BILIARY DECOMPRESSION IN PANCREATIC CANCER

Up to 75% of patients with pancreatic cancer develop symptomatic biliary obstruction[1] and both the most recent guidelines from the European Society of Medical Oncology (ESMO)[2] and the National Comprehensive Cancer Network (NCCN) strongly recommend the endoscopic approach for the placement of a metallic biliary stent. Although biliary drainage (BD) is strongly recommended as palliation in advanced pancreatic cancer to provide relief of biliary and/or duodenal obstruction, malnutrition, and pain,[2] studies do not recommend presurgical BD.[3,4] However, based on the most recent evidence, including a randomized controlled trial, both the ESMO and NCCN guidelines suggest routine preoperative BD only in selected patients with symptomatic jaundice, cholangitis, or with an expected delay to surgery.[2,5,6]

The endoscopic method is the first-line treatment for biliary obstruction. A recent study compared endoscopic and percutaneous drainage in a population of 9135 patients from the Nationwide Inpatient Sample;[7] it showed that endoscopic BD through endoscopic retrograde cholangiopancreatography (ERCP) has fewer adverse events compared to the percutaneous approach for malignant biliary tract obstruction (8.6% vs. 12.3%; P < 0.001), even considering only the pancreatic cancer subgroup (2.9% vs. 6.2%; P < 0.001). Despite this, the results of another meta-analysis have found a better outcome, although no significant, in favor of percutaneous biliary drainage (PTBD) over ERCP in the drainage of malignant biliary obstruction.[8]

ERCP is limited in cases of gastric outlet or duodenal obstruction not susceptible for endoscopic dilation and enteral stenting and in cases of postsurgical altered gastrointestinal anatomy (Roux-en-Y gastric bypass, Kausch–Whipple resection, pylorus-preserving Whipple resection, Roux-en-Y hepaticojejunostomy, cholecdochojjunostomy, and pancreaticojjunostomy), while patients with a previously performed surgical Billroth I and II gastrectomy may be not an issue for conventional ERCP.[9] When ERCP fails, PTBD with subsequent internalization may be necessary. PTBD is a well-recognized treatment modality in the management of biliary obstruction and above all in cases of failure of the endoscopic approach and altered gastrointestinal anatomy. There is no absolute contraindication for PTBD.

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and relative contraindications are limited to coagulation disorders, allergy to iodinated contrast agents, and ascites. Coagulopathy may be corrected or adjusted before the procedure, and an allergic reaction can be prevented.

An alternative method to PTBD is endoscopic ultrasound-guided BD (EUS-BD). There is growing evidence that the EUS-guided approach is comparable to PTBD in terms of efficacy and safety. However, its application is available only in a few centers and significant expertise is required to perform reliable examinations. Currently, it has not yet found a recommendation, and randomized controlled trials are required to further evaluate its efficacy and safety in comparison with the traditional modalities.

**STANDARDS OF PRACTICE FOR PERCUTANEOUS TRANSHEPATIC CHOLANGIOGRAPHY**

Before any procedure, patients should undergo multiphase contrast-enhanced computed tomography and/or magnetic resonance imaging with magnetic resonance cholangiopancreatography. PTBD should never be performed without a proper noninvasive evaluation of the biliary tree.

In accordance with the “quality improvement guidelines for percutaneous transhepatic cholangiography and biliary drainage” published by the Society of Interventional Radiology and shared by the Cardiovascular and Interventional Society of Europe, the threshold of technical success rates after PTBD should be as high as 95% and 70%–80% in cases of dilated and nondilated bile ducts, respectively. To improve the procedure success rate, especially in patients with nondilated ducts and for the left-sided approach, ultrasound (US) guidance should be considered. Reported rates of clinical success, defined as the resolution of symptoms, are above 75% to improve the clinical outcome the radiologist should monitor and manage the patient who has undergone PTBD.

One of the main advantages of PTBD over ERCP is the possibility of avoiding cannulation of the papilla, virtually nullifying the risk of acute pancreatitis, especially in surgical patients. When ERCP is performed, the risk of developing pancreatitis is about 3.5%, however, in some studies, rates reached up to 15.7%. Moreover, in our opinion, percutaneous cholangiography allows a clearer representation of the biliary tree and a better comprehension of anatomic variants, than ERCP. This is particularly relevant in case of abnormal insertion of biliary ducts that, if not detected and are excluded by the placement of covered stents, may evolve to cholangitis.

Adverse events include hemorrhage (1.42%), biliary leak (1.42%), sepsis (6.25% including abscess, peritonitis, pancreatitis), and recurrence of obstructive jaundice (3.27%). Most of the complications are immediate and are treated conservatively or by interventional radiology. According to “quality improvement guidelines,” the ceiling for all major complications of percutaneous transhepatic BD should be 10%; centers with higher complication rates should make an internal review of methods and procedures.

