ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Prateek Sharma, MD

Esophageal Motility Disorders in Gastroesophageal Reflux Disease

John E. Pandolfino, MD, MSCI
Hans Popper Professor of Medicine
Division Chief, Gastroenterology and Hepatology
Northwestern University Feinberg School of Medicine
Chicago, Illinois

G&H What clinical factors raise suspicion for esophageal dysmotility in patients with dysphagia?

JP The clinical factors that raise suspicion for dysmotility in patients with dysphagia are typically a result of significant trouble with the transit of food from the mouth into the esophagus. Patients with esophageal dysphagia can generally get food down into their throat, but once it is in the esophagus, they feel like it is stuck in their chest. Sometimes patients may point to their throat and say they feel food stuck there, even though the dysmotility or blockage is further down the esophagus. This is because when food and liquids get backed up to a certain level, for example, the top of the esophagus, and more is packed on top of that, the patient starts to feel pressure at the level where there is food. Patients tend to feel chest discomfort, an inability to clear things, and then, of course, at the end stage, regurgitation. The patient will get food down into their esophagus and then regurgitate undigested food.

G&H How prevalent are esophageal motility disorders in gastroesophageal reflux disease?

JP The most common motility pattern in gastroesophageal reflux disease (GERD) is actually normal motility. Studies show that more than 50% of patients with reflux will have decent esophageal motility. The most common abnormal pattern in terms of being a dysmotility or esophageal motility disorder (EMD) is ineffective esophageal motility. Essentially, the peristaltic waves are either weak, meaning that they are not strong enough to generate pressure, or fail (they sometimes are not triggered and there is no contraction in the esophagus). A combination of failed swallows and weak swallows that accounts for more than 7 of 10 swallows (>70%) is typically defined as ineffective esophageal motility. However, 5 failed swallows are also considered to be ineffective esophageal motility.

G&H How does the pathogenesis of EMDs differ from that of GERD?

JP There is a little bit of overlap. When one thinks about the function of the lower esophageal sphincter (LES) at the esophagogastric junction (EGJ) where the esophagus meets the stomach, the sphincter has two seemingly opposite jobs. It must open upon swallowing to allow food into the stomach in a seamless way, and then after swallowing, it must close to become an antireflux barrier. The main difference in terms of motility between GERD and EMDs, like achalasia, which is the most well-described EMD, is at the sphincter. The two disease states are essentially on opposite ends of the spectrum. In GERD, the antireflux barrier is defective, and the LES pressures are weak. This allows gastric juice to come up into the esophagus at will, with minimal pressure elevations. In contrast, in patients who have dysmotility with dysphagia—for example, patients with achalasia, EGJ outflow obstruction (EGJOO), or spasm—the LES fails to relax and open, creating an obstruction during swallowing.

Some EMDs are associated with very strong contractions like hypercontractile esophagus (also called jackhammer esophagus). Other EMDs are associated with complete absence of peristalsis, which is seen with achalasia and scleroderma. Again, although there is a little bit of overlap in the esophagus body between reflux patterns and dysmotility, the real differentiating part is at the sphincter.

G&H What is the current standard for diagnosing EMDs?

JP The test that all esophageal disorders are based on is manometry. An EMD can also be diagnosed with other devices such as a timed barium esophagram, during which the patient drinks a specified amount of barium a few minutes before the test is performed. Based on the pattern observed, a dysmotility can be diagnosed because the gastroenterologist can see when there is a failure of peristalsis. For example, when there is a spasm, the esophagus will have a corkscrew appearance, and when the LES fails to open, it looks like a bird's beak at the end of the esophagus. Functional lumen imaging probe (FLIP) panometry, which is a platform I helped develop, can also assess motility. One can measure how much the LES opens and can look at patterns of contraction as they are stimulated by distention of a balloon in the esophageal body. FLIP panometry is like a stress test on the esophagus. Often information can be gleaned from an endoscopy that will suggest a motility disorder.

G&H How are EMDs classified?

