

# ADVANCES IN ENDOSCOPY

Current Developments in Diagnostic and Therapeutic Endoscopy

Section Editor: Todd H. Baron, MD

## Endoscopic Management of Incidentally Identified Gastrointestinal Stromal Tumors



Michael B. Wallace, MD, MPH  
Professor of Medicine  
Mayo Clinic  
Jacksonville, Florida

**G&H** How common are gastrointestinal stromal tumors, and how often are they identified incidentally?

**MW** Gastrointestinal stromal tumors (GISTs) are quite common and include a wide variety of completely benign, potentially malignant, and frankly malignant lesions. The current estimate of the frequency in which they are incidentally identified is uncertain, but, generally speaking, GISTs are found in 2% to 3% of endoscopic procedures.

**G&H** Where along the gastrointestinal tract are GISTs most likely to be found?

**MW** GISTs can be found anywhere in the gastrointestinal tract, from the esophagus, stomach, and small intestine to the large intestine. However, GISTs are most commonly found in the stomach.

**G&H** What are the indications for endoscopic resection of gastric GISTs?

**MW** Endoscopic resection of gastric GISTs is performed for either diagnostic or therapeutic reasons. In cases where the diagnosis is uncertain, endoscopic resection can be used to confirm findings. Diagnostic resection is appropriate for subepithelial lesions located in the submucosal layer, and the procedure is relatively easy and safe to perform. For larger lesions, particularly those arising in the muscle layer, the goal of resection is often therapeutic. In

these cases, the risks of endoscopic resection are greater; thus, lesion removal is a more selective process. It is uncertain as to whether all GISTs need to be removed. In general, GISTs that are at high risk for progression are resected. Factors for progression include size (typically  $\geq 3$  cm), irregular shape, and, based on the results of a preresection fine-needle biopsy, a high mitosis count or a high proliferation index such as a *Ki-67* stain. It is likely that smaller GISTs have a very low risk of progression and, therefore, may not need to be removed, but this is a controversial topic.

Of note, a very specific subgroup of these lesions consists of the carcinoid tumors. It is not uncommon to find carcinoid tumors in the stomach, and it is important to remember that the carcinoid tumors that are associated with chronic atrophic gastritis are often very benign and do not require resection at all. However, such lesions are often referred for resection; thus, gastroenterologists should keep in mind that if they see a carcinoid tumor, it is helpful to assess whether the patient has chronic atrophic gastritis. This can be done by taking a gastric aspirate and checking the pH level, performing a gastric biopsy to assess for signs of atrophic gastritis, or measuring a gastrin level.

**G&H** What endoscopic methods are available to manage GISTs? How are they performed?

**MW** Lesions can generally be resected with endoscopic mucosal resection techniques, such as injection, lift, and

snare or band and snare resection with a cap. For the injection, lift, and snare technique, the lesion is first identified based on an endoscopic ultrasound. If the lesion is located in the submucosa, an injection is performed underneath, in the deep layer of the lesion. The area is then lifted, and a snare device is used to resect the entire lifted submucosal lesion and surrounding normal submucosa. The cap method is performed most commonly with a band and snare device. An injection is made, followed by suctioning of the lesion into the cap. A band is deployed and the banded tissue is resected. Another technique is the unroofing procedure, which generally involves a submucosal injection on the superficial side of the lesion followed by a needle-knife excision over the top of the lesion. A direct submucosal snare is used to resect the lesion. A variant of this method is when the lesion is entrapped with an endoloop and is left to slough off. The most recent advance in this field is a procedure called a submucosal tunneling endoscopic resection, which is similar to an endoscopic submucosal dissection. A fluid-like cushion is injected 2 to 3 cm on the proximal side of the lesion, creating a small incision into the submucosal space. An endoscope is then tunneled into the submucosal layer until the lesion is reached. The lesion is dissected using the same needle knives that are used for endoscopic submucosal dissection, and is removed usually with a snare or net device (eg, Roth Net, US Endoscopy). The entrance to the tunnel is then closed with standard clipping devices.

### G&H How should the appropriate treatment be chosen?

**MW** In a lesion that is suspicious for subepithelial tumor, an endoscopic ultrasound is the most valuable test to determine the type of lesion and in which layer it is located. Some lesions, such as lipomas, are completely benign and do not require any resection, and some lesions are actually not even subepithelial lesions but are extrinsic structures (eg, a blood vessel, the gallbladder, a bone spur in the esophagus) that are pressing on the gastrointestinal wall. Fine-needle biopsy is also helpful and can be done through endoscopic ultrasound. The appropriate treatment can be chosen once the type and location of the lesion is determined.

### G&H What are the main benefits and limitations associated with each procedure in relation to the management of GISTs?

**MW** The main advantages associated with the standard injection, snare, and cap methods are that they are relatively easy, safe, and quick to perform; most endoscopists who perform endoscopic mucosal resection can perform

these procedures. However, these procedures are largely limited to lesions located in the submucosa and to lesions that are relatively small. The cap method in particular is intended for lesions that are approximately 1 cm or smaller due to the diameter of the cap. The more complex procedures, such as the unroofing technique and the submucosal tunneling endoscopic resection procedure, allow much larger and deeper lesions to be removed, including lesions in the muscle layer as well as lesions that are exophytic (ie, the predominant lesion is extending outside the wall of the gastrointestinal tract). However, these procedures generally require advanced skills in endoscopic submucosal dissection or submucosal endoscopy, such as peroral endoscopic myotomy. Only endoscopists with significant expertise in these procedures should perform them.

