ADVANCES IN ENDOSCOPY

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Endoscopic Management of Gallbladder Disease

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G&H What are the main types of gallbladder disease, and how have they traditionally been managed?

SI Benign gallbladder conditions such as gallstones, inflammation (cholecystitis), and polyps are the most common forms of gallbladder disease. Gallbladder cancers, although rare, can be very aggressive and often present late in the disease course.

Cholecystectomy continues to be the standard of care for managing all gallbladder diseases, both benign and malignant, although treatment of acute cholecystitis has evolved over the last 5 to 10 years. Patients who are not surgical candidates were traditionally managed with percutaneous drainage of the gallbladder, a procedure that started in the 1970s in which an interventional radiologist passes a needle through the abdominal wall, often through the liver, and into the gallbladder, most commonly under ultrasound guidance. A guidewire is then placed in the gallbladder, over which an 8-French percutaneous drain is placed to allow the gallbladder to decompress or drain externally. Challenges with percutaneous drains are the pain and dyscosmesis associated with an external drain and the need for multiple reinterventions due to dislodgements or occlusion.

G&H What endoscopic approaches are available, and how are they performed?

SI Two endoscopic drainage options are currently available. Transpapillary drainage of the gallbladder has been used since 1984, when Dr Richard Kozarek first described transpapillary drainage of the gallbladder via endoscopic retrograde cholangiopancreatography (ERCP). This method involves placing a 7-French, double pigtail stent, usually 12 to 15 cm in length, via ERCP. The stent is passed through the major papilla, common bile duct, and cystic duct into the gallbladder to relieve the cause of obstruction that is driving the process of acute cholecystitis. Most often, the obstruction is a gallstone or a stricture. However, malignancies (such as pancreatic, gallbladder, and bile duct cancers) can cause a blockage to the cystic duct, and, occasionally, the placement of metal stents in the bile duct can cause an occlusion to the takeoff of the cystic duct, leading to acute cholecystitis. Therefore, endoscopists have to navigate the cystic duct, place a guidewire into the gallbladder, and then deploy a stent over the guidewire to allow decompression of the infected gallbladder.

In 2007, Dr Todd Baron and Dr Mark Topazian described the first transmural drainage of the gallbladder, through the wall of the duodenum or stomach, via endoscopic ultrasound (EUS). This procedure was initially performed using a plastic, 7-French, pigtail stent. After puncturing the gallbladder with a needle, a guidewire was advanced into the gallbladder. The stent was passed over the guidewire, and the gallbladder was then decompressed and drained directly into the duodenum. Since then, endoscopists have employed fully covered self-expanding metal stents (FCSEMSs) that are designed for use in the bile duct. FCSEMSs, although capable of reducing the risk of bile leaks that can be encountered with transmural plastic stents, are more prone to migration due to their length and absence of flares at the ends. Lumen-apposing

metal stents (LAMSs), used to drain pancreatic fluid collections, offer the same benefits as FCSEMSs with the additional advantages of being short and including wide flanges that allow for better apposition of the gallbladder lumen and enteric wall, thus creating fairly secure fistulas with minimal risks of bile leaks or stent migration.

G&H What factors should be considered when selecting a drainage approach?

SI A discussion with the patient's surgeon is necessary to determine whether the patient is currently, or will be, a candidate for cholecystectomy. If surgery is needed, a transpapillary approach may be more appropriate, as a transmural stent could make a future operation more challenging due to the need to close a duodenal or gastric fistula to the gallbladder. Another factor is the severity of the patient's disease. In patients with Grade III cholecystitis (according to the Tokyo Guidelines), imaging studies are needed to confirm there is no free perforation of the gallbladder. In such patients, who may not be able to tolerate anesthesia, a percutaneous approach may be more appropriate. A third factor is whether a patient has an indication for an ERCP, such as associated jaundice. In this instance, a transpapillary gallbladder stent placement is appropriate. The last factor is the presence of significant ascites. Percutaneous drains and transmural gallbladder drainage are associated with higher risks of bile leaks in this setting, and a transpapillary gallbladder stent via ERCP should be considered. However, a transmural approach using EUS may be feasible if transpapillary drainage fails.

G&H What are the advantages and disadvantages associated with transpapillary drainage?

SI Transpapillary drainage is a feasible and reasonable option if there is already an indication for an ERCP (eg, a common bile duct stone). Transpapillary stent placement does not violate the duodenal or the gastric wall, keeping intact the normal anatomy. By not breaking these luminal boundaries, the transpapillary approach makes any future surgery less challenging; the surgeon just has to remove the pigtail stent from the gallbladder. However, it is critical to determine the potential need for surgery so that the cystic duct and gallbladder stent are not inadvertently stapled off without the stent first being removed. Another advantage of this method is cost; a plastic stent at my institution costs $50, while a LAMS costs $3500 to $5000. Additionally, transpapillary drainage does not increase the risk of bile leaks in the setting of ascites.

On the other hand, transpapillary stent placement can be technically more challenging than placing a transmural stent due to a tortuous cystic duct, which may be occluded by a gallstone, a stricture, or an uncovered biliary metal stent. Furthermore, gallstones cannot pass through a 7-French pigtail stent; thus, placement of a transpapillary stent does not treat cholecystitis caused by gallstone disease. Lastly, there are risks associated with performing ERCP, one of which is developing pancreatitis. One paper has been published thus far that suggests lower technical and clinical success rates with transpapillary stenting vs transmural stenting, with higher rates of recurrent obstruction with transpapillary stents.

