

# ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

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## Diagnosis and Management of Esophageal Chest Pain

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### G&H What are the various causes of chest pain?

**SR** Chest pain can arise from a number of disorders. A cardiac source is the most concerning cause, as it is the most life-threatening; thus, it must be excluded as soon as possible.

Once a cardiac source of pain has been excluded, a variety of other sources should be considered, such as muscular skeletal or pulmonary causes. For example, an individual who is exercising after a period of physical inactivity may experience discomfort, heaviness, chest pain, and possibly even damage or trauma. Muscular skeletal causes are common sources of chest pain. Chest pain can also be triggered by pulmonary conditions such as an infection in the lungs.

Once cardiac, muscular, and pulmonary conditions have been excluded, the vast majority of patients are found to have an esophageal source for their chest pain. The 3 main causes of esophageal chest pain result from an underlying disturbed nerve sensation and muscle and mucosal dysfunction. The most common esophageal cause of pain is gastroesophageal reflux disease. Reflux of acid can present with chest pain, heartburn, or swallowing difficulties; chest pain is only 1 manifestation of this condition. Esophageal chest pain can also occur when the esophagus undergoes a strong spasm caused by a motility disorder of the esophagus. The third cause of esophageal chest pain, which has been a focus of my research for the last one-and-a-half decades, is an abnormal sensory function of the esophagus called esophageal hypersensitivity. In this sensory disorder, the muscle, nerve, and receptors of the esophageal wall are overly sensitive.

Finally, anxiety or an underlying psychiatric disorder can manifest as chest pain in some individuals.

### G&H How are cardiac and esophageal causes of chest pain differentiated?

**SR** It is often difficult to distinguish between cardiac and esophageal causes of chest pain based upon symptom presentation alone because the nerves that supply the heart also supply the esophagus. Therefore, patients may think they are experiencing pain of a cardiac origin when the pain is, in fact, coming from the esophagus. Likewise, individuals who think that they are experiencing heartburn may actually be having a heart attack. Another example is an individual who is exercising and experiencing chest discomfort and pain radiating to the arm; this scenario may appear to suggest a cardiac etiology, but exercise is also known to trigger reflux, which could result in reflux pain. Thus, physicians are increasingly relying less upon symptoms and more upon objective data.

Nevertheless, symptoms may offer some hints. For example, it is not very likely that a 20-year-old nonsmoker complaining of chest pain who is otherwise fit and active has coronary artery disease. On the other hand, it is not possible to judge whether chest pain in a 50-year-old smoker with a family history of hypertension is due to a cardiac or a noncardiac source.

For cardiac evaluation, patients should undergo a stress test and angiogram performed via magnetic resonance studies or other techniques. These tests are the most effective methods for excluding vascular disease in the heart.

### G&H Beyond excluding other sources, how can physicians determine whether chest pain is esophageal in origin?

**SR** If a patient does not have vascular disease in the heart, the physician should consider an esophageal source for the chest pain. The first course of action is to perform an endoscopy to search for reflux disease. If reflux disease is

present (ie, there is ulceration in the esophageal walls), reflux is most likely the source of the chest pain and should be treated. As very effective treatments are available for reflux, the pain will disappear in 90% of cases.

If the pain does not disappear or endoscopic testing does not show any mucosal disease, the physician should further examine the patient for reflux. To determine whether the patient has reflux disease despite no visible damage to the lining of the esophagus, the patient should undergo a 24- to 48-hour acid reflux monitoring test, which can be performed via a wire (by placing a probe in the esophagus) or wirelessly (by affixing a capsule to the esophageal lining) and recording the amount of acid reflux occurring over 1–2 days. This test is, by far, the most accurate test currently available for quantifying the amount of acid reflux over a 24- to 48-hour period and thereby provides both symptom correlation and a clear, objective definition of acid reflux disease. If a patient has chest pain but does not have reflux disease according to an endoscopy or 24- to 48-hour pH monitoring, then the chest pain is not related to acid reflux. In a small proportion of patients, the chest pain may be related to nonacid reflux.

The vast majority of the remaining patients have visceral or esophageal hypersensitivity. The best test for detecting this condition is a balloon distention test. A small balloon is inserted into the esophagus and distended. At a particular level of balloon distention, the patient will feel a sensation. If the balloon is distended further, the patient will feel discomfort. If the balloon is distended even further, the patient will feel pain. This test has been performed in healthy individuals in order to record “normal” pain thresholds. If the same balloons are placed in patients complaining of noncardiac chest pain, a large proportion of these patients will report discomfort and pain at much lower thresholds, where normal individuals report merely some sensation. Lower pain thresholds suggest that these patients have an extremely sensitive esophagus whose sensitivity is manifesting as chest pain.

