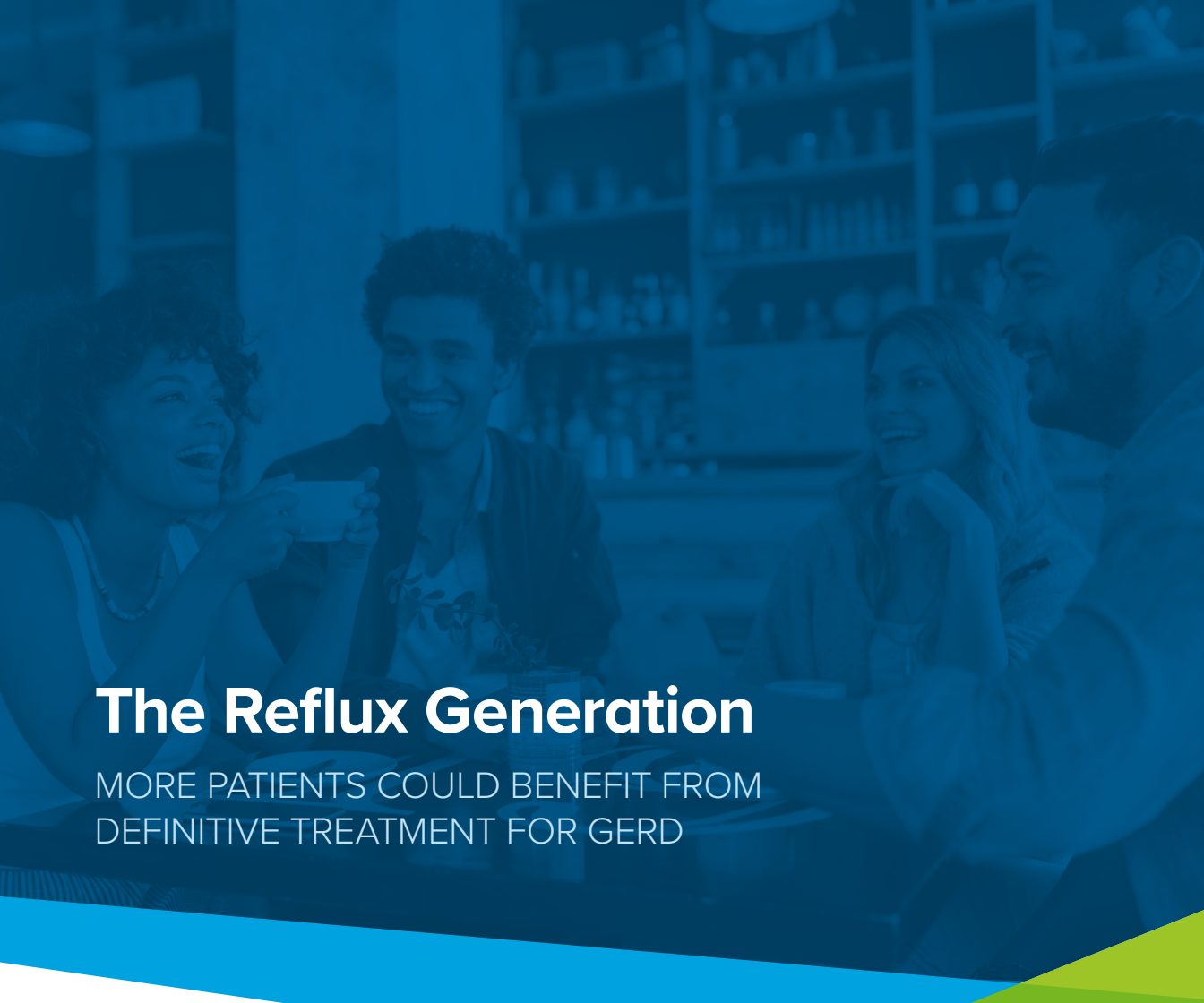

The Reflux Generation

MORE PATIENTS COULD BENEFIT FROM DEFINITIVE TREATMENT FOR GERD

AdventHealth
Medical Group

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Mickle Center for Reflux and Esophageal Disorders

The Digestive Health Institute at AdventHealth Tampa dedicated the Center for Gastroesophageal Reflux and Esophageal Cancer in remembrance of George Mickle, a former patient who passed away from esophageal cancer at age 52. The Mickle Center for Reflux and Esophageal Cancer is a symbol of the Institute's focus and commitment to provide education, awareness, research, and innovation to citizens of the Tampa Bay area for appropriate treatment options available for gastroesophageal reflux disease (GERD) and other esophageal disorders, including esophageal cancer. George was a patient of Dr. Sharona Ross, who is nationally recognized in endoluminal, laparo-endoscopic single site (LESS) and complex abdominal robotic surgery.

George's widow, Maeve Mickle, continues to work with the hospital and the Digestive Health Institute to help raise awareness about the prevalence and consequences of GERD, which can be a precursor to esophageal cancer.

> **"George was the love and light of my life. He valiantly and bravely fought, and I promised him that I would continue the fight and our journey, with the hope that we can help prevent another family from going through what we endured"**
>
> **Maeve Mickle**

The Mickle family, through their generosity in George's memory, has given the Digestive Health Institute an invaluable podium from which to speak about GERD and esophageal cancer. Their generosity compels our team to continue to push for advances in patient education and care.

Medical Management of Acid Reflux Is Doing Little to Mitigate the Rise of Esophageal Adenocarcinoma

Gastroesophageal reflux disease, or GERD, is a major health concern, with an estimated 60 million people in the United States living with this condition, whether diagnosed or not. Reflux symptoms are experienced by a third of American adults monthly, more than one in seven have them weekly, and nearly one in ten suffer from them daily.

Upon diagnosis, GERD is almost always medically managed, with most patients being prescribed proton pump inhibitors (PPIs). PPIs have their role in treating GERD, but they were never intended for long-term use; studies suggest about one of four patients taking PPIs on a long-term basis are progressing to Barrett's esophagus and even esophageal cancer. Unfortunately, because most patients' acid reflux is well-controlled on PPIs, they are not aware they are still refluxing, and lacking acid, this reflux is actually more carcinogenic. The impact of the introduction of PPIs has been catastrophic. Since the first one was approved by the FDA, esophageal adenocarcinoma rates have increased astronomically.

60 million
people in the United States
live with acid reflux

1/3 of American adults
experience reflux symptoms **monthly**

1 out of 4
patients taking PPIs
on a long-term basis are progressing to **Barrett's esophagus and even esophageal cancer**

What is GERD?

