

## Preoperative biliary drainage in pancreatic head cancer patients

Pancreatic cancer is considered the second most common gastrointestinal malignancy and the fourth deadliest cancer in the USA. Despite decades of efforts, five-year survival rate remains only close to 5%. The most common risk factor for pancreatic adenocarcinoma is cigarette smoking.<sup>[1]</sup> Another risk factor is long-standing type 2 diabetes mellitus. Patients with type 2 diabetes of >10 years duration have a 1.5-fold increased risk compared with nondiabetics.<sup>[2]</sup> In addition to environmental risk factors, hereditary risk factors such as *BRC A2* and *PALB2* (partner and localizer of *BRC A2*) mutations are strongly linked to pancreatic cancer. Several factors, in addition to disease stage, need to be considered in the selection of patients who will benefit from surgical resection. These include patient's overall health, tumor biology, and the use of neoadjuvant therapy. The required operation for a given patient depends on the location of the tumor. Tumors arising from the head of the pancreas require a pancreaticoduodenectomy (Whipple procedure), while those in the pancreatic tail require a distal pancreatectomy.

Preoperative biliary stenting was introduced in the 1960s and 1970s in an attempt to improve surgical outcomes in patients with pancreatic cancer undergoing curative resection. The theoretical benefit was to correct physiological disturbances caused by hyperbilirubinemia secondary to malignant biliary obstruction prior to operation for improving perioperative morbidity and mortality. Small prospective randomized trials<sup>[3]</sup> and early retrospective studies<sup>[4]</sup> yielded mixed results. In practice, those theoretical benefits of preoperative biliary stenting have not been consistently demonstrated. Plastic stents tend to occlude more rapidly than metal stents and are unable to maintain patency long enough through neoadjuvant therapy for pancreatic cancer.<sup>[5]</sup> A large retrospective analysis comparing stented to unstented patients showed either no significant differences in surgical outcome or increased rates of infection with preoperative biliary stenting.<sup>[6]</sup> Several meta-analyses published over the past decade recommend against routine preoperative biliary stenting in pancreatic cancer patients undergoing curative pancreaticoduodenectomy.<sup>[7]</sup> A recent prospective randomized trial reported a significant increase in overall complication rate in stented patients compared to those proceeded directly to surgery. Many of the reported

complications were related to the stenting itself.<sup>[8]</sup> The efficacy of preoperative biliary drainage (PBD) in patients with malignant biliary obstruction remains controversial.

In this issue the Journal, Togawa *et al.*<sup>[9]</sup> present findings from a multicenter prospective study that assessed the feasibility and safety of PBD using a fully covered self-expandable metallic stent (SEMS). The study was conducted to examine perioperative adverse events related to stent placement. The study involved 26 patients treated for pancreatic head cancer with distal bile duct obstruction from April 2011 to March 2013. Two patients were excluded due to failed SEMS placement. Fully-covered SEMS was endoscopically placed in 24 patients. Among those patients, 7 were deemed unresectable, and 17 underwent surgery at a median of 18 days after stent placement. In the 17 patients who underwent surgery, only two developed preoperative adverse events (one developed cholecystitis and the other had incomplete resolution of jaundice). In this study, the surgeons encountered no intraoperative difficulties attributable to the use of SEMSs in PBD. The patients were then followed-up for 90 days for postoperative adverse events. Study limitations include the small sample size with single-arm nature and inability to enroll the originally planned number of patients.

In their report,<sup>[9]</sup> patients were followed up to eight weeks after stent insertion during which jaundice and liver enzymes were monitored. Only one patient (6%) experienced insufficient resolution of jaundice. The elevated total bilirubin gradually decreased within 45 days after stent placement and before surgery. The optimal duration of biliary drainage before surgery was not established yet. However, a period of at least four to six weeks is needed for the restoration of normal or near-normal liver enzymes.<sup>[10]</sup>

In the study by Togawa *et al.*,<sup>[9]</sup> two of the 24 patients who underwent fully-covered SEMS placement developed cholecystitis, which is similar to the incidence of 10% in previous reports. Several studies reported mixed results regarding the possible association between SEMSs and the risk of cholecystitis. Invasion of the cystic duct by the tumor is considered a risk factor for developing cholecystitis.<sup>[11]</sup>

Many factors can affect postoperative outcomes in patients undergoing pancreatic cancer resection including surgeon/hospital volume, age, sex, reduced serum albumin, elevated serum creatinine, jaundice, and presence of comorbidities.<sup>[12]</sup> Pancreatic surgery performed in high-volume centers is associated with death rates of less than 5%.<sup>[10]</sup> Togawa *et al.*<sup>[9]</sup> conclude that PBD using fully covered SEMSs is safe, feasible, and can reduce the rate of preoperative adverse events in patients with resectable pancreatic head cancer.

In summary, the adverse effects of biliary obstruction on multiple organ systems may adversely impact the postoperative outcome in patients with pancreatic cancer. PBD has the potential to improve surgical outcomes by reversing the detrimental effects through the restoration of bile flow. Percutaneous biliary drainage can be cumbersome for patients to manage and requires significant maintenance. Endoscopic biliary drainage is generally preferred over percutaneous biliary drainage to achieve PBD. SEMSs are favored over plastic stents because of its superior patency rate and less risk of therapy interruption and delay of surgery. However, in light of these findings, more randomized clinical trials with larger cohorts are needed to provide additional insights.

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