My colleagues and I have conducted extensive studies on this topic and have found that in a group of patients who do not have cardiac or reflux disease, up to 75% have a positive balloon distension test. This hypersensitivity is a problem in the lining of the esophagus, where the receptors are located; in the connections between the esophagus and the brain; and in the brain's perception of esophageal sensation. Throughout the entire pathway, dysregulation leads to abnormal perception of what should be considered normal sensory information. When healthy individuals experience some tension, the esophagus may also experience some tension, but not pain; unfortunately, patients with noncardiac chest pain experience pain because of alterations in tension receptors in the esophageal wall. We believe that there is a dysfunction

in the communication between the gut and the brain in these patients and that this gut-brain dysfunction is the underlying source of esophageal hypersensitivity.

### G&H Are there any other tests that can be used in these patients?

**SR** In my opinion, the 24- to 48-hour pH monitoring test is the gold standard diagnostic approach. However, not all physicians have access to this test, and patients may be reluctant to undergo it. An alternative diagnostic test is a therapeutic drug trial, called the omeprazole test, in which the patient takes a proton pump inhibitor—it does not matter whether it is omeprazole, lansoprazole, esomeprazole, or dexlansoprazole—twice daily for 1 week. If the patient has reflux disease, in most cases—though not all—the symptoms will resolve. This test detects reflux disease; however, it may not help to identify hypersensitivity in patients.

An ultrasound test has been used in a small, select group of patients, not as a diagnostic test, but as a mechanistic test to understand the mechanism for pain. A research group from San Diego has shown that when patients experience chest pain, there is a significant shortening in the longitudinal muscle of the esophageal wall.

Another test currently being used is an impedance pH test, which looks for reflux of both acid and nonacid materials. This test provides some useful information. However, although it is beginning to be used a bit more frequently, it has not yet been well tested in chest pain patients.

Several centers across the country offer specialized services that may be helpful to patients with esophageal chest pain; if gastroenterologists have trouble diagnosing the mechanisms of these patients, I would encourage them to send patients to these centers for more thorough evaluation.

### G&H How is chest pain of esophageal origin usually treated?

**SR** Based upon studies that my colleagues and I have conducted as well as studies by other researchers, my current recommendation, in the absence of any contraindications, is theophylline. This drug is best known for relaxing muscles in the lungs, though it has also been shown to relax other muscles in the body, including the gut and esophageal wall. Theophylline also appears to have another very important specific property as an adenosine receptor antagonist. The esophageal wall and the nerve that supplies the esophagus have these receptors, which are important for modulating pain throughout the body. An adenosine infusion administered into the vein of a

healthy individual lowers balloon distension thresholds. In other words, by administering adenosine, a healthy individual can be temporarily converted into a patient with noncardiac chest pain; the pain threshold that they experienced before the adenosine infusion significantly decreases, so that they now experience pain where they previously could tolerate balloon distension. Because theophylline is an antagonist to adenosine, it relieves chest pain. Several double-blind studies have shown that up to approximately 60% of patients who took 200-mg doses of theophylline twice daily reported improvement in chest pain.

### **G&H** Is theophylline associated with any significant side effects or concerns?

**SR** Unfortunately, theophylline is not a “clean” drug; it has several side effects, including heartburn, palpitations, sleep disturbance, and indigestion-like symptoms. Occasionally, it may cause jitteriness because of its caffeine-like effects. A drug that specifically antagonizes adenosine without causing the side effects seen in theophylline is needed. However, such a drug is not yet available; until one is, theophylline will remain in our therapeutic armamentarium.

Many gastroenterologists are uneasy about using theophylline. They should start with small doses. Although clinical trials have used 200-mg doses, I recommend starting patients on 100 mg per day with meals. If patients do not respond over several weeks of therapy and experience no side effects, they can take 100 mg twice daily and then gradually work up to 200 mg twice daily.

### **G&H** What other medical therapies are available to treat esophageal chest pain?

**SR** I try to use a mechanism-based approach for diagnosing and managing esophageal chest pain. If the mecha-

nism is identified as reflux disease, patients are treated aggressively with proton pump inhibitors, which are very effective. If the mechanism is identified as hypersensitivity, I first try to treat patients with theophylline. If they cannot tolerate this drug or it is contraindicated, low-dose antidepressants can be used. Several uncontrolled studies have been performed with sertraline, trazodone, and citalopram and have shown small improvements in chest pain. If gastroenterologists are uneasy about treating patients with low-dose antidepressants, they should follow the gradual dosing schedule I suggested with theophylline. In the small proportion of patients who have chest pain caused by spasms in the esophagus, nifedipine may be useful. Botulinum toxin type A (Botox, Allergan) has also been injected into a small number of these patients and has shown improvement.

### **G&H** Are there any endoscopic or surgical options for treating esophageal chest pain?

**SR** Several experimental therapies have been attempted; however, none have been shown to be effective.

### **Suggested Reading**

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