Gastroesophageal reflux occurs when stomach acid refluxes back into the esophagus. Some reflux is normal, and almost everyone will experience it from time to time. However, when reflux produces negative health consequences, including severe or persistent symptoms, it can be classified as gastroesophageal reflux disease (GERD). Excessive reflux is generally caused by esophageal dysmotility, loss of lower esophageal sphincter function or delayed gastric emptying.

Patients with GERD may experience esophageal and/or extraesophageal symptoms, including:

- Heartburn
- Noncardiac angina (marked by severe pain in the chest)
- Dysphagia
- Hoarseness or voice changes
- Sinusitis
- Recurrent pneumonia
- Cough
- Exercise-induced asthma or asthma-like symptoms

In particular, dysphagia, or the sensation of food getting stuck in or passing slowly through the esophagus, is an ominous symptom because it could denote the presence of strictures or cancer. If left untreated or undertreated, GERD can lead to sequelae such as pulmonary insufficiency, esophageal strictures, Barrett's esophagus and esophageal adenocarcinoma.

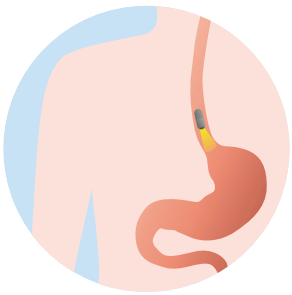
Diagnosing GERD

GERD diagnoses are often based exclusively on the presentation, or patient report, of symptoms. While diagnosis begins with a thorough review of medical history and symptoms, it is crucial the condition be objectively established by means such as physical measurement of reflux, and therapy (open-ended or definitive) should be undertaken only after objective documentation of excessive reflux is obtained.

There are three primary tests that assist in the diagnosis of GERD:

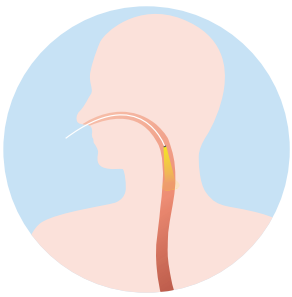
An **upper gastrointestinal barium study,** also known as a swallow study, uses a barium laden food bolus (usually a marshmallow or bite of bagel) to measure how well food travels down the esophagus and into the stomach. The test provides tremendous information about esophageal and gastric motility. This study can also define esophagogastric anatomy and the presence and extent of hiatal hernia, providing a road map to definitive therapy.

Esophagogastroduodenoscopy (EGD) has emerged as a useful study because it can identify sequelae of GERD (e.g., inflammation) including precancerous changes (e.g., Barrett's esophagus) and cancer. EGD also identifies the squamocolumnar junction, pinpointing where the esophagus and stomach meet, which allows for a Bravo pH measuring capsule to be placed accurately.



Bravo capsule

Ambulatory devices that measure pH including the Bravo capsule that gauges the amount of liquid acid refluxing into the esophagus, and the Restech probe, placed transnasally and down behind the uvula, that measures aerosolized as well as liquid reflux.



Restech probe

Laryngopharyngeal Reflux

What is Laryngopharyngeal reflux?

Laryngopharyngeal reflux (LPR) is a condition that occurs when contents from the stomach travel up through the esophagus and into the throat. Anyone can develop LPR, but aging, certain dietary habits, stress and obesity make one particularly susceptible to LPR.

What are the symptoms of LPR?

The symptoms of LPR are very different from the symptoms associated with gastroesophageal reflux disease (GERD). For example, with LPR, most people do not experience heartburn. For this reason, LPR is often referred to as 'silent reflux.' Common symptoms of LPR include:

- Hoarseness
- The sensation of a 'lump' in the throat
- Cough
- Increased mucus in the throat
- Frequent throat clearing
- Food sticking in the throat when swallowing
- Bad taste in the mouth
- Post-nasal drip

How is LPR tested?

At the Digestive Health Institute, our team specializes in the evaluation and treatment of laryngopharyngeal reflux. In order to get objective data related to the presence of acid in your throat, we use the Dx-pH system. The Dx-pH system utilizes a small probe that is placed in the throat. This probe takes continuous measurements of the acid that enters the throat in either an aerosolized or liquid form. Due to the sensitivity of the throat, even aerosolized acid exposure could potentially cause tissue damage.

How is LPR treated?

If you test positive for LPR via the Dx-pH system, our team will discuss the various treatment options with you. Treatment options typically include lifestyle modifications, medications and/or surgical intervention.

What if LPR is left untreated?

It is known that the tissue in your throat is much more sensitive that the tissue in your esophagus and stomach. As such, laryngopharyngeal reflux can be dangerous if left untreated. Untreated LPR can lead to chronic sore throat, chronic cough, pulmonary complications, voice changes, lesions on the vocal cords, vocal cord abnormalities, dental erosion & cancer. If you are experiencing LPR symptoms, it is important that you speak with your doctor.

The role of a hiatal hernia

The term hiatal hernia was introduced into the American lexicon in the 1950s. It describes the herniation of the stomach through the hiatus into the chest, and progressively it has been interpreted as an abnormal condition denoting disorder or disease. While gastroesophageal reflux disease and hiatal hernia are distinct conditions that occur independently, it is important to recognize that a large hiatal hernia can lead to symptoms of reflux or dysphagia. The presence of a large hiatal hernia indicates the phrenoesophageal membranes that help control reflux have become weakened or stretched out, rendering them ineffective. The herniation of the stomach into the chest can also displace the esophagus, leading to relative esophageal outlet obstruction.

Hiatal hernia is anatomically normal and is present in most people over the age of 50. By itself, in almost all cases, a hiatal hernia is not the issue; the reflux is, and from a patient perspective, treatment should focus on the symptoms related to GERD or esophageal outlet obstruction. Only when surgical intervention for reflux or outlet obstruction is sought is the presence of a hiatal hernia of particular interest because ultimately, the contents of the hiatal hernia must be replaced within the high-pressure zone of the abdomen.