G&H What are the benefits and limitations of EUS-guided transmural drainage?

SI EUS-guided transmural drainage has high technical and clinical success rates, more than 90% to 95% in published series. This approach eliminates the risk of post-ERCP pancreatitis and is capable of treating the underlying cause of cholecystitis (if it is gallstone disease) by allowing either spontaneous passage of gallstones or cholecystoscopy with lithotripsy. However, there is a lack of long-term data on the recurrence of gallstones once cleared.

Ascites are a concern when performing EUS-guided transmural drainage due to the risk of bile leak and inability to form a mature fistula. Stent misdeployment, although uncommon, can also lead to a bile leak, which could require the use of a percutaneous drain or, rarely, be life-threatening. Although rare, the gallbladder may be located too far from the duodenal or gastric wall to allow safe stent deployment. A transmural stent placed into an intraperitoneally perforated gallbladder risks opening the digestive tract up to the peritoneum. As discussed previously, this method could make future cholecystectomy more challenging. Lastly, the cost of a cautery-enhanced LAMS remains prohibitive.

G&H What adverse events are associated with endoscopic drainage of gallbladder disease?

SI The adverse events associated with transpapillary drainage are the same as those that are associated with ERCP, such as sphincterotomy, bleeding, perforation, and pancreatitis. There are anesthesia-associated risks with every endoscopic procedure, and, in the moribund patient, it is a factor that has to be weighed against percutaneous drainage. Specific to gallbladder stents, there is the risk of injury or perforation of the cystic duct, which could lead to stent misdeployment and bile leaks.

Transmural drainage is associated with a risk of stent misdeployment as well, but could have more severe

consequences due to the size of the stents (10, 15, and 20 mm vs a 7-French plastic stent). Bleeding may also occur, although the self-expanding nature of a LAMS may provide tamponade in several patients. Gastric and duodenal perforations seem to be rare but are similarly possible with stent misdeployments. Delayed stent migrations, inward or outward leading to recurrent cholecystitis, have been described. Finally, due to the larger diameter of the stents, there are also several reports of food material occluding the stents, leading to recurrent pain and cholecystitis.

Despite these mentioned risks, the rates of adverse events seem to be low with both endoscopic approaches. Several published studies have shown the adverse-event rate with endoscopic approaches to be significantly lower than with percutaneous gallbladder drains. Most of these complications can be treated endoscopically or with the help of interventional radiology. Mortality from either of these procedures appears to be rare.

G&H Have any comparative trials evaluated the transpapillary and transmural drainage approaches?

SI Dr Dongwook Oh and colleagues conducted a retrospective review of a prospectively maintained database from a single center in Korea. A total of 172 patients were included, 76 of whom had undergone EUS-guided transmural drainage and 96 of whom had undergone endoscopic transpapillary drainage. They found that EUS-guided transmural drainage was associated with higher technical and clinical success rates than transpapillary drainage (99.3% vs 86.6% and 99.3% vs 86.0%, respectively), both of which were statistically significant. The transpapillary group also had a higher rate of procedure-related adverse events (19% vs 7%), as well as a higher recurrence rate of cholecystitis and cholangitis (12.4% vs 3.2%, respectively) compared to the EUS-guided transmural drainage group.

My colleagues and I have similarly conducted a series (not yet published) at Virginia Mason that retrospectively compares EUS-guided transmural drainage to transpapillary gallbladder drainage in 78 patients, with similar results.

Importantly, a meta-analysis of 5 studies comparing EUS-guided transmural drainage with percutaneous drainage was recently published in *Surgical Endoscopy*. The study found similar technical and clinical success rates between the 2 methods, but a significantly lower rate of reinterventions, pain scores postprocedure, and adverse events in the endoscopic group vs the percutaneous group.

G&H Are there any approaches to the management of gallbladder disease that are currently under development?

SI Beyond what is already available, I am not aware of any additional approach that is under development. However, transmural drainage of the gallbladder has allowed clinicians to clear gallstones from the gallbladder, which prior treatments could not do. Cholecystoscopy allows for lithotripsy of large stones (6-7 cm), and there are reports that cholecystoscopy has allowed for polypectomy, leading clinicians to analyze and surveil patients who may be at a higher risk of cancer but who are not ideal surgical candidates.

G&H What research is needed in this field?

SI There is a need for more randomized, controlled trials comparing not only percutaneous drainage with endoscopic drainage of the gallbladder, but also the 2 different types of endoscopic drainage techniques. Long-term data on gallstone recurrence following clearance from the gallbladder with LAMSs are lacking. Following patients in this setting, and identifying whether leaving pigtail stents in the gallbladder indefinitely prevents gallstone formation or serves as a nidus for recurrent stones, could be useful information. Finally, it is important to understand that even though the options for minimally invasive methods of managing gallbladder disease continue to improve, especially with the use of LAMSs, a multidisciplinary approach, especially with surgeons and interventional radiologists, remains paramount to providing the best care for patients.

Dr Irani serves as a consultant for Boston Scientific.

Suggested Reading

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