; 14 (56%) were placed entirely intraductally. After 3 months, these stents were removed, and 1 case of downstream migration of the stent (after complete resolution of the stricture) was observed. Stricture resolution and pain relief were noted in all patients after stent removal. No de novo strictures or episodes of cholangitis occurred after stent placement. With regard to long-term outcomes, at a median follow-up time of 34 months, pain redeveloped in 3 (12%) patients, with recurrence of pancreatic duct stricture in 2 of these patients (18 and 24 months after stent placement), and repeated stent placement was performed in both.

The authors should be applauded for this prospective pilot study investigating the use of a novel stent. In the nearly 3 years of follow-up, the need for repeated stent

placement in only 2 patients is encouraging, although information regarding sustained pain improvement on visual analog scales, hospitalizations, and requirement for pain medication is lacking. Fully covered self-expanding metal stents have consistently shown high stricture resolution rates in patients with refractory pancreatic duct strictures, but the primary advantage of the studied stent is its low adverse event rate. Stent migration remains a concern with any form of stent placement, particularly if it occurs before stricture resolution. In prior studies, stent migration rates have been reported as high as nearly 50%, particularly with shorter stents.<sup>5</sup> Although theoretically this may be due to the central saddle shape of the stent to mold better in addition to the shorter length of this stent, larger studies will be needed to verify the low rate of migration.

Over half of the stents were placed intraductally, which presents another potential advantage of this stent. The lasso feature facilitated removal of the stents, and future studies should examine the possibility of placing several intraductal stents to treat multiple strictures across the pancreatic duct, including tail strictures that were excluded from this study. The concept of multiple short intraductal stents needs to be tempered, however, in multifocal strictures where a single long stent may suffice and in diffuse strictures where the central saddle portion may be too short to cover the stricture adequately. Perhaps most importantly in the study, no de novo strictures associated with stent placement occurred, which has previously been an unfortunate adverse event of both plastic and metal stents that is difficult to manage.<sup>9</sup> This may be related to the relatively short period before stent removal, and studies are needed to see whether longer indwell times (ie, 6 months, as in biliary stents) will be associated with stent-associated strictures but possibly more durable resolution of stenoses.

As for the risk of blocking or “jailing” the side branches of the pancreatic duct, this remains a concern with fully covered metal stents; however, recent studies examining these stents in the pancreatic duct have reported low rates of postprocedure pancreatitis or pancreatic sepsis, which raises the question of what role side branch occlusion plays in pain pathogenesis.<sup>5-7</sup> Regardless, the short length of these stents minimizes the area of coverage, which may reduce the risk of side branch obstruction.

In terms of future directions, multicenter prospective studies examining the use of fully covered metal stents are under way (NCT02802020), and comparative studies between different types of stents within populations around the world will be needed. Much as metal stents designed for biliary indications were found to be noninferior to plastic stents in resolving benign biliary stricture and decreased the number of ERCPs needed for stricture resolution, randomized trials comparing metal stents

specifically designed for the pancreatic duct with plastic stents as first-line therapy with cost-effectiveness analyses should be a future goal.<sup>10</sup> Additionally, although a prior randomized controlled trial demonstrated superiority of surgical drainage over endoscopic stenting in obstructive chronic pancreatitis, it remains true that ductal hypertension represents only a single component of the multifactorial pain mechanism and that many patients prefer nonsurgical options; therefore, well-designed studies are needed comparing metal stents with surgery to help guide endoscopic treatment algorithms.<sup>11</sup>

Most importantly, studies in which the primary outcome is a technical outcome rather than a patient-centered outcome, assessing the patient's life and health outcomes with these treatments is a limitation. We may be seeing morphologic improvement, but is the patient's quality of life or functional status improving? Certainly, in a pilot study, an outcome such as stricture resolution is perfectly acceptable, but to get to the next level of meaningful impact, future studies involving this stent and pancreatic endotherapy in general for this population would best serve these patients by focusing on patient-centered outcomes such as quality of life (NCT03632616).

Finally, the study by Lee et al<sup>8</sup> provides further evidence of the safety and efficacy of modified fully covered metal stents for recalcitrant pancreatic duct strictures. For a chronic disease in which no treatment other than complete removal is curative, the treatment options remain limited. This approach adds another tool to the arsenal available to endoscopists in the management of this difficult disease process.

## DISCLOSURE

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## REFERENCES

1. Majumder S, Chari ST. Chronic pancreatitis. *Lancet* 2016;387:1957-66.
2. Drewes AM, Kempeneers MA, Andersen DK, et al. Controversies on the endoscopic and surgical management of pain in patients with chronic pancreatitis: pros and cons! *Gut* 2019;68:1343-51.
3. Olesen SS, Poulsen JL, Broberg MC, et al. Opioid treatment and hypoalbuminemia are associated with increased hospitalisation rates in chronic pancreatitis outpatients. *Pancreatology* 2016;16:807-13.

4. Chandrasekhara V, Chathadi KV, Acosta RD, et al. The role of endoscopy in benign pancreatic disease. *Gastrointest Endosc* 2015;82:203-14.
5. Tringali A, Vadala di Prampero SF, Landi R, et al. Fully covered self-expandable metal stents to dilate persistent pancreatic strictures in chronic pancreatitis: long-term follow-up from a prospective study. *Gastrointest Endosc* 2018;88:939-46.
6. Oh D, Lee JH, Song TJ, et al. Long-term outcomes of 6-mm diameter fully covered self-expandable metal stents in benign refractory pancreatic ductal stricture. *Dig Endosc* 2018;30:508-15.
7. Sharaiha RZ, Novikov A, Weaver K, et al. Fully covered self-expanding metal stents for refractory pancreatic duct strictures in symptomatic chronic pancreatitis, US experience. *Endosc Int Open* 2019;7:E1419-23.
8. Lee YN, Moon JH, Park JK, et al. Preliminary study of a modified, non-flared, short, fully covered metal stent for refractory benign pancreatic duct strictures (with videos). *Gastrointest Endosc* 2020;91:826-33.
9. Adachi K, Yamauchi H, Kida M, et al. Stent-induced symptomatic pancreatic duct stricture after endoscopic prophylactic pancreatic duct stent placement for the normal pancreas. *Pancreatology* 2019;19:665-71.
10. Cote 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.
11. Cahen DL, Gouma DJ, Nio Y, et al. Endoscopic versus surgical drainage of the pancreatic duct in chronic pancreatitis. *N Engl J Med* 2007;356:676-84.

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