ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: Klaus Mergener, MD, PhD, MBA

Interventional Endoscopic Ultrasound: Next Frontier or Dead End?

Marc Giovannini, MD
Scientific Director of Interventional Gastroenterology
IRCAD
Strasbourg, France

G&H Could you describe how the field of interventional endoscopic ultrasound evolved?

MG The endoscopic ultrasound (EUS) technique was initially used in the early 1980s as a combination of ultrasound imaging and endoscopic examination. A mechanical radial ultrasound probe was placed on the tip of the endoscope to perform an EUS examination of the esophageal wall, gastric wall, duodenum, and rectum. During the first 10 years, from 1980 to 1990, this technique was used only for diagnostic purposes because the radial probe provided transverse images similar to computed tomography scans. Although the probe scans allowed easier assessment of the anatomy, the view is perpendicular to the endoscope's axis, rendering it impossible to obtain even a small biopsy or to perform an intervention with the endoscope. Early in 1990, an electronic linear probe was introduced that had many advantages over the mechanical radial probe. The goal of the electronic linear probe endoscope was to perform a transmural biopsy using fine-needle aspiration (FNA) to target the lesion, such as a lymph node or pancreatic lesion. Prior to this innovation, in a patient with an isolated lymph node in the abdomen, for example, obtaining the histology of the lymph node required open surgery, which, of course, is associated with high risk and poor outcome for the patient. In the early 1990s, the first clinical use of the electronic linear probe for EUS-guided FNA was pioneered by Vilmann and colleagues in Copenhagen, Wiersema and Chang in the United States, and myself. Together, we published in 1997 the first combined study of more than 400 patients who underwent EUS-FNA. The linear echoendoscope was the first step in the development of therapeutic EUS. However, at that time, therapeutic EUS was limited by the small size of the working channel of the endoscope; the 2-mm working channel made it impossible to use larger therapeutic accessories. Another limitation of older fiberscopes was the lack of an elevator, which made it impossible to target lesions adequately. The development of the video echoendoscope with large working channel and elevator was an important innovation that helped the transition to therapeutic EUS. In 2001, I had the opportunity to perform the first EUS-guided bilioduodenal anastomosis using this therapeutic echoendoscope in a patient with obstructive jaundice caused by a pancreatic mass. These milestones marked the beginning of the story of therapeutic EUS.

> The development of the video echoendoscope with large working channel and elevator was an important innovation that helped the transition to therapeutic EUS.

G&H What are the latest stent technologies used for EUS-guided drainage of pancreatic pseudocysts and walled-off necrosis?

MG The luminal-apposing metal stent (LAMS) is the latest technology and could potentially replace the plastic stent, although there is some debate among the experts regarding use of the LAMS vs the plastic stent. The first

LAMS (AXIOS stent, Boston Scientific) was developed by Binmoeller and Shah, with the goal of being able to perform an anastomosis between a cyst and the gastric wall. With this stent, it is possible to push the structures close together, creating a large opening to enter the cyst and perform necrosectomy, debridement, and fluid aspiration. However, there is always a place for the plastic stent because the LAMS is not a panacea. A LAMS is useful in the case of infected necrosis and in patients with acute pancreatitis because it facilitates easier access and cleaning of the cavity. Use of a LAMS has replaced the surgical procedure, which has high morbidity and mortality for the patient. Today, first-line treatment of walled-off necrosis is to perform debridement through a LAMS, which is later replaced with double-pigtail plastic stents. These are kept in for a minimum 6 months to 1 year to prevent disconnected pancreatic duct syndrome owing to a huge pseudocyst. Now, many medical device manufacturers provide the LAMS, which is useful for more than just pseudocysts.

G&H Since the early days of therapeutic EUS, how has the range of EUS-guided interventions expanded?

