ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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Insights on Extraesophageal Gastroesophageal Reflux Disease



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G&H What are common and less common symptoms of extraesophageal gastroesophageal reflux disease?

AS Rather than defining symptoms of extraesophageal gastroesophageal reflux disease (GERD) as common and less common, it might be better to define them as those that have evidence-based associations suggestive of GERD vs those that have proposed associations. Based on the Montreal definition of GERD, established associations exist between certain syndromes such as reflux cough, reflux laryngitis, reflux asthma, and dental erosion. Examples of proposed associations include globus sensation, throat pain, chronic throat clearing, pharyngitis, sinusitis, and recurrent otitis media. It is difficult to determine whether these symptoms are attributed to GERD or not. In the right setting, cough, hoarseness, laryngitis, and asthma appear to have a stronger association with GERD.

G&H How prevalent are extraesophageal symptoms in patients with GERD?

AS Pinpointing prevalence is a challenge because of how extraesophageal symptoms may present themselves. From what is currently known, the prevalence rate of GERD in North America and Western Europe is approximately 10% to 20%. It is more likely that symptoms such as cough and those that have proposed associations with GERD are manifestations of extraesophageal GERD in patients who have a confirmed diagnosis of GERD. Such symptoms likely have other causes in patients who

do not experience reflux symptoms such as heartburn or regurgitation. Also, GERD is rarely the sole cause of an extraesophageal symptom. Another primary cause may be present.

Three large population-based surveys have been conducted that examine ear, nose, and throat (ENT) and pulmonary symptoms in which the odds ratios were calculated for laryngeal and pulmonary conditions among patients with GERD. One of the studies was a local population-based study pertaining to Olmsted County, Minnesota. Another study involved US military veterans, and the third study was a European population-based study. The odds ratios ranged from 1.2 to 3, with nocturnal cough having the strongest association with GERD. These findings confirm that having extraesophageal symptoms is more likely in the presence of typical reflux symptoms, whereas GERD is probably unlikely as the sole cause of the extraesophageal symptoms.

G&H What are the challenges of timely diagnosis of extraesophageal GERD?

AS The most important challenge is the lack of a gold-standard diagnostic test for a suspected extraesophageal symptom. The sensitivity and specificity of existing tests are not quite sufficient. Especially challenging is that the symptoms are so varied. This makes extraesophageal GERD a diagnosis of exclusion. If a patient has a cough or has asthmatic symptoms, he or she needs to submit to a pulmonary workup or allergy testing. Symptoms such as laryngitis, sinusitis, and pharyngitis require ENT evaluation. Computed tomography of the sinuses or a

challenge of nasal corticosteroids may be required to rule out sinusitis or rhinitis from another cause.

G&H What diagnostic testing can be used when extraesophageal GERD is suspected?

AS Causes of ENT, pulmonary, or other symptoms, such as cardiac cause of chest pain, need to be ruled out first. If there is still suspicion of extraesophageal GERD, a proton pump inhibitor (PPI) challenge is recommended to observe whether the symptoms persist or improve. If they

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improve, the dose should be adjusted to what is optimal for the patient. If no resolution of symptoms is seen following a PPI challenge, then further evaluation is needed regarding whether suspicion of GERD is still high.

Typically, a lower suspicion of GERD is reserved for patients who do not have the typical GERD symptoms of heartburn or regurgitation and who have a lower body mass index (BMI), perhaps less than 25. In this situation, pH testing in the absence of PPI therapy might be useful. If the suspicion of GERD is high—for example, in a patient with a BMI of 25 or more or if the patient has typical reflux symptoms—then pH testing and pH monitoring should be performed while on PPI therapy. Other tests, such as salivary pepsin or mucosal impedance, also can be introduced.

G&H How can mucosal impedance aid in the diagnosis of extraesophageal GERD?

AS Mucosal impedance is a novel and perhaps time-saving modality. A catheter or balloon probe is inserted during endoscopy. It allows for direct contact of sensors on the catheter with the mucosa and measures changes in the mucosal current conduction to assess epithelial integrity.

Mucosal impedance measurements take approximately 5 seconds. This procedure can replace several currently used tests that take much longer, such as catheter-based pH monitoring with impedance, which typically requires 24-hour testing, and wireless capsule pH monitoring, which requires between 48 and 96 hours of testing.

Based on preliminary data, mucosal impedance testing appears to be more efficient than current forms of testing. It eliminates the need for a patient to go on a strict diet or endure home monitoring, which involves having the patient manipulate buttons and measures so that the treating clinician can measure the symptom index.

That being said, traditional tests are reliable, and patience pays off. For example, studies of wireless capsule pH monitoring show that the longer the testing period, the more effective the analysis is. However, if an endoscopy is going to be performed to rule out esophagitis or reflux-related pathology, it is more efficient and easier on the patient to undergo mucosal impedance.

