

## Management of distal malignant biliary obstruction

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Biliary strictures remain a conundrum regarding diagnostic and management approaches. Traditionally, biliary strictures have been considered indeterminate when the diagnosis could not be established after basic laboratory workup, abdominal imaging, and endoscopic retrograde cholangiopancreatography (ERCP). Although up to 30% of the cases can be benign,<sup>[1]</sup> the vast majority of biliary strictures are considered malignant. Pancreatic adenocarcinoma and cholangiocarcinoma are considered the two major biliary malignancies. In some cases, there are no clinical or radiological features to reliably distinguish benign from malignant strictures. According to the literature, 15–24% of the patients undergoing surgical resection for suspected biliary malignancy have a benign etiology.<sup>[2,3]</sup> Therefore, preoperative determination of malignancy is highly desirable to help plan appropriate treatment, including the need for any type of surgery. The most common causes of benign biliary strictures include chronic pancreatitis, primary sclerosing cholangitis, autoimmune disease (autoimmune pancreatitis or cholangitis), Mirizzi syndrome, ischemic cholangiopathy, and iatrogenic (post-liver transplant or cholecystectomy). Malignant bile duct strictures are usually due to pancreatic adenocarcinoma and cholangiocarcinoma. Less common causes of malignant biliary stricture include metastatic cancer of the pancreas or liver, gallbladder cancer obstructing the bile duct, ampullary tumors growing into the bile duct, or malignant periportal lymph nodes.

ERCP and endoscopic ultrasound (EUS) are the two major endoscopic modalities used in the evaluation of patients with biliary obstruction. ERCP with sampling has been the mainstay, but it is limited by low sensitivity and the risk of post-ERCP pancreatitis. Burnett *et al.*<sup>[4]</sup> reviewed 16 studies with over 1500 patients who underwent ERCP with biliary strictures brushing and found an overall sensitivity of 41.6% and a negative predictive value of 58%. The diagnostic yield of biliary cytology can be increased to 60–70% by using both brushings and biopsies.<sup>[5]</sup> EUS-guided fine needle aspiration is increasingly being used in the diagnostic evaluation of biliary strictures, with sensitivity ranging from 40% to 90%.<sup>[6,7]</sup> Intraductal ultrasonography (IDUS) that involves the insertion of a high-frequency ultrasound probe

into the bile duct over a guidewire has shown a diagnostic accuracy of around 90% in some studies.<sup>[8]</sup> IDUS has not been widely used due to limited experience and availability. Single-operator cholangioscopy system, commonly known as SpyGlass (Boston Scientific, Natick, MA, USA), is another diagnostic modality for biliary strictures, with the ability to obtain direct tissue samples using a 3-Fr biopsy forceps.

Both self-expandable metal stents (SEMS) and plastic stents (PS) can be used in palliation for inoperable distal malignant biliary obstruction (MBO). In a meta-analysis conducted by Harsha *et al.*,<sup>[9]</sup> 11 studies were reviewed, including 947 patients with distal MBO who underwent endoscopic palliative drainage using either SEMS or PS. Pooled analysis showed SEMS to be superior to PS, with better patency periods (167.7 days compared to 73.3 days in PS). Furthermore, lower occlusion rates, cholangitis, and reintervention rates have been associated with SEMS. SEMS have also been shown to be better than PS for biliary drainage in patients going for neoadjuvant chemotherapy and radiation in the setting of borderline-resectable disease.<sup>[10]</sup> Lee *et al.*,<sup>[11]</sup> in a retrospective cohort study, compared covered self-expandable metal stents (CSEMSs) with uncovered self-expandable metal stents (USEMSs) in 749 patients with distal malignant biliary obstruction. The study concluded that there was no significant difference in patency rate or overall survival between CSEMSs and USEMSs groups for distal MBO. A higher rate of stent migration and pancreatitis was noted in the CSEMSs group.<sup>[11]</sup>

For patients with distal MBO, metal stent placement above or across sphincter of Oddi (SO) remains controversial. Jo *et al.*<sup>[12]</sup> compared the efficacy of suprapapillary and transpapillary placement of CSEMSs and USEMSs in patients with MBO. Most of those patients had distal MBO. The suprapapillary stent group had 74 patients (28 USEMSs and 46 CSEMSs), and the transpapillary group had 81 patients (19 USEMSs and 62 CSEMSs). Pancreatitis occurred in 3 patients (4.1%) in the suprapapillary group and 20 patients (25.0%) in the transpapillary group. Stent occlusion by the tumor was more frequently observed in the suprapapillary group, whereas stent occlusion by sludge was more observed in the transpapillary group. No significant difference in cumulative stent patency or patient survival was noted between the groups.

In their study, Zhang *et al.*<sup>[13]</sup> demonstrated efficacy between the suprapapillary and transpapillary placement of USEMS in the management of distal MBO. Retrospectively, they studied 59 patients who underwent USEMS placement for distal MBO between January 2012 and March 2016. In group A, stents were placed above the SO and across the SO in group B. They compared the two groups regarding early-cholangitis, stent occlusion, and overall survival time. Study limitations include retrospective nature and inability to determine the cause of stent occlusion (clogging or tumor growth). The study concluded that the two approaches were not significantly different regarding early-cholangitis, stent patency, or overall patient survival. These data were similar to what was published before. Unlike the previous study, pancreatitis was not significantly different between the two groups. However, no meaningful statistical comparison could be performed because of the small number of patients.

In summary, Zhang *et al.* support the fact that there is no significant difference in the rate of SEMS-related early-cholangitis, stent patency, and overall survival. Whether transpapillary metal stenting in MBO is associated with increased risk of pancreatitis remains unclear, and further randomized control studies with larger sample size are required to answer this question.

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