MG Interventional endoscopists have many procedures to choose from. Starting from the early more simple procedures to the more difficult and more recent procedures, the first, of course, is EUS-FNA with biopsy. This is just to obtain histology of the mass, but this is the first preliminary step. After this is celiac neurolysis, which is the injection of alcohol into the celiac plexus to treat pain of the patient with advanced pancreatic cancer. Another procedure is pancreatic fluid collection drainage using a LAMS with a double-pigtail stent. After that is biliary drainage, or hepaticogastrostomy, which is the drainage of the left lobe of the liver into the stomach with a partially covered stent or fully covered stent. The next step after this procedure is EUS-guided gastrojejunal anastomosis, which establishes a connection between the stomach and the jejunum using a 20-mm dedicated LAMS; this will likely replace the gastrojejunal surgical approach. The LAMS can also be used for patients who have had gastric bypass for obesity. In these patients, a stone in the common bile duct (CBD), pancreatic cancer, or other pathology can develop years after the procedure. In this case, the endoscopist needs to reconnect the 2 stomachs—the small residual stomach with the larger excluded stomach. A LAMS can be placed to reconnect the 2 stomachs and to pass the endoscope inside to reach the excluded stomach. Considered the most technically difficult EUS-guided procedure, drainage of the pancreatic duct is performed in patients with chronic pancreatitis when endoscopic retrograde cholangiopancreatography (ERCP) fails. EUS-guided ERCP is another procedure. One of the most recent therapeutic EUS procedures is radiofrequency ablation of a tumor (eg, for neuroendocrine tumors or for some pancreatic metastasis from renal cancer). Another new EUS-guided treatment being studied is radiotherapy, involving the local injection of phosphorus-32, a radioactive liquid, into a tumor. All these procedures represent the vast range of therapeutic EUS interventions available today, and this is likely just the beginning.

G&H Could you give a brief overview of recent advances in EUS-guided biliary access and drainage techniques, such as hepaticogastrostomy and bilioenteric stenting?

MG Today, there is a question about whether to perform ERCP or EUS first. The answer is not so clear, for example, with choledochoduodenostomy for a patient with tumoral invasion, pancreatic cancer, or tumoral invasion of the distal part of the bile duct or the proximal part of the bile duct. For EUS, a large CBD of more than 15 mm is needed to insert the LAMS safely.

> The fully covered stent with side holes is a recent development designed to prevent obstruction of the side branch and may be the best stent to use today to perform hepaticogastrostomy.

However, if the CBD is less than 15 mm, it is better to do ERCP. In fact, the best indication for EUS-guided choledochoduodenostomy is the patient with a large CBD with high risk of acute pancreatitis because there is no risk of acute pancreatitis with EUS. In particular, the female patient with a normal pancreatic duct, I think, is the best indication to start with EUS-guided choledochoduodenostomy. In other cases, it is better to start with ERCP and, if unsuccessful, then proceed to EUS-guided choledochoduodenostomy.

The best indication for hepaticogastrostomy is the patient with altered anatomy or duodenal cancer leading to stenosis, in which it is impossible to reach the papilla.

Of the 2 types of stents available today, the partially covered stent is easy to insert and there is no risk of migration, but the patency of this stent is lower than that of a fully covered stent. However, the fully covered stent may occlude the side branch and induce cholangitis. The fully covered stent with side holes is a recent development designed to prevent obstruction of the side branch and may be the best stent to use today to perform hepaticogastrostomy. Another recent development for EUS-guided biliary drainage is the multiple axillary access technique for patients with complex biliary stenosis, in particular patients with cholangiocarcinoma of the ileum with multiple stenoses. It is now possible to do one drainage of the right lobe of the liver by ERCP, the left lobe of the liver by EUS, or everything by EUS, or to combine EUS, ERCP, and percutaneous transhepatic biliary drainage to have the best drainage. The reason for this is because effective treatment for cholangiocarcinoma, including immunotherapy, can now be provided by the oncologist. The goal is to obtain the best drainage for the patient, and this can increase patient survival. It is essential to work closely with the oncologist and to adapt the drainage for the patient with cancer.

G&H How has interventional EUS influenced the field of endo-hepatology?

MG This is not my specialty, but the field of endo-hepatology is interesting because the goal is to use EUS to perform in one visit every step of management for the patient with advanced liver disease. This includes staging of portal hypertension, gastric varices, and portal vein thrombosis, with splenic vein measurement and measurement of portal vein pressure, hepatic vein pressure, and portal pressure gradient. The results of these tests are important in patients with cirrhosis or metabolic dysfunction-associated steatohepatitis to detect and prevent the development of fibrosis. EUS-guided portal pressure measurement can potentially replace the current standard transjugular hepatic venous pressure gradient measurement, an invasive procedure that requires feeding a catheter into the jugular vein to the hepatic vein. The single visit could also include EUS-guided liver biopsy, which is possible with the new 19-gauge histology needle. The needle provides access in the portal space to evaluate for fibrosis and to biopsy both the left and right lobes of the liver. Lastly, shear wave elastography can be used with the latest generation of EUS scanner, as studies show that shear wave elastography under EUS guidance performs similarly to vibration-controlled transient elastography (FibroScan) for assessing liver fibrosis. Having a 1-step evaluation for staging of the potential fibrotic liver is appealing. The goal now is to convince the pathologist.