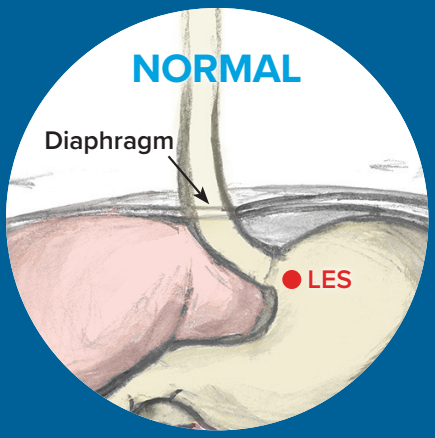
Four basic types of **hiatal hernia**

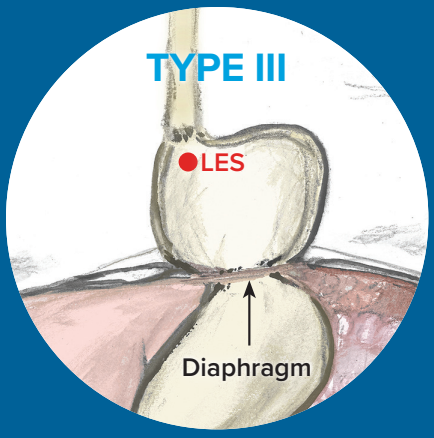
Sliding hiatal hernia (I), caused when a portion of the proximal stomach has migrated into the mediastinum such that the gastroesophageal junction resides well above the esophageal hiatus. The symptoms most commonly associated with this hernia are symptoms of excess acid reflux.

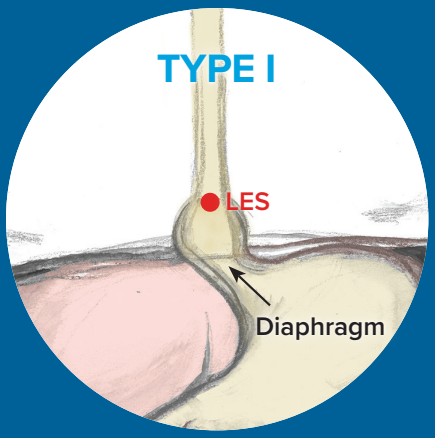
Paraesophageal hernia (II), in which the gastroesophageal junction resides in the high-pressure zone of the abdomen caudal to the esophageal hiatus. A portion of stomach has herniated through the esophageal hiatus. This hernia is cause for concern because while uncommon, it can lead to gastric incarceration and strangulation. Symptoms associated with this hernia are often related to esophageal outlet obstruction rather than GERD per se.

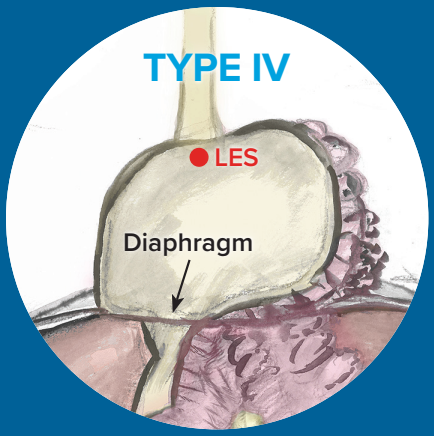
Large hiatal hernia (III), where a significant portion of the stomach has herniated into the chest (i.e., mediastinum). With this hernia, the gastroesophageal junction lies well cephalad to the esophageal hiatus. Symptoms associated with this hernia are generally related to GERD.

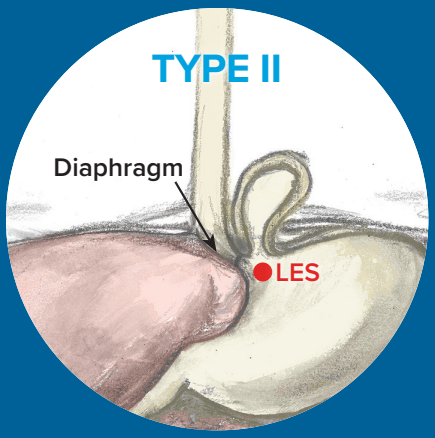
Giant hiatal hernia (IV), which includes a significant portion of the stomach and adjacent organs, often including the colon, small intestines, omentum, spleen and, very occasionally, the pancreas. The gastroesophageal junction is well within the mediastinum, and associated symptoms may be related to excess acid reflux, esophageal outlet obstruction, or both.


NORMAL
Diaphragm
LES


TYPE III
LES
Diaphragm


TYPE I
LES
Diaphragm


TYPE IV
LES
Diaphragm


TYPE II
Diaphragm
LES

Medical management and lifestyle modifications in the treatment of GERD

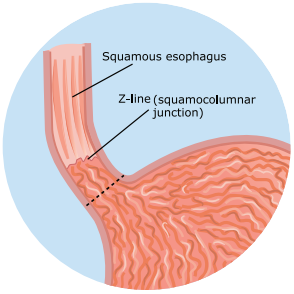
Medical management is the mainstay of treatment for GERD, and proton pump inhibitors (PPIs) or H2 blockers are the principal anti-acid drugs used to treat the condition. Weight loss; smoking cessation; avoiding caffeine, alcohol and chocolate; avoiding medicines that relax the lower esophageal sphincter mechanism; and avoiding increases to intra-abdominal pressure(e.g., heavy lifting) are also crucial to medical management.

Unfortunately, for a variety of reasons, medical management is often unsuccessful:

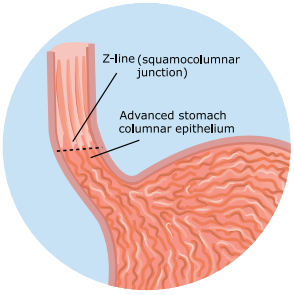
- **It is expensive.** Medications, doctors' visits, tests, procedures and time lost attending to health care makes medical management of GERD pricey.
- **It is difficult, and sometimes impossible.** Lifestyle changes are typically not easy to make or maintain, and they can be impractical. For example, a man working on a loading dock may not have the option of moving to a desk job just to avoid repetitive heavy lifting.
- **It treats the symptoms, not the cause.** Prescription and over-the-counter reflux medications suppress or neutralize acid, but do not stop reflux. Patients taking proton pump inhibitors still reflux, and they will continue to experience symptoms such as exercise-induced asthma, hoarseness, sinusitis and cough. Additionally, their esophagi are exposed to non-acid reflux, which often contains bile acids and bile salts—both potential carcinogens.

Despite these issues, efforts to resolve chronic reflux with medical management should be actively pursued before definitive treatment options are considered. However, medical management, and specifically proton pump inhibitors, should not be used for extended periods. PPIs are not approved for this purpose, and the consequences of open-ended use are many and severe. It may be tempting to continue medical management for patients who achieve symptom control on pharmacotherapy, but it's important to consider that these are often the same patients who do best with definitive therapy.

Risks of Untreated GERD



Normal esophagus



Barrett's esophagus

The sequelae of GERD are even more serious conditions, including esophageal strictures, Barrett's esophagus and esophageal cancer. A **stricture**, or scar tissue that narrows the esophagus, can lead to dysphagia, or the delaying of food traveling down the esophagus, and in extreme cases, the inability of food to reach the stomach. The difficult and painful swallowing, odynophagia, caused by a stricture can cause patients to become malnourished or dehydrated. A stricture can also lead to regurgitation and aspiration, which can in turn cause pneumonia and pulmonary insufficiency.