G&H How should treatment be approached in terms of specific extraesophageal symptomatology?

AS In a general clinical scenario, patients typically present to gastroenterologists after they have seen other specialists, such as ENT doctors, pulmonologists, or cardiologists. In many instances, the patient is referred to a gastroenterologist by these specialists after they have ruled out causes of the patient's symptoms, or perhaps laryngoscopy was performed and detected laryngopharyngeal reflux, leading to the suspicion of GERD and, in turn, a referral to a gastroenterologist.

Occasionally, a primary care physician might directly refer a patient with chronic throat clearing or globus sensation to a gastroenterologist for evaluation, but typically a patient presenting to a gastroenterologist with complaints of laryngitis or asthma would have already seen an ENT doctor, pulmonologist, or allergy specialist. When a patient presents to a gastroenterologist with such symptoms and no prior workups have been performed, the patient is then referred to appropriate specialists to rule out other causes before considering GERD as a possible association or attribution.

G&H Once a diagnosis of extraesophageal GERD has been established, what is the treatment protocol?

AS Treatment takes the form of a stepwise approach that starts with lifestyle modification, then medical therapy, and then endoscopic or surgical therapy.

Lifestyle modification may include a weight loss regimen and arranging sleeping quarters so that the patient reclines with the head and upper body elevated perhaps to a 30-degree angle, which can help alleviate symptoms, especially in a patient with postnasal drip. Avoidance of caffeine, alcohol, cigarette smoking, and/or trigger foods that the patient associates with symptoms also may be recommended in accordance with the patient's lifestyle habits. In addition, waiting approximately 3 hours between a meal and sleep is strongly recommended, as is eating small, rather than large, meals. Patient education and adherence, as well as good physician-patient communication about these lifestyle habits, are important for improved clinical outcomes.

Medical therapy, which is the next step, can include use of antacids and a range of other medications: H2 blockers, PPIs, alginates, baclofen, and prokinetic agents. Generally speaking, a short course of PPI therapy is given to a patient suspected of having GERD whereby the medication is taken twice daily for 2 to 3 months. This regimen is sufficient to assess for response. Once the patient responds to PPI therapy, it can be taken once daily or on an as-needed basis.

Endoscopic antireflux procedures can include transoral incisionless fundoplication, radiofrequency ablation, or endoluminal fundoplication. These have traditionally been tested in patients with typical GERD, and not patients with extraesophageal GERD.

Finally, surgical modalities may include fundoplication or a magnetic sphincter augmentation using a ring. Surgical therapies are typically reserved for patients with anatomic defects such as a large hiatal hernia or patients with moderate to severe GERD who are looking for an alternative to long-term medical therapy.

G&H What symptoms would benefit from behavioral management?

AS Lifestyle modification is the foundation. Behavioral management would focus on particular symptoms, such as chronic throat clearing, globus sensation, nonspecific throat pain, and symptoms that appear to be habit-forming or caused by oversensitization. Patients with these symptoms do well with a referral for cognitive behavioral therapy or a similar modality. Behavioral therapy can be useful alone, along with lifestyle modification, or as an adjunctive treatment to medical therapy.

Disclosures

Dr Sathyamurthy has no relevant conflicts of interest to disclose

Suggested Reading

Durazzo M, Lupi G, Cicerchia F, et al. Extra-esophageal presentation of gastro-esophageal reflux disease: 2020 update. *J Clin Med.* 2020;9(8):2559.

El-Serag HB, Sonnenberg A. Comorbid occurrence of laryngeal or pulmonary disease with esophagitis in United States military veterans. *Gastroenterology*. 1997;113(3):755-760.

Gislason T, Janson C, Vermeire P, et al. Respiratory symptoms and nocturnal gastroesophageal reflux: a population-based study of young adults in three European countries. *Chest.* 2002;121(1):158-163.

Locke GR 3rd, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ 3rd. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. *Gastroenterology.* 1997;112(5):1448-1456.

Sidhwa F, Moore A, Alligood E, Fisichella PM. Diagnosis and treatment of the extraesophageal manifestations of gastroesophageal reflux disease. *Ann Surg.* 2017;265(1):63-67.

Vaezi MF, Katzka D, Zerbib F. Extraesophageal symptoms and diseases attributed to GERD: where is the pendulum swinging now? *Clin Gastroenterol Hepatol.* 2018;16(7):1018-1029.

Vakil N, van Zanten SV, Kahrilas P, Dent J, Jones R; Global Consensus Group. The Montreal definition and classification of gastroesophageal reflux disease: a global evidence-based consensus. *Am J Gastroenterol.* 2006;101(8):1900-1920.