Biliary stents for pancreas cancer with obstruction: the problem with plastic

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Patients with pancreatic cancer are often diagnosed after progression to a locally advanced or metastatic stage. Medical students are taught to recognize the classic "painless jaundice" from malignant obstruction of the distal common bile duct in the setting of this dreaded disease, which continues to have dismal survival rates of only 5% (1). Endoscopic placement of a biliary stent is a standard palliative measure for patients with metastatic disease, to relieve jaundice and associated pruritus during the last months of life. Self-expanding metal stents (SEMS) have been found to be more cost-effective than plastic stents for patients whose life expectancy exceeds 6 months (2). In contrast, for patients who present with resectable disease, a multicenter randomized controlled trial has shown that placement of a biliary stent prior to pancreaticoduodenectomy leads to increased rates of complications, and that these patients should proceed directly to surgery (3). This trial did not address the population of patients who undergo neoadjuvant therapy, in an attempt to downstage locally advanced disease and make curative resection possible. Little data exists to guide the decision of which stent-plastic or metal- is best in this population.

The proportion of patients undergoing neoadjuvant chemoradiotherapy for pancreatic cancer is estimated to be only 4.5%. This number stands to grow following the recent publication of data demonstrating a survival benefit, which will likely prompt more centers to adopt neoadjuvant therapy as a standard of preoperative care (4). Patients undergoing this therapy require biliary decompression to safely receive chemotherapeutic agents. The ideal biliary stent in this setting must remain patent for the duration of the pretreatment evaluation, chemoradiotherapy regimen, and post-treatment recovery period. This time interval in most patients amounts to an average of 130-140 days (5). Stent occlusion in these patients can lead to life-threatening

cholangitis and hospitalizations, as well as interruptions in therapy and delays in eventual surgery.

Until the past decade, the use of SEMS was discouraged in preoperative pancreatic cancer patients owing to concerns that these stents might interfere with reconstruction during pancreaticoduodenectomy. The higher costs of SEMS (as much as 15-40 times as much as plastic stents) was also a barrier to their routine use in these patients. As surgeons have become comfortable with removal of metallic stents, this concern no longer has merit and the door has opened to more common use of SEMS during neoadjuvant therapy. In theory, the larger diameter and longer patency rates of SEMS should make them a more attractive option than plastic stents. Metal stents may also reduce the need for unplanned stent exchange in those patients who fail neoadjuvant therapy and need continued palliation until end of life.

Data on stent performance in these patients remains limited, however. A retrospective review of patients undergoing neoadjuvant chemoradiotherapy who had plastic stents placed at the time of diagnosis revealed that more than half of the patients underwent unplanned stent exchange due to stent occlusion or cholangitis. Most of these patients required hospitalization and suffered a delay in their neoadjuvant regimen (5). By way of contrast, a recent prospective evaluation of SEMS by Aadam et al. showed stent malfunction in only 15% of patients who were treated with neoadjuvant therapy (6). Retrospective comparison studies have shown higher rates of occlusion and complications when plastic stents were used during the neoadjuvant period compared to SEMS (7,8). These studies have been somewhat limited by the small numbers of patients who were treated with SEMS, though the favorable performance of metal over plastic was impressive.

In this issue of the Journal of Gastrointestinal Oncology, Adams et al. (9) report a retrospective cohort of 52 patients who underwent biliary stent placement for relief of malignant obstruction from pancreas cancer. All of the patients underwent gemcitabine-based neoadjuvant therapy and 71% of the patients eventually underwent surgery. The investigators collected data on complications, including the need for stent exchange or hospitalization. Patients were followed until surgery, death, or loss to follow-up. Only 11 of 52 patients (21% of the cohort) made it to surgery with their initial stent in place. The authors note that 7 of these patients had an initial plastic stent and 4 had metallic stents. The authors compared stent performance as a ratio of complications per month with indwelling stent, and found that the complication rate in plastic stents was nearly seven times higher than with metallic stents.

The study by Adams *et al.* adds to the growing body of evidence to support the use of SEMS for malignant biliary obstruction in patients undergoing neoadjuvant therapy for pancreas cancer. The strengths of this study include the focus specifically on this subset of patients and the ability to directly compare plastic and metal stent performance. The neoadjuvant regimen and duration between stent placement and surgery is consistent with previous studies.

Limitations of the study include its retrospective design and the small number of patients who initially were treated with SEMS. The authors attempt to overcome the latter limitation by measuring the complication rate per stent, rather than per patient. While this shows a superior complication rate for a metallic stent versus a plastic stent, the authors do not fully describe how much of this time actually includes the period prior to surgery (including the neoadjuvant therapy itself), and how much includes the time following surgery for those 52% of patients who did not have a successful resection.

It is notable that despite the superior performance of SEMS described by Adams *et al.*, the complication rate for stents during neoadjuvant therapy remains quite high. Seven of the 43 patients with an initial plastic stent made it to surgery without a stent exchange (either planned or unplanned). Of the patients with initial placement of SEMS, only 4 of 9 made it to surgery with their initial stent. Both results are disappointing and show a need for improved understanding of the factors that lead to complications in these patients. Metallic stents may perform better in these patients, but there remains room for improvement.

Is the question of plastic versus metal stents now settled in patients undergoing neoadjuvant therapy for pancreatic malignancy? While there is no randomized controlled head-to-head trial between plastic and metallic stents, the evidence thus far is overwhelmingly in favor of improved performance with SEMS. Given the known poor performance of plastic stents - combined with new evidence of the effectiveness of metallic stents - in this population, such a prospective comparison study may be difficult to justify.

Obstacles still remain to the routine use of SEMS for distal biliary obstruction in the setting of presumed pancreatic cancer. When the diagnosis is still in question, the endoscopist may be hesitant to place a metallic stent due to concerns about cost or removability. Certainly some strictures which initially appear malignant may later be found to be due to treatable causes such as chronic pancreatitis or autoimmune pancreatitis. If endoscopic ultrasound with fine-needle aspiration and on-site cytologic review is available, then this dilemma can often be solved at the time of the procedure.

However, EUS is not at widespread at ERCP and many endoscopists (particularly in community settings) will have to rely on a high index of suspicion for placing a metallic stent across a presumed malignant stricture. The concern about removal of the stent in cases of benign disease would seem to be addressed by the use of a covered metallic stent. At this time there is no data specifically on the performance of covered metallic stents in patients undergoing neoadjuvant therapy, though the main factor which makes metallic stents preferable (i.e., larger diameter) is still present.

In summary, the study by Adams *et al.* lends further support to the notion that SEMS are a superior device for management of malignant obstruction in pancreatic cancer patients undergoing neoadjuvant therapy. This patient population is likely to grow as more centers embrace neoadjuvant therapy, so this kind of knowledge is critical to providing the best outcomes for patients facing this lifethreatening illness. It seems increasingly clear that plastic stents are now an obsolete device for management of strictures in pancreatic cancer, and that it is time to embrace metallic stents for all patients with this disease who are not sent immediately to curative surgery, or expected to survive less than six months.

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Boulay. Biliary stents for pancreas cancer with obstruction

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308