Barrett's esophagus is a neoplastic condition in which the cells at the junction between the esophagus and stomach start to become goblet cells, which are normally only present farther down the digestive tract. This condition increases the risk for esophageal cancer by about 50 times. Patients with Barrett's esophagus must be followed closely to make sure their condition does not progress to high-grade premalignant disease or esophageal adenocarcinoma; sometimes definitive treatment for Barrett's esophagus such as radiofrequency ablation is warranted.

Among the U.S. population, since the early 70s, the incidence of **esophageal adenocarcinoma** has increased more than fifty times; this increase can almost entirely be attributed to GERD, especially as the population's average BMI has been on a steady incline since then. (The relationship between increased BMI and the severity and frequency of GERD symptoms has been well documented.)

Esophageal squamous cell carcinoma v. esophageal adenocarcinoma

The most common histological subtypes of esophageal cancer, accounting for more than 98 percent of diagnoses, are squamous cell carcinoma and adenocarcinoma. While the squamous cell subtype is commonly caused by factors such as drinking, smoking, poor diet and the consumption of very hot beverages, esophageal adenocarcinoma is directly linked to GERD; it is the cancer that develops from the neoplastic response to the presence of reflux contents in the esophagus.

Proton pump inhibitor
precautions

Despite their prevalence, PPIs such as Prilosec, Pevacid and Nexium, are not risk-free. They do not stop reflux; they merely reduce or eliminate acid production; thereby decreasing the amount of acid contained in the reflux material. With PPIs, patients still experience gastroesophageal reflux, but without acid, reflux material is often alkaline and contains potent carcinogens that can lead to neoplastic, pre-cancerous changes such as Barrett's esophagus and ultimately, adenocarcinoma in the lower esophagus. In fact, a 2012 study of patients under routine medical maintenance care including PPI therapy found that 1 in 4 progressed to more severe forms of reflux, and one large-scale Danish study even concluded that the more compliant a patient was in taking prescribed PPIs, the more likely his or her Barrett's esophagus was to progress to a higher grade or to adenocarcinoma. (See p. 24 for detail.)

Proton pump inhibitors have been grossly overprescribed in recent decades, and these medications have done nothing to stall the increase in incidence of esophageal cancer. Rather, they have contributed to the drastic rise in adenocarcinoma. A review of the SEER database found the number of esophageal cancer cases, including both esophageal squamous cell carcinoma and esophageal adenocarcinoma, rose approximately seven and a half times in less than 40 years, increasing from 326 cases per 100,000 in 1973 to 2,525 per 100,000 in 2010. During this time period, the incidence of squamous cell carcinoma cases increased two and half times, while adenocarcinoma increased 57-fold—not 57 percent, more than 50 times.

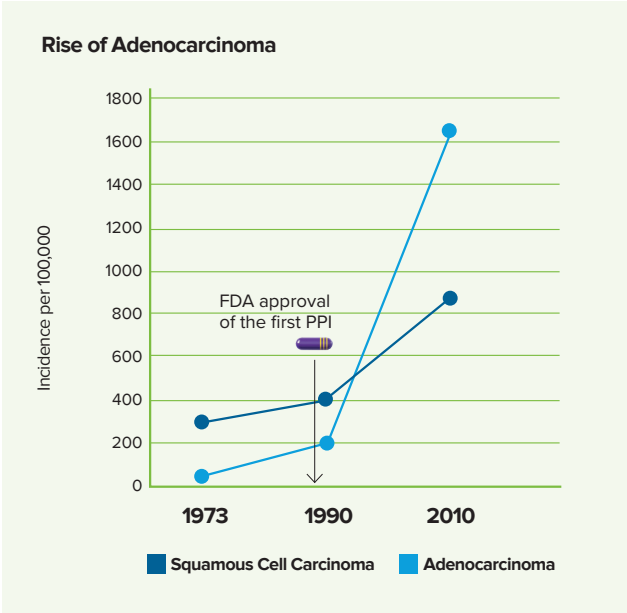
In 1973, less than 1 of 10 patients with esophageal cancer had adenocarcinoma, but by 2010, nearly 66 percent—or 2 out of 3—had adenocarcinoma. In other words, what once may have been considered a rare subtype has rapidly become an epidemic, with the most dramatic increase occurring in the decades immediately following FDA approval of the first PPI in 1989. The impact of PPIs has been cataclysmic by any standard and is cause for great concern.

The overprescription of PPIs has contributed to a
57-fold increase in adenocarcinoma

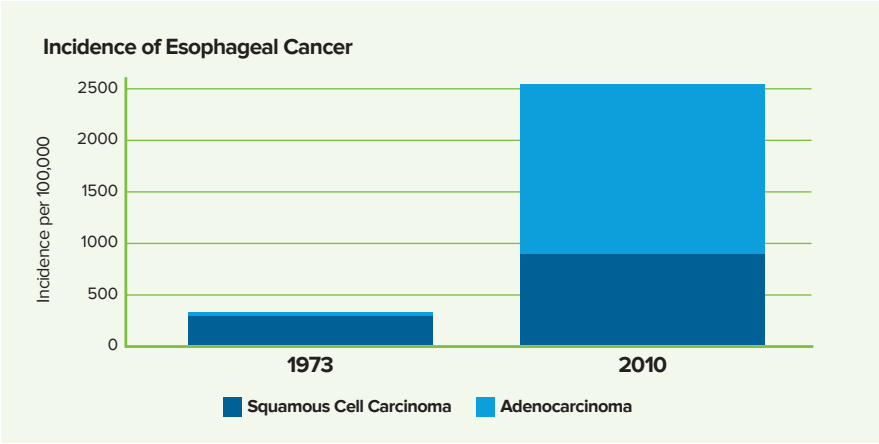
In addition to increasing the risk for esophageal cancer, PPIs contribute to the development and/or progression of osteoporosis by decreasing calcium and magnesium absorption, particularly in postmenopausal women as well as men over age 50, and they are associated with a 27 to 39 percent increased risk of community-acquired pneumonia. Long-term PPI use has also been linked to early-onset dementia, renal dysfunction and failure and colonic infections with Clostridium difficile.

PPIs are associated with many drug interactions and can lead to malabsorption and reduced bioavailability. For example, PPIs impede the activation of Plavix (clopidogrel bisulfate), a common anti-platelet therapy. Clopidogrel is a prodrug that cannot be activated in patients on proton pump inhibitors. In addition, many drugs depend upon the acidic environment of the stomach to degrade their capsule or covering, and in the absence of acid, they go unabsorbed.