G&H From a technical standpoint, what principal equipment-related limitations or challenges remain in interventional EUS practice?

MG First, it is important to know the anatomy of the patient. It is not possible to do a good therapeutic procedure without knowing the anatomy. Artificial intelligence (AI) will probably help endoscopists and endoscopy beginners understand the anatomy better. Regarding the technology, the current echoendoscope and EUS machine are good. Having a larger working channel is probably not needed. Perhaps a thinner echoendoscope with the same large working channel and elevator will be developed and more dedicated accessories may be needed. A limitation of therapeutic EUS is the repeated exchange of accessories. Reducing the number of accessory exchanges or having a 1-step or 2-step procedure with accessories would be best.

G&H What is the recommended training route for endoscopists aiming to gain expertise in interventional EUS, and where should this training ideally take place?

MG There is a major debate in Europe, and probably in the United States, regarding the curriculum for therapeutic EUS. For younger endoscopists, the goal is to learn ERCP and therapeutic EUS in parallel and to be focused on hepatobiliary therapeutic procedures. With the current number of procedures, it is impossible to become an expert in all of them. I do not recommend having the endoscopist choose between performing endoscopic submucosal dissection and endoscopic mucosal resection or performing hepatobiliary endoscopic procedures because it is time-consuming, and the endoscopist needs to be more specialized than before. The general endoscopist is finished, in my opinion. During my scientific life, when I started 40 years ago, I performed everything. However, over time, as procedures have become more and more complex, I have reduced the number of procedures I perform and have focused on the hepatobiliary procedure. Regarding the training for interventional EUS, endoscopists need to learn in parallel and to have a staging unit in which to perform a huge number of therapeutic EUS procedures. In the future, the curriculum for therapeutic EUS will probably be for a limited number of endoscopies, not for every kind of endoscopy.

G&H Will AI in EUS be a valuable training tool or just an expensive toy?

MG AI will be helpful not for performing therapeutic EUS, but for training to reduce the learning curve. The most advanced AI program available can show the

trainee the anatomy. AI can also show the position of the endoscope in the patient and indicate whether the trainee has performed a complete examination. For example, if a trainee missed one of the stations in the pancreas, the EUS system will give a warning that the examination is incomplete, and the trainee can go back to see the area that was missed. This use of AI is helpful. I am against use of AI to show whether tissue is a tumor. The AI tool can show some abnormality in the pancreas; however, the endoscopist must interpret the finding and determine whether the lesion is malignant, benign, or something else. If not, we will disappear.

G&H Has interventional EUS reached a plateau, or are there still meaningful opportunities for growth and innovation?

MG Not mentioned yet is the potential for interventional EUS to be used for other indications, for example, to treat gastric varices with coiling or injecting glue. It is possible that the field is in a plateau, but it is a plateau in which there will be development of some small niches for any new indication. This plateau is necessary because what is needed now is to find the real place for each therapeutic EUS procedure that is being performed today. Again, therapeutic EUS is not always the panacea. For the best therapeutic decision-making, we need to choose what is best for the patient. During the last 5 to 10 years, multiple indications have been explored. The development of accessories such as the LAMS has opened many other possibilities. In the future, other accessories will probably become available, and there may be a slight increase after this plateau.

Disclosures

Professor Giovannini has no relevant conflicts of interest to disclose.

Suggested Reading

Binmoeller KF, Shah J. A novel lumen-apposing stent for transluminal drainage of nonadherent extraintestinal fluid collections. *Endoscopy.* 2011;43(4):337-342.

Giovannini M, Moutardier V, Pesenti C, Bories E, Lelong B, Delpero JR. Endoscopic ultrasound-guided bilioduodenal anastomosis: a new technique for biliary drainage. *Endoscopy.* 2001;33(10):898-900.

Wiersema MJ, Vilmann P, Giovannini M, Chang KJ, Wiersema LM. Endosonography-guided fine-needle aspiration biopsy: diagnostic accuracy and complication assessment. *Gastroenterology.* 1997;112(4):1087-1095.