JP EMDs are classified using the Chicago Classification version 4.0. This updated hierarchal classification scheme undergoes a reappraisal every 3 to 5 years to ensure that it is keeping current with technology advances and research. Of course, diagnostics need to keep up with technology advancements, which may not only make testing easier and more tolerable for the patient but also help the gastroenterologist see things better. Regular reappraisal of the classification also provides an opportunity to correct mistakes and look for ways to improve diagnostic accuracy. The classification scheme is based on an improvement in measurements and an appreciation that now gastroenterologists can be more definitive and accurate with the esophagus anatomy and the pressure patterns.

The tendency is to classify an EMD by determining whether the patient has a problem with the LES relaxing. If there is a problem, then the patient probably has achalasia or one of its subtypes and/or an EGJOO. If the LES is performing well, then the esophageal body patterns are assessed, and patients are classified into a specific subcategory. This depends on whether contractions are weak or absent; very hypercontractile; or premature, spastic, or chaotic. Patients with no evidence of an impaired LES have normal motility, have no problem with the sphincter relaxing or the integrated relaxation pressure (IRP) is normal, and the esophageal body pattern is normal.

G&H Which manometric patterns require further evaluation for diagnosis?

JP I think that a patient who has an abnormal IRP and evidence of peristalsis, meaning that testing showed propagating contractions, has an EGJOO. All patients with this pattern require further evaluation with either a timed barium esophagram or a FLIP device. This will definitively address whether there is an abnormality at the EGJ that would be akin to achalasia. A conclusive diagnosis cannot be made by manometry alone when a patient has only an EGJOO pattern.

Similarly, patients with a normal IRP but complete absence of peristalsis (ie, there is no activity and no contraction with each swallow) most likely have a scleroderma-like pattern, which is consistent with scleroderma the disease or severe reflux. However, many of these patients can also have a diagnosis of achalasia that may have been missed because of a flaw in the IRP measurement. For these patients as well as those with EGJOO, the Chicago Classification Working Group recommends that gastroenterologists have a low threshold for performing an esophagram or a FLIP device assessment.

G&H How are patients with both EMDs and GERD managed?

JP Management of the two disease states is very different because they are diametrically opposed in most cases based on the sphincter. Most important is that when a patient has an EMD, the first question to ask, which I mentioned from the Chicago Classification version 4.0, is: Does the patient have an abnormality in the esophageal sphincter? (Is the sphincter not relaxing, and is it causing an obstruction?) If an obstruction is noted, the first step is to remove it. This can be done primarily with either endoscopic balloon dilation or peroral endoscopic myotomy (POEM), or potentially with laparoscopic myotomy.

If a patient has both an obstruction at their sphincter and a severe abnormality in peristalsis where a spasm occurs, the entire muscle may be cut; typically, this would be done with POEM. However, complementary therapy with smooth-muscle relaxants, such as nitrates, calcium-channel blockers, or even sildenafil, can also be tried.

In patients with GERD, typically the problem is that their LES is defective, meaning it is weak or even wide open. GERD patients typically have severe symptoms and poor clearance (poor peristalsis and ineffective esophageal motility). Almost always in severe GERD, there is also an anatomic issue like a hiatus hernia. For severe GERD with a hiatus hernia, the hernia is repaired, and a valve is created either surgically with Nissen fundoplication or endoscopically with transoral incisionless fundoplication.

There are many patients who have reflux disease without a large hernia, and their main symptom is related not just to the fact that they are having reflux but how

they react to reflux. How intense is their reflux? Is it stimulating their esophagus, and is it injuring their esophagus? For almost all types of reflux, the first treatment should be a trial of acid suppression therapy with proton pump inhibitors, because acid suppression will treat about 50% to 60% of reflux patients adequately. Also, it is low risk. However, not all patients respond to proton pump inhibitors. It is for those patients that one would start to think about whether it is necessary to fix the physiology or the anatomy. Honestly, current treatment strategies are not very good at fixing the physiology. Because the medicines that focus on improving peristalsis and LES pressure are not great, the tendency is to try treating the anatomy, which in essence would treat the defects in the physiology, meaning the disrupted antireflux barrier.