Proton pump inhibitors are approved only for short-term use. Long-term and open-ended PPI therapies are off-label indications accompanied by high risk for complications – not to mention that even with them, patients will continue to experience the extraesophageal symptoms of reflux. Extended use is indicated only in patients who are not suitable candidates for definitive therapy, such as the elderly or those with short life expectancy.



*Data provided by SEER database



*Data provided by SEER database

Over-the-counter medications

Over-the-counter medications for GERD are meant to be taken intermittently, as-needed for quick relief, and only for short periods of time. While they can help alleviate symptoms, they should not be used on a daily basis.

Antacids are generally safe for most people. Unlike H-2 blockers or PPIs, they don't reduce gastric acid secretion; rather, they chemically neutralize acid, and because they work on contact, relief of symptoms can be immediate. Side effects are rare, but depending on the formulation, diarrhea or constipation can be notable. Antacids can also interfere with the function or absorption of other drugs.

The effects of antacids can vary considerably depending on the buffers they contain. Most contain aluminum hydroxide, calcium carbonate, magnesium trisilicate or a combination. Additional antacid ingredients include sodium and aspirin. With chronic ingestion, those containing aluminum may raise aluminum levels in the body, especially in patients with renal dysfunction. Calcium may cause significant acid secretion, high levels of sodium is a concern for individuals with fluid retention and aspirin can inactivate platelets. In fact, in response to reports of serious bleeding, in 2016 the U.S. FDA issued a safety alert about aspirin-containing antacids.

H-2 receptor blockers decrease acid secretion by blocking the activation of the Histamine-2 receptors in the stomach lining. Generally, they have a short half-life and are only marginally effective. They are readily available at a low cost and are typically used in conjunction with PPI therapy when better nighttime control of reflux is needed.

Common prescription and over-the-counter reflux medications

Category	How They Work	Examples
Antacids (including foaming agents)	Neutralize acid	Alka-Seltzer, Maalox, Mylanta, Rolaids, Riopan, Tums, Amphogel, Gaviscon, Gelusil
H2 blockers	Decrease acid production	famotidine (Pepcid, Pepcid AC), ranitidine (Zantac), nizatidine (Axid), cimetidine (Tagamet, Tagmet HB)
Proton Pump Inhibitors (PPIs)	Decrease acid production	omeprazole (Prilosec, Zegerid), lansoprazole (Prevacid), pantoprazole (Protonix), rabeprazole (Aciphex), esomeprazole (Nexium), esomeprazole (Nexium)

Definitive treatment of GERD

Because proton pump inhibitors should be restricted to short-term symptom control, and they do not protect against reflux-associated aspiration or the progression of Barrett's esophagus to cancer, patients with GERD require a definitive modality to manage or remedy their condition. Operative treatment is proven effective for GERD, and unlike medical management, should be curative. Ninety-five percent of the patients who undergo surgery to strengthen the lower esophageal sphincter (LES) experience cessation of excess gastroesophageal reflux, resulting in a significant reduction in GERD symptoms.

Surgical treatment for GERD should be pursued only after a thorough preoperative evaluation, including documentation of excess acid reflux, endoscopy (with biopsies as indicated), and documentation of esophageal motility and function have been completed. For the latter, an upper GI contrast series with a barium-laden food bolus (e.g., bite size portions of a bagel or campfire-sized marshmallows) seems to be a better predictor than manometry of how a patient will handle a food bolus after fundoplication.

Unless they have specific contraindications to definitive care, patients should be considered candidates for definitive GERD therapy. Advanced age is generally not a singular contraindication because people are consistently living longer, and definitive cessation of reflux can palliate many GERD-associated complications that often plague the elderly.

Surgical care for GERD should be considered when a patient:

- **Continues to have esophageal or extraesophageal symptoms** on medical management, including pharmacotherapy.
- **Is at risk for esophageal stricture or Barrett's esophagus** as a result of chronic irritation. Once transmural injury has occurred, it is unlikely esophageal motility and function will ever be the same, so strictures should be prevented through definitive therapy. Likewise, definitive therapy is warranted before the development of neoplastic changes such as Barrett's esophagus occur.
- **Has developed an esophageal stricture.** The stricture should be corrected through the use of dilation. Once the stricture has been dilated, cessation of reflux is imperative and pharmacotherapy alone is insufficient for this. Dilation may be temporarily necessary after a definitive control of reflux as well.

(Definitive Treatment of GERD continued on next page)

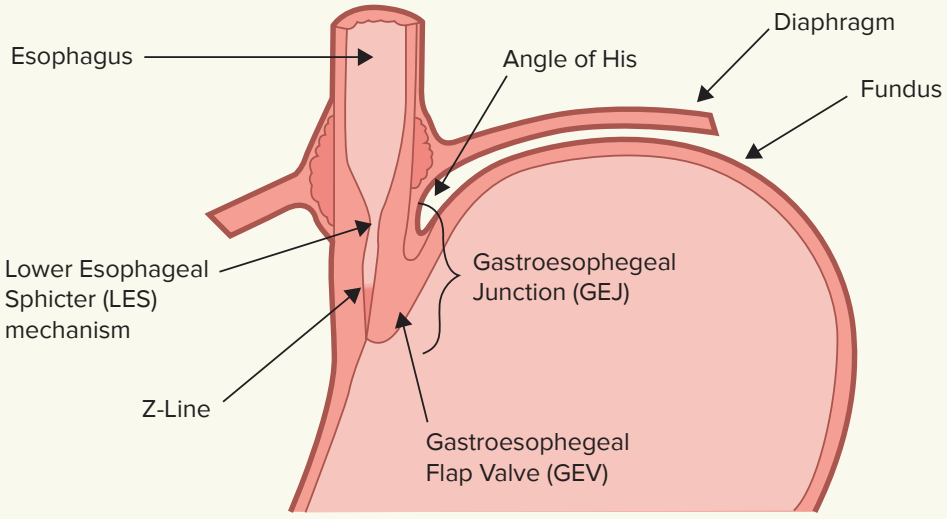
Definitive treatment of GERD (continued)

Has been diagnosed with Barrett's esophagus. With the cessation of reflux brought on by definitive treatment, regression of neoplastic changes is possible and even likely (provided they are in early stage).

- **Has been on PPIs for extended periods.** Although some patients do well with pharmacology in terms of alleviation of symptoms, open-ended medical therapy presents significant risk. Patients who experience symptom control with PPIs often do the best with definitive therapy; success with medical therapy strongly predicts success with definitive therapy.