For distal obstructions, right-sided procedures are preferred, since left-sided PTBD is associated with a slight, but no significant increase in clinically relevant hemobilia of 1.5%–5.2%. Internal/external tubes may present problems related to inadequate bile flow or dislodgement, leading to septic complications and hemorrhage; these risks can be minimized with 8-10 Fr locking catheters placed through the ampulla or anastomosis. Appropriate antibiotics should be administered before initiating the procedures to prevent sepsis, and the duration of antibiotic therapy should be tailored on the clinical course of individual patients. With the percutaneous approach, in addition to internal/external drainage, a biliary stent can be placed. An uncovered self-expandable metal stent is the most common, with or without balloon (pre-) dilatation and with the distal end going across the papilla. This improves BD and reduces the risk of postprocedure cholangitis. A transprosthesis internal/external 8 Fr tube (or a smaller catheter) is left along the percutaneous/transhepatic track for the first 48–72 h following stent placement to minimize the risk of postprocedure biliary sepsis and bleeding from the liver capsule at the puncture site. In case of stent obstruction, due to biliary sludge or tumor growth, PTBD can be repeated with a coaxial metal stent placement.

Procedure-related death has been reported with rates of up to 5.6% in an old published series, but technical improvements and implementation of US guidance for bile duct puncture have dramatically reduced the rates of morbidity and mortality. However, the “standard of practice” suggests a threshold for mortality of 3%, which, in our opinion, is still too high to be tolerated.
HOW TO IMPROVE PERCUTANEOUS BILIARY DRAINAGE

We analyzed multiple aspects that should be improved for a better PTBD outcome. First of all, the use of US for puncture guidance [Figure 1] reduces the risk of hemorrhage and pleural transgression, preventing pneumothorax, hemothorax, and biliary pleural effusions. Patient selection and classification by risk stratification can also be useful to predict rates of possible complications, and sometimes, can intervene where possible to reduce risks. As for ERCP procedures, where in high volume centers, each endoscopist performs >25 ERCP per year, we should reserve the performance of PTBD only to such specialized centers, since in a comparison of PTBD performed in centers with low and high volumes, the rates of adverse events are significantly different ($P = 0.001$), 7.61% and 5.62%, respectively. Ultimately, a preoperative anesthesiologic evaluation, perioperative support and dedicated materials and devices can also change the outcome of the procedure.

FUTURE PERSPECTIVES

The latest generation of flexible fiberoptic choledochoscopes has increased the interest of interventional radiologists for direct visual exploration of the biliary tree; under direct vision, it is possible to perform bioptic sampling and narrow differential diagnosis of biliary strictures. With modern equipment and flexible fiberoptic choledochoscopes, the percutaneous transhepatic access is limited to 9–10 Fr and the complication rate of cholangioscopy does not exceed that of PTBD. Rather than in the first-line treatment of patients with pancreatic cancer, this method finds more application for upper biliary tract diseases, in patients with previous surgeries, and/or altered gastrointestinal anatomy.

PERCUTANEOUS BILIARY DRAINAGE AT LARGE-VOLUME CENTER

In 2016, in our institution, considered of high volume according to ERCP considerations (defined as >25/year/interventional radiologist), four interventional radiologists performed 128 percutaneous transhepatic BDs; each interventional radiologist performed about 32.5 PTBD per year. Our results are comparable with those of recently published series. Technical success was reached in 125 cases (98%); 42 of 128 cases presented with a previously failed ERCP; in this subgroup, technical success was 100%, and a percutaneous drainage or an uncovered self-expandable metal stent was placed respectively in 30 and 12 cases. Forty-six patients presented altered anatomy due to previous surgery and were not eligible for ERCP, one of which underwent a Rendezvous technique. A Rendezvous approach was also applied in two other patients with normal anatomy after a failed ERCP. No deaths due to PTBD complications were recorded. Of note, no cases of clinically relevant pancreatitis were observed. Cases of hemorrhage were successfully managed with intra-arterial embolization by the same interventional radiologists. Septic adverse events were managed with intravenous antibiotics and positioning of larger internal/external catheters (10–12 Fr), with a resolution of symptoms. Annual clinical records of PTBD in our institution are shown in Table 1.

CONCLUSION

In patients with pancreatic cancer presenting with distal biliary obstruction, the first-line treatment should be endoscopic. In case of failed ERCP, the PTBD is a valid method that presents a low complication rate, with even better rates when performed in high-volume centers. Furthermore, the US-guided percutaneous...
puncture reduces complications, that are mostly treated conservatively or in the interventional radiology (IR) theater. An alternative to PTBD may be EUS-guided BD, but this approach still lacks sufficient evidence to be applied on a large scale; prospective robust randomized trials are necessary. In conclusion, in large volume center with qualified interventional radiologists, in case of ERCP unfeasibility or failure, we still recommend the percutaneous approach, favored by higher rates of technical success and lower rates of complications.

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