

ADVANCES IN GERD

Current Developments in the Management of Acid-Related GI Disorders

Section Editor: Joel E. Richter, MD

Regurgitation in Patients with Gastroesophageal Reflux Disease



Peter J. Kahrilas, MD
Professor of Medicine
Division of Gastroenterology
Northwestern University Feinberg School of Medicine
Chicago, Illinois

G&H What are the most common symptoms associated with gastroesophageal reflux disease?

PK The most common, or cardinal, symptoms of gastroesophageal reflux disease (GERD) are heartburn and regurgitation. Heartburn is sometimes described as chest pain and other times described as a burning sensation under the sternum; however, regardless of the description, heartburn is reported in nearly all GERD patients and is usually considered to be the defining feature of GERD. Regurgitation occurs with varying degrees of severity in approximately 80% of GERD patients. This symptom is usually described as a sour taste in the mouth or a sense of fluid moving up and down in the chest.

The third most common symptom is dysphagia. At least half of GERD patients describe a sensation of food sticking in the chest or not going down the esophagus easily, or even just an abnormal awareness of food passing through the esophagus. This symptom can be a manifestation of a stricture, but it is more commonly a manifestation of increased sensitivity of the esophagus.

Symptoms associated with GERD that occur at a much lower frequency include chest pain, cough, sore throat, laryngitis, and water brash (very profound salivation).

G&H How often does regurgitation usually occur in GERD patients (ie, on a daily or weekly basis)?

PK On symptom surveys such as the Reflux Disease Questionnaire, GERD patients generally rate symptoms based on how many days per week they occur. A minority of GERD patients report experienc-

ing symptoms on a daily basis; symptoms are more commonly experienced either 2–3 days per week or 4–6 days per week. Approximately 13% of GERD patients complain of regurgitation at least 4 days per week, which is a frequency sufficient for causing a measurable decrement in their quality of life.

In addition, certain factors—such as eating large meals, exercising, or bending over after eating—tend to compress the stomach and trigger regurgitation. It is also thought that regurgitation is more common in GERD patients with anatomically disrupted esophagogastric junctions, which compromise the ability to prevent reflux.

G&H What causes of regurgitation other than GERD should be excluded during the diagnostic process?

PK There are 2 circumstances in which regurgitation is not due to GERD per se but can easily be confused with it. One is in the setting of achalasia, where retained food and fluid reside in and are regurgitated from the esophagus, not the stomach. Thus, achalasia-induced regurgitation has no gastric acid or bile; it is composed of partially digested food and, occasionally, very mucoid saliva (which does not go down the esophagus).

The other condition that may be confused with GERD-induced regurgitation is rumination. This condition occurs while individuals are eating. It is a learned behavior in which an individual subconsciously causes gastric content to come back up the esophagus into the mouth and subsequently reswallow it. The term “rumination” comes from “ruminant” species, such as cows. Cows have 2 stomachs; they regurgitate

food from 1 stomach and swallow it into the other stomach. People are not meant to do this.

G&H If left untreated, could regurgitation lead to more significant problems?

PK The main impact of regurgitation is a decrease in one's perceived quality of life. My colleagues and I recently conducted a study on specific symptoms of GERD and found that regurgitation was 1 of the dominant symptoms that led to the downgrading of quality-of-life indices. This was particularly true when regurgitation occurred at least 4 days per week and was demonstrated irrespective of whether or not heartburn was effectively treated with acid suppression.

G&H According to the data currently available, how effective is standard medical therapy for treating heartburn in GERD patients?

PK Most of the medical treatments for GERD, such as proton pump inhibitors, work by neutralizing or suppressing gastric acid secretion; thus, these treatments are effective at reducing heartburn, which is strongly linked to the reflux of gastric acid in the esophagus. Studies have shown that standard medical therapy for GERD has an efficacy of approximately 50% if the outcome measure is the complete elimination of heartburn. This rate increases if the outcome measure is expanded to include partial resolution of heartburn (although most studies analyze GERD in terms of complete resolution of heartburn).

G&H Is standard medical therapy as effective at treating regurgitation in GERD patients?

PK It is a common misconception that standard medical GERD therapies are also very effective at treating regurgitation. Their efficacy for treating regurgitation is significantly less (by 10–20%) than their efficacy for treating heartburn. Thus, regurgitation is a more resistant symptom than heartburn in GERD patients, and this is true for both definitions of regurgitation (the perception of sour taste in the mouth and, especially, the perception of movement in the chest).

It has been proposed by some gastroenterologists that the failure of a symptom to respond to proton pump inhibitor therapy implies that it is not related to GERD. This is not true. Proton pump inhibitors are excellent at healing esophagitis and are approximately 50% effective at eliminating heartburn, as previously mentioned; however, the efficacy of proton pump inhibitors diminishes precipitously when moving farther away from those 2 endpoints (to chest pain, regurgitation, laryngitis, or any other potential GERD symptom).