Trial Evidence of Medical Management vs. Surgical Treatment

In looking at trial studies that compare medical management to surgical treatment of GERD, it is important to note that these two therapies are often held to different standards. Surgical treatment is often considered a failure if the patient resumes taking PPIs or antacids after surgery. Unfortunately, too often, patients resume medical management after surgery without objective evidence of excess reflux. In the experience of the surgeons at the Digestive Health Institute, 19 out of 20 patients experience a complete cure, signified by the cessation of symptoms, after definitive care.



Surgical Solutions for GERD

GERD is a mechanical problem that requires a mechanical solution, and there are multiple mechanical treatment approaches for the condition. Goals for definitive treatment of GERD include constructing a valve mechanism at the gastroesophageal junction, commensurate with esophageal motility, in the high-pressure environment of the abdomen, while ensuring adequate gastric outlet and emptying. All approaches to surgical treatment for GERD involve augmenting the lower esophageal sphincter (LES) mechanism, most often involving augmenting the Angle of His and thereby augmenting the gastroesophageal flap valve.

The surgeons at the Digestive Health Institute use minimally invasive procedures whenever possible for definitive resolution of GERD. They have completed more than 3,000 minimally invasive anti-reflux procedures, that is, wrapping part of the stomach completely or partially around the LES to strengthen this valve.

The two approaches to eliminate GERD used at DHI are minimally invasive surgery, either laparoscopic or robotic-assisted, and endoscopic solutions.

3,000+ minimally invasive fundoplication procedures have been completed

Laparoscopic and Robotic-Assisted Surgical Solutions

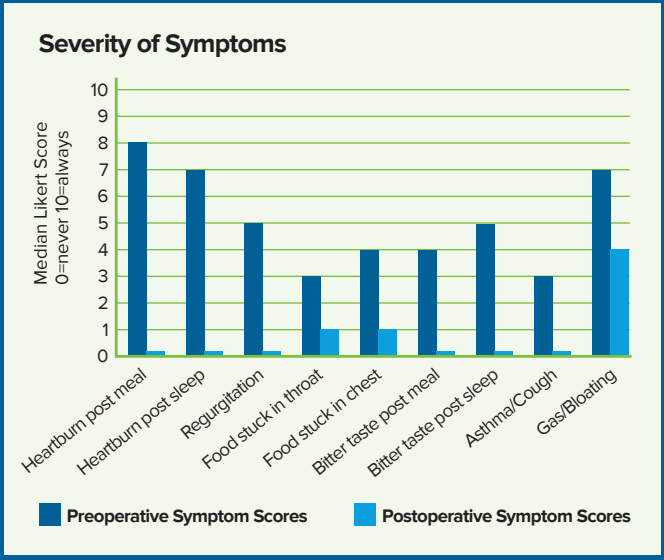
The most common approach to minimally invasive fundoplication involves laparoscopy or robotic-assisted procedures. This approach nearly always involves constructing one of two types of fundoplication:

Nissen fundoplication, also called a 360° wrap, involves wrapping the entire esophagus with stomach. In other words, the back of the stomach (posterior fundus) is brought around the esophagus and sutured to the front of the stomach (anterior fundus) so that the esophagus is completely covered by stomach.

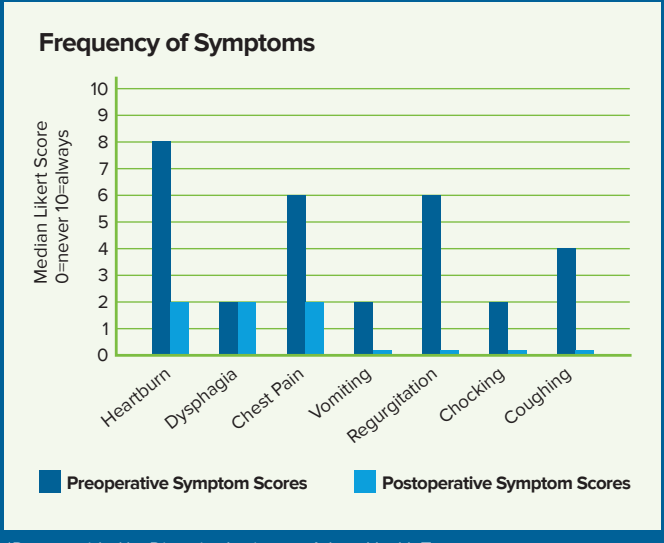
Toupet fundoplication, also known as a 270° posterior fundoplication or partial wrap, involves wrapping a portion of the esophagus with stomach. As with a Nissen fundoplication, the posterior fundus of the stomach is brought around behind the esophagus, but with a Toupet fundoplication, the posterior fundus is sewn to the esophagus rather than the anterior fundus. Then, the anterior fundus is sewn to the left side of the esophagus rather than the posterior fundus. This results in a portion of the esophagus being covered by stomach.

The fundoplication approach chosen by the surgeon is generally based on preoperative evaluations of esophageal motility as determined by the preoperative upper GI barium study. (It is difficult to establish motility and gastric emptying intraoperatively or endoscopically.) Generally, the Nissen fundoplication is preferable because it constitutes a more competent valve mechanism. For this approach, the esophagus should be able to clear a food bolus with two or fewer stripping motions on an upper GI barium study. Toupet fundoplication has its place when there is moderate esophageal dysmotility as measured by the moderate inability to clear a bolus.

In the case of severe dysmotility, such as when the esophagus struggles further with more than four contractions with both a bite of a bagel and a bite of marshmallow, approaches other than an operatively constructed fundoplication should be discussed. These approaches could include the endoscopically constructed procedures that will be discussed later or an uncommon form of fundoplication construction. Uncommon constructions such as the Hill procedure or the Belsey Mark IC procedure might have application in these cases, but these fundoplications are not widely used because they are technically demanding operations and their results have been inconsistent.