### G&H What risks are associated with endoscopic resection of GISTs?

**MW** The main risks associated with endoscopic resection of GISTs, which are similar to the risks of all endoscopic resection procedures, are perforation and bleeding, which can be acute. The majority of bleeds can be controlled endoscopically with cautery tools and, occasionally, clipping. In the past, perforation has been a highly feared complication because it required surgical management; in the current era, virtually all endoscopic perforations can be managed with closure devices. Some perforations are even considered intentional or necessary to fully resect the lesion. For example, for an exophytic GIST, a physician would often have to create an intentional perforation or a full-thickness resection. Now that the tools to close those perforations are available, they are less concerning. The most feared complication, which fortunately is very rare, is now a delayed perforation, which does often require surgery to repair.

### G&H How significant is the learning curve for these procedures?

**MW** Primary learning curve data are not available for GISTs, but data exist for endoscopic mucosal resection and endoscopic submucosal dissection procedures. According to a study published in *Gastrointestinal Endoscopy*, the learning curve to achieve proficiency for endoscopic mucosal resection techniques is approximately 100 to 125 procedures. Those numbers should be considered a baseline before an endoscopist starts to practice more complex procedures. Separately, endoscopic ultrasound has its own set of learning curves. Guidelines exist for credentialing in endoscopic ultrasound, but typically, approximately 75 procedures are necessary to assess the competency of performing diagnostic endoscopic

ultrasound. The endoscopic submucosal dissection and submucosal tunneling endoscopic resection techniques are the most complex and should only be undertaken by endoscopists who have mastered endoscopic mucosal resection. Thus, in addition to the 100 to 125 endoscopic mucosal resection procedures, at least 25 to 50 endoscopic submucosal dissection procedures are required to achieve a degree of mastery.

### **G&H** Have any studies evaluated the short- and long-term effects of these procedures for the management of GISTs?

**MW** Currently, we only have results on short-term efficacy, which, along with short-term safety, appears to be very high, provided that the complex procedures are performed by experienced endoscopists. The procedures in general are highly effective for the removal of smaller lesions. Although long-term results regarding the management of GISTs are lacking, we do have long-term natural history data on small lesions that suggest that such lesions, including small stromal tumors, have a very low risk of progression to advanced cancers. Thus, most small lesions (<3 cm) do not need to be resected.

### **G&H** How should patients be followed up?

**MW** In patients who do not undergo resection because they have low-risk lesions, a repeat endoscopic ultrasound in 1 to 2 years is appropriate follow-up, with an extended interval if the lesion remains stable. For example, a patient may undergo a repeat endoscopic ultrasound in 1 year, with the interval increased to 1.5 to 2 years if no change is observed. Based on the patient's age and comorbidity, that interval may be continued; often, if the lesion is stable for 5 to 10 years, follow-up is discontinued.

In terms of follow-up after resection, the most important issue is that the lesion is completely resected; this is confirmed with a pathologic analysis of the margins. If the margins are truly negative and the lesion is low risk, then often no surveillance is needed. If there

are worrisome features such as an unclear margin or high-risk factors, then follow-up would occur according to current guidelines (eg, the National Comprehensive Cancer Network guidelines). This usually involves periodic imaging, including cross-sectional imaging such as computed tomography or positron emission tomography, at regular intervals.

### **G&H** What are the priorities of research in this field?

**MW** One of the major dilemmas in this field is that the small lesions that are the easiest and safest to remove are often the lesions that do not necessarily need to be resected. Another challenge is that preoperative biopsy, even with fine-needle biopsy or multiple endoscopic biopsies, can actually make subsequent endoscopic resection more difficult. Thus, it would be helpful to have better tools to assess the risk of these lesions without a biopsy in order to identify low-risk and high-risk lesions and resect only the latter.

*Dr Wallace serves as a consultant to Aries Pharmaceuticals Inc and Lumendi and has received research support from Olympus, Fujifilm, BSCI, and Medtronic paid to his institution.*

### **Suggested Reading**

- Bamboato ZM, Dematteo RP. Updates on the management of gastrointestinal stromal tumors. *Surg Oncol Clin N Am*. 2012;21(2):301-316.
- Bhurwal A, Bartel MJ, Heckman MG, et al. Endoscopic mucosal resection: learning curve for large nonpolypoid colorectal neoplasia. *Gastrointest Endosc*. 2016;84(6):959-968.e7.
- El-Menyar A, Mekkodathil A, Al-Thani H. Diagnosis and management of gastrointestinal stromal tumors: an up-to-date literature review. *J Cancer Res Ther*. 2017;13(6):889-900.
- Kim HH. Endoscopic treatment for gastrointestinal stromal tumor: advantages and hurdles. *World J Gastrointest Endosc*. 2015;7(3):192-205.
- Tan Y, Tan L, Lu J, Huo J, Liu D. Endoscopic resection of gastric gastrointestinal stromal tumors. *Transl Gastroenterol Hepatol*. 2017;2:115.
- von Mehren M, Joensuu H. Gastrointestinal stromal tumors. *J Clin Oncol*. 2018;36(2):136-143.