Gastroenterologists must be careful when repairing the antireflux barrier to not make it too tight, because the esophagus in patients with severe ineffective esophageal motility is already weak and may not be able to clear its contents. This is why an assessment of emptying or motility is always performed before even contemplating a surgical correction like a fundoplication.

G&H How might advances in diagnostic testing improve management of EMDs?

JP Certainly, manometry can be improved. There may be opportunities to use combined manometry with impedance, which helps us see whether there is liquid or air in the esophagus. Using more-advanced computation, we can get a better sense of how well the esophagus is emptying or functioning as a tool to move fluid and food into the stomach. By incorporating impedance into manometry, the field could move closer to understanding why patients have symptoms related to the motility abnormality.

Another technology that could potentially improve patient tolerance is FLIP panometry. Its major advantage is that it can be performed during index endoscopy when the patient is asleep. It is well known that at least 50% to 60% of motility disorders can be diagnosed up front during that initial visit. Many patients may not need a manometry. In contrast, manometry is performed transnasally when patients are not sedated and can last up to 30 minutes. However, manometry and FLIP panometry may be complementary, which may be an improvement in management. In a recent study, my colleagues and I found shared features between evaluations of secondary peristalsis on FLIP manometry and primary peristalsis on manometry, although discordant responses also occurred.

I think there is also the opportunity for X-rays to become more advanced, and for artificial intelligence to help with classifying motility disorders. Some variants in spasm and in hypercontractile swallows may be related to anatomy and not motility problems. If these tests and technologies can help identify which are the true motility problems, that would be a major improvement in the management of these conditions.

G&H What is the focus of research on EMDs?

JP Researchers are thinking about how current diagnostic tools can be used complementarily to provide a complete picture of how the esophagus is working. An interesting area of research focuses on the cause of dysmotility. Some believe that a virus, possibly a herpes virus, triggers an autoimmune process that causes nerve damage. However, it is not known how or why spastic motor disorders occur, or whether they are truly a primary abnormality of neuromuscular function or a response to an anatomic issue.

Another area of research is looking at how the geometry of the esophagus may change. Some patients present at the end stage of their motility disorder with esophageal dilatation, which is a poor prognostic indicator. It would be helpful to know how the esophagus becomes dilated and how that can be prevented or reversed.

In terms of treatment, I think there should be more focus on procedures such as pneumatic dilation, balloon dilation, POEM, and Heller myotomy. POEM especially, being less invasive than surgery but more precise than pneumatic dilation, can be utilized to personalize the approach to each patient's motility disorder. The fine-tuning of anatomic corrections, whether endoscopic or surgical, to prevent patients from having bad outcomes is also a hot topic.

Disclosures

Dr Pandolfino holds shared intellectual property rights and ownership surrounding FLIP panometry systems, methods, and apparatus with Medtronic Inc. He has consulted for Medtronic, Ironwood Pharmaceuticals, and Diversatek; has received research support from Ironwood Pharmaceuticals and Takeda; and has served on the advisory board for Medtronic, Diversatek, EndoGastric Solutions, and Ethicon.

Suggested Reading

Carlson DA, Baumann AJ, Prescott JE, et al. Validation of secondary peristalsis classification using FLIP panometry in 741 subjects undergoing manometry. *Neurogastroenterol Motil.* 2022;34(1):e14192.

Mittal R, Vaezi MF. Esophageal motility disorders and gastroesophageal reflux disease. *N Engl J Med.* 2020;383(20):1961-1972.

Yadlapati R, Gyawali CP, Pandolfino JE; CGIT GERD Consensus Conference Participants. AGA Clinical Practice Update on the Personalized Approach to the Evaluation and Management of GERD: expert review. *Clin Gastroenterol Hepatol.* 2022;20(5):984-994.e1.

Yadlapati R, Kahrilas PJ, Fox MR, et al. Esophageal motility disorders on high-resolution manometry: Chicago Classification version 4.0©. *Neurogastroenterol Motil.* 2021;33(1):e14058.