*Data provided by Digestive Institute at AdventHealth Tampa



*Data provided by Digestive Institute at AdventHealth Tampa

Conventional laparoscopic fundoplication

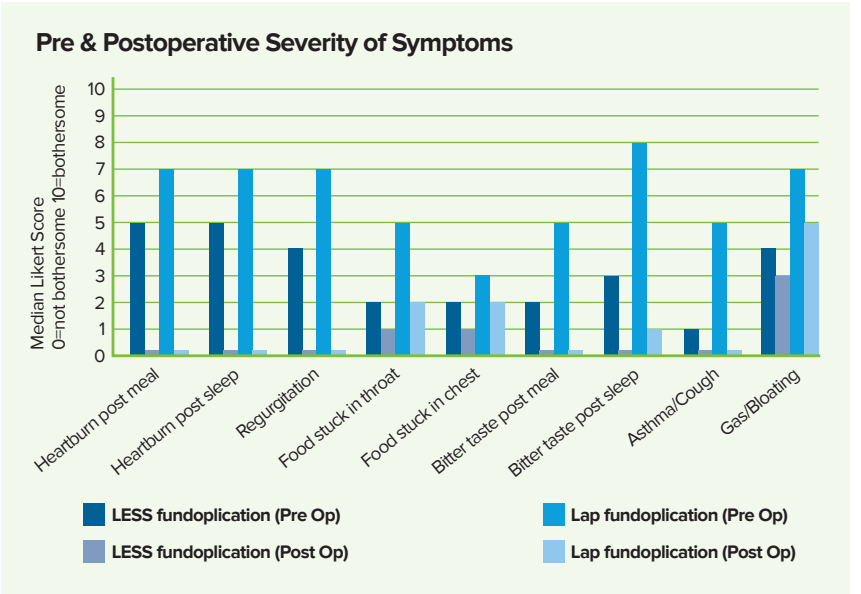
Laparoscopic fundoplications are performed conventionally with five trocars and incision sites, one of which is usually at the umbilicus. This operative approach has been in use for more than 25 years. Fundoplications constructed through this approach are effective and durable. The Digestive Health Institute team has operated on more than 2,000 patients with this approach with superior results. In short, after this procedure, patients have:

- Effective control of gastroesophageal reflux
- Amelioration or elimination of gastroesophageal reflux symptoms
- Few persistent troublesome symptoms
- Few new troublesome symptoms

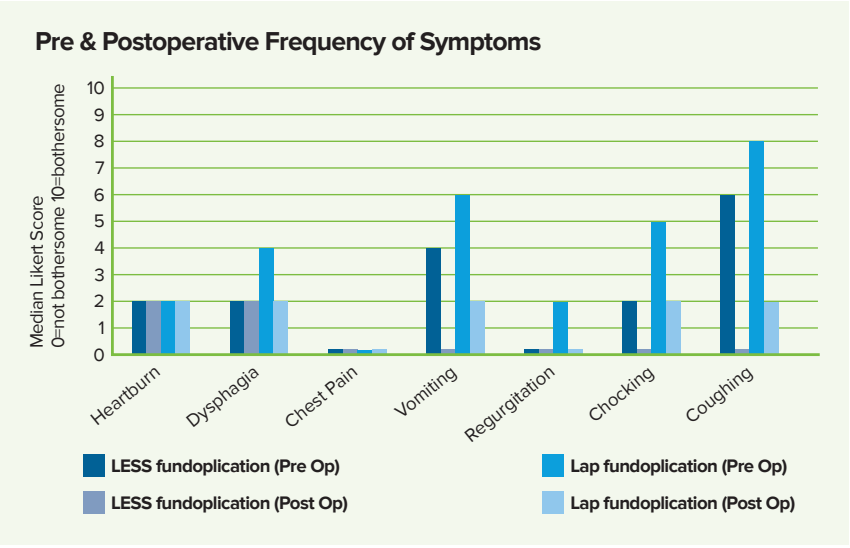
Our physicians have been thought leaders in the diagnosis, evaluation, treatment and follow-up of patients who have gastroesophageal reflux and who have had laparoscopic fundoplication. Comparisons of preoperative and postoperative symptoms clearly document the salutary benefits of a laparoscopic fundoplication.

Robotic-assisted fundoplication

The advent of the daVinci® Surgical System has made it possible for patients unable to have a conventional laparoscopic fundoplication procedure to have one in the context of a surgical robot. While this approach modestly increases the length of the operation, it provides a minimally invasive option for patients who may have otherwise needed an open procedure.



**Data provided by Digestive Institute at AdventHealth Tampa*



*Data provided by Digestive Institute at AdventHealth Tampa

LESS fundoplication

The conventional laparoscopic approach continues to be the preferred approach for most surgeons. Because it is safe, efficacious and durable, the conventional laparoscopic approach is not to be denigrated; however, the surgeons at DHI believe there is a better approach. This better approach—laparo-endoscopic single site (LESS) fundoplication—is equally efficacious, safe and durable but with a much better cosmetic outcomes, less pain and increased patient satisfaction.

Our team began performing anti-reflux fundoplications with the LESS approach in 2008 and have now performed more than 500 fundoplications with this approach, made possible by the development of the 5 mm deflectable-tip laparoscope. Our treatment results from this approach parallel the ones we have achieved with conventional laparoscopy.
After LESS fundoplication, amelioration of GERD symptoms is impressive with few persistent bothersome symptoms and few new symptoms. However, patient satisfaction is higher after LESS fundoplication compared to conventional laparoscopy because of fewer trocar site complications and a seemingly faster return to normal activities. Further, patients report being pleased they are left with only one scar — one that is hidden in their umbilicus.

Whenever possible, we now use the LESS approach for fundoplication, and we are strong advocates of this approach for treating GERD in our publications and presentations at conferences and regional and national professional surgery society meetings. Given that it leaves patients with fewer adverse physical effects, LESS fundoplication should be in every surgeon's armamentarium. While most surgeons find the procedure technically challenging and thus prefer conventional laparoscopy, with proper training, this hesitation can be overcome. We have trained more than 250 surgeons in the LESS approach, and with our instruction, surgery residents and fellows master this technique safely.

An 8mm incision,
made at the umbilicus
(belly button), **is less than half the width of a dime.**

Robotic-assisted fundoplication and hiatal hernia repair

The advent of the daVinci® Surgical System has made it possible for patients unable to have LESS fundoplication procedure to have one in the context of a surgical robot. This provides a minimally invasive option for patients who had history of previous abdominal operations, have a large hiatal hernia, and/or BMI slightly above 26. The daVinci® Surgical System is a very stable surgical platform with superior 3D HD optics and 7degree hand motion with elimination of tremor and increased dexterity. The platform provides more accurate dissections which allows surgeons to offer complex operations with a very minimally invasive approach.

Temporary Side Effects from
Laparoscopic and Robotic-assisted Approaches

Regardless of fundoplication type constructed, there are a few physical consequences that often result from a laparoscopic or robotic-assisted approach:

- Temporary shoulder pain as a result of carbon dioxide insufflation of the peritoneal cavity irritating the urogenital and pelvic diaphragms.
- Food catching at the new valve (improved by starting off on a liquid diet and slowly advancing the diet to more solid foods).
- Bloating as a result of learned aerophagia while experiencing GERD symptoms; chronic swallowing of air can take some time to unlearn.
- Increased flatulence as a result of bloating.
- Increased frequency of defecation (generally a short-term issue).
- Nausea as a result of aerophagia.
- Early satiety because of a decreased stomach size after fundoplication (which quickly resolves itself).
- Pain at the incision(s).

