

## Hot topics in therapeutic EUS

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Over the years, EUS has become an important tool for diagnosis in gastrointestinal diseases. Fine needle aspiration (FNA)/fine needle biopsy (FNB) has opened a path for interventional EUS that nowadays, it is gaining an increased interest in the therapeutic arsenal.<sup>[1]</sup> The possibility to reach such deep structures as pancreas and biliary tree under real-time imaging extended the uses of therapeutic EUS from clinical to experimental applications, especially in oncologic treatment.<sup>[1]</sup>

For decades, ERCP and percutaneous biliary drainage (PTCD) are the first choices in malignant biliary obstruction. EUS-guided biliary drainage (EUS-BD) is now an alternative when ERCP or PTCD fails.<sup>[2]</sup> EUS-BD includes EUS-guided choledochoduodenostomy for distal biliary obstructions, EUS-guided hepaticogastrostomy (EUS-HGS) for proximal biliary obstructions, or EUS-guided hepaticoduodenostomy for isolated right intrahepatic duct dilatation.<sup>[2-4]</sup> Combined approaches through EUS-guided rendezvous for failed biliary cannulation during ERCP with intrahepatic or extrahepatic approaches have a technical success rate over 80%.<sup>[5]</sup> EUS-guided antegrade stenting is also feasible but

with a relatively high rate of complications.<sup>[6]</sup> Studies comparing ERCP or PTCD with EUS-BD techniques for the treatment of distal biliary obstructions are still very limited but showed similar clinical success rate and adverse events for ERCP *vs.* EUS-BD and slightly better clinical success and fewer adverse events for EUS-BD *vs.* PTCD.<sup>[2]</sup> Some centers prefer EUS-BD over PTCD because of low risk of cholangitis and displacement of the biliary drain. However, complexity of interventional EUS makes it available for now only in high-volume centers with expertise in this field.

Stereotactic body radiation therapy (SBRT) has an important role in the treatment of pancreatic ductal adenocarcinoma.<sup>[7]</sup> SBRT requires fiducial placement for better tracking the target and avoiding radiation to the adjacent normal structures.<sup>[8]</sup> Fiducials are liquid (hydrogel) or solid (gold, platinum, or carbon) radiopaque markers with high contrast and different shapes placed in the tumor through an FNA 19- or 22-gauge needle or preloaded EUS needles.<sup>[8]</sup> The 22-gauge needles are preferred because of the easy

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introduction of the markers when the access to the tumor needs transduodenal approach.<sup>[8]</sup> Studies reported a technical success rate of 96.27% in 820 patients with pancreatic cancer that received EUS-guided fiducials placement.<sup>[9]</sup> The migration rate of fiducials was reported to be 4.33% in a systematic review of seven studies conducted by Patel *et al.* and 3% in another review of five studies.<sup>[10]</sup> In a small study on 51 patients, Sanders *et al.* had a 7% rate of migration.<sup>[11]</sup> Minor adverse events have been reported with an incident rate of 4.85%.<sup>[12,13]</sup> Small pancreatic neuroendocrine tumors (PNETs) that are impossible to be palpated by the surgeon intraoperatively can be efficiently marked before surgery with fiducials.<sup>[14]</sup>

EUS-guided ablation therapy has already been described for the treatment of inoperable PNETs, pancreatic cystic neoplasms (PCNs), and pancreatic metastases using radiofrequency ablation (RFA) with results compared to surgery.<sup>[15]</sup> In the past, ablation therapy for locally advanced pancreatic cancer (LAPC) was performed intraoperatively or percutaneous but with a relatively high rate of major complications. Recently, there is an increased interest for EUS-RFA in the palliation treatment of LAPC because of the easy and minimal invasive approach. EUS-RFA for PNET and PCNs showed partial or complete resolution of the cysts and central necrosis of the PNET with no major complications.<sup>[15]</sup> EUS-RFA for functioning insulinomas obtained complete resolution of the symptoms in 100% of the cases after single or multiple sessions.<sup>[16]</sup> A prospective study of 12 patients with pancreatic metastases from renal cell carcinoma in whom EUS-RFA was performed, with a median follow-up of 27.7 months, obtained complete response at 12 months in 40% of the treated lesions.<sup>[17]</sup> Major complications were represented by duodenal and hepatic abscess.<sup>[17]</sup> EUS ablation for LAPC was described in few studies, with a short follow-up but with satisfactory results in terms of safety and technical success rate. Adverse events reported were managed medically, and no major complications were reported.

Until recently, pancreatic drainage of collections, obstructed biliary, and pancreatic ducts was performed using double pigtail plastic or metal stents designed for ERCP use. Lumen-apposing metal stent (LAMS) with cautery-tipped was designed for better drainage and debridement of necrotic pancreatic collections and represents the first option for EUS-BD, EUS-guided gallbladder drainage, and gastrojejunostomies. For EUS-HGS, a hybrid biliary partially half-covered and uncovered self-expandable metal stent is usually used.

Axios (Hot Axios, Boston Scientific) and Spaxus (Niti-S Spaxus, Taewoong Medical) are the main LAMSs at the moment, made of nitinol wire, with double flanges for lumen apposing and fully coated to prevent leakage.<sup>[18]</sup> The only preloaded fiducial needles are the Echotip 22-gauge needle manufactured by Cook Medical that contains four fiducial markers and both 19-gauge and 22-gauge needles preloaded with two markers produced by Medtronic.<sup>[18]</sup> The RFA probes available used until now are represented by monopolar Habib, EMCision Ltd. That require the introduction through a 19- or 22-gauge FNA needle and a specially designed RFA bipolar probe, with variable length of the active tip, inserted directly into the tumor through the working channel of the echoendoscope, VIVA RF generator, STARmed.<sup>[18]</sup>

Another application of diagnosis and therapeutic EUS under the concept of “Endo Hepatology” includes liver biopsies, liver ablations, measurement of portal pressure gradient (PPG), and EUS-guided treatment of gastric varices. For the assessment of liver fibrosis, EUS-guided liver biopsy is noninferior in terms of safety, efficiency, and diagnostic accuracy compared with percutaneous or transjugular liver biopsy.<sup>[19]</sup> Measurement of hepatic venous pressure gradient is the gold standard for the evaluation of portal hypertension. EUS-guided measurement of the PPG is possible through a compact manometer attached to a 25-gauge FNA EUS needle introduced in the portal vein. PPG measurement has excellent accuracy with the results obtained by the transjugular route and strong correlation with clinical parameters of portal hypertension.<sup>[20]</sup>

Recent development of therapeutic EUS and technological improvement of the accessories used are providing various modalities of innovative treatment in different pancreatic and biliary diseases.

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