It should also be noted that, thus far, essentially all placebo-controlled trials that have been conducted on the treatment of GERD have examined the resolution or reduction of esophagitis or heartburn as the primary outcome measure; no studies have used the elimination of regurgitation as the primary outcome measure. Thus, all of the available data on regurgitation in GERD patients have been obtained from secondary outcomes and usually have been investigator-assessed rather than patient-assessed.

G&H Are there any other medical therapies for treating regurgitation in GERD patients?

PK Beyond acid suppression and neutralization, secondary treatments for GERD include promotility drugs; however, at the present time, no drugs in this class are available for chronic use in the United States.

Recently, there was a major initiative for the development of a class of drugs called reflux inhibitors. These drugs inhibited transient lower esophageal sphincter relaxations, which are 1 of the main mechanisms of GERD and are likely 1 of the main mechanisms of regurgitation as well. The drug that was furthest along in development was lesogaberan, a gamma-aminobutyric acid B agonist. Lesogaberan underwent a study in which relief of refractory heartburn was the primary outcome measure and relief of regurgitation was a secondary outcome measure. Unfortunately, the study's findings were very marginally positive in terms of treating regurgitation, and lesogaberan's development was suspended due to unimpressive efficacy and the possibility of liver toxicity.

G&H If GERD patients are still experiencing regurgitation after receiving standard medical therapy, what is the next step for treatment?

PK The next step is surgical treatment, such as Nissen fundoplication. Refractory regurgitation is 1 of the main indications for antireflux surgery (both conventional and newer surgeries). These surgeries involve mechanical manipulation of the esophagogastric junction or the lower esophageal sphincter, which prevents reflux and controls regurgitation much better than acid suppressive therapy.

G&H At what point is antireflux surgery considered for these patients?

PK This is a patient-driven decision. Ultimately, it is the patient who should decide when more intensive therapy is warranted, and this decision should be based on how significantly his or her quality of life is being compromised. This decision should never be driven by fears of developing esophageal cancer—which, unfortunately, may be the rationale for some patients—as none of these treatments

have been shown to alter the incidence of esophageal cancer in GERD patients. The incidence of esophageal cancer is very low in GERD patients and remains very low following surgical interventions.

G&H Could you discuss the efficacy and safety of antireflux surgery?

PK When performed by an experienced surgeon, antireflux surgery is very effective at resolving regurgitation. However, a small subset of GERD patients who undergo antireflux surgery actually end up worse off than before the surgery.

The array of potential complications associated with antireflux surgery is fairly broad. The most common complications are severe dysphagia and gas retention in the stomach (sometimes called gas bloat); less common complications include inadvertent injury to the vagus nerve resulting in gastroparesis and complications that can occur with any surgical procedure, such as hernias, bleeding, or perforations.

G&H Could you discuss any ongoing or upcoming studies in this area?

PK Current research in this area appears to be focused on intermediate interventions between acid suppressive medical therapies and Nissen fundoplication. Two such interventions have recently been investigated. In the LINX

procedure, a device that looks like a necklace of small magnetic beads is implanted around the lower esophageal sphincter, externally augmenting sphincter pressure. Pivotal data on this procedure were sufficiently robust to gain US Food and Drug Administration approval. This procedure is now being performed in several centers in the United States in a limited fashion.

The other new procedure, which is called transoral incisionless fundoplication (TIF), is performed endoscopically with an EsophyX device by creating a fundoplication through the mouth without any skin incisions. Although TIF is currently being performed, it is still being examined in controlled trials in order to determine the ideal construction of the fundoplication and the appropriate criteria for patient selection.

Suggested Reading

Kahrilas PJ, Jonsson A, Denison H, Wernersson B, Hughes N, Howden CW. Regurgitation is less responsive to acid suppression than heartburn in patients with gastroesophageal reflux disease. *Clin Gastroenterol Hepatol.* 2012;10:612-619.

Kahrilas PJ, Boeckxstaens G. Failure of reflux inhibitors in clinical trials: bad drugs or wrong patients? *Gut.* 2012;61:1501-1509.

Kahrilas PJ, Howden CW, Hughes N. Response of regurgitation to proton pump inhibitor therapy in clinical trials of gastroesophageal reflux disease. *Am J Gastroenterol.* 2011;106:1419-1425, quiz 1426.

Lipham JC, DeMeester TR, Ganz RA, et al. The LINX reflux management system: confirmed safety and efficacy now at 4 years. *Surg Endosc.* 2012;26:2944-2949.

Muls V, Eckardt AJ, Marchese M, et al. Three-year results of a multicenter prospective study of transoral incisionless fundoplication. *Surg Innov.* 2012 Sep 11. Epub ahead of print.