LINX® not a suitable alternative to fundoplication

The LINX® reflux management system is an attempt at definitive treatment for GERD that does not involve anatomical structure modification, although if a hiatal hernia is present, it must be reduced and the esophageal hiatus reconstructed. LINX consists of a band of magnetized titanium beads wrapped around an elastic-type wire placed circumferentially around the gastroesophageal junction.

While LINX was in development, the FDA had numerous reports of serious adverse events that led to explantations of the device. Some surgeons and many gastroenterologists perceive LINX to be a particularly minimally invasive approach for definitive reflux control, but our physicians avoid using it in their practice. Their explantations of LINX have revealed impressive fibrous reactions around these devices, making it inconceivable that the proposed mechanism of these devices could be realized. Because the LESS fundoplication approach is safe, efficacious and durable, the DHI surgeons find the LINX device unnecessary.

Endoscopic Solutions

In addition to laparoscopic and robotic-assisted procedures involving anywhere from one to five incisions, there are also endoscopic solutions for the definitive treatment of GERD that involve no external incisions at all. These involve transoral incisionless fundoplication (TIF), also known as EsophyX™, and the Stretta procedure.

Transoral incisionless fundoplication (TIF/EsophyX)

A TIF, created by using the EsophyX device, reestablishes the primary natural barrier to reflux by constructing a robust valve at and above the gastroesophageal junction. This approach should greatly augment the angle of His and augment the gastroesophageal flap valve.

Candidates for TIF are patients with:

- A hiatal hernia ≤ 2 cm in size
- A body mass index less than 35 kg/m^2
- Excess acid reflux

Patients with previous abdominal surgeries that would contribute to a reoperative field and patients with a failed previous fundoplication are ideal candidates for TIF as long as they meet other criteria such as adequate esophageal motility and adequate gastric emptying.

The EsophyX device constructing the TIF results in a 2 to 3 cm 270° esophagogastric fundoplication that utilizes full-thickness polypropylene H-fasteners. The TIF procedure is performed with concomitant flexible video endoscopy, which provides visualization.

Endoscopic Solutions (continued)

TIF is an ambulatory procedure with immediate return to functional activities. Durability results at five years are very promising. After TIF, the vast majority of patients can suspend PPI therapy. Consequently, their qualities of life are tremendously improved, and resolution of esophagitis should be expected. Given that the large majority of patients opt out of follow-up ambulatory pH testing, available data indicates postintervention pH normalization should be expected. In short, TIF is a safe and efficacious procedure.

Stretta Procedure

The Stretta procedure involves a catheter passed transorally into the esophagus and stomach which delivers low, 5-watt radiofrequency energy at the lower esophageal sphincter mechanism and gastric cardia. While being applied, the Stretta generates temperatures of 65°C to 85°C during a series of 14, one-minute cycles that remodel the lower esophageal sphincter muscle and gastric cardia.

Stretta results in a statistically significant decrease in GERD symptoms and subsequent PPI use. The treatment is effective and durable beyond five years. Unfortunately, as with all procedures aimed at definitive relief for GERD, there is a lack of pH testing to document the efficacy of Stretta because, for most patients, when permanent relief of symptoms is achieved, they are unlikely to find such testing necessary.

The role of proton pump inhibitors in causing esophageal adenocarcinoma

A large epidemiological study published in 2014 of all Danish patients diagnosed with Barrett's esophagus—a metaplastic condition caused by GERD—between 1995 and 2009 was very telling. In this case-controlled study of 9,833 patients, the officers were unable to prove that proton pump inhibitors prevented the progression of Barrett's esophagus. Rather, they documented an increased risk of esophageal adenocarcinoma and high-grade dysplasia related to long-term PPI therapy. Notably, with long-term, low-adherence PPI use, the risk of high-grade dysplasia and adenocarcinoma was increased 2.2 times. With long-term, high-adherence PPI use, the risk of dysplasia and adenocarcinoma was increased 3.4 times. In sum, the study did not find a preventive effect from PPIs but rather an increased risk of high-grade dysplasia and esophageal adenocarcinoma.

The ProGERD study, a prospective multicenter open cohort study undertaken in Germany, Austria and Switzerland, was published in 2012. Study participants were stratified into two cohorts: those with nonerosive reflux disease and those with erosive reflux disease. Patients were given a short course (2 to 8 weeks) of esomeprazole to achieve endoscopically confirmed healing in erosive reflux disease and symptom relief in nonerosive reflux disease. Patients were then sent back to their physicians for routine treatment, as ordered at the discretion of their physicians, and followed annually by protocol.

Within two years of study initiation, adenocarcinoma was confirmed in 6 patients. At five years, 44 percent, or 2,721, of the patients underwent endoscopies by the study group to measure disease progression, defined as nonerosive reflux disease becoming erosive reflux disease, worsening of erosive reflux disease (class A/B becoming class C/D), or the development of Barrett's esophagus or esophageal adenocarcinoma. While the study concluded that most patients' Barrett's esophagus does not worsen while under medical management, after five years, 25 percent of patients from the nonerosive reflux disease cohort had developed erosive reflux disease; 50 percent of patients with LA class C/D erosive reflux disease had persistent erosive reflux disease; and nearly 1 in 10 of these patients had persistent class C/D erosive reflux disease. Overall, 25 percent of patients on standard therapy (i.e., PPIs) had persistence of, or progression to, erosive reflux disease. Moreover, 5.9 percent of the nonerosive reflux disease cohort, 12.1 percent of those with LA class A/B erosive reflux disease, and 19.7 percent of those with LA class C/D erosive reflux disease had progressed to Barrett's esophagus. Ten percent of all patients had progression to visible columnar-lined epithelium, and 6 percent of all patients had progression to visible columnar-lined epithelium with intestinal metaplasia. This progression was particularly notable in patients with erosive reflux disease. Regular PPI therapy was a significant factor in promoting progression to Barrett's esophagus: The more compliant the patient, the bigger the problem.

In sum, PPI therapy was effective in controlling symptoms of reflux but was not particularly effective in healing erosive esophagitis. Under routine medical care including PPI therapy, progression to more severe forms of reflux occurred in 25 percent of patients with nonerosive reflux disease. The takeaway from this study is that current medical therapeutic management with proton pump inhibitors is usually adequate, but it is also often inadequate. Routine treatment of gastroesophageal reflux disease with acid-suppressive drugs does not always—and often does not—prevent progression to Barrett's esophagus and the sequela of Barrett's esophagus. Patients with more severe forms of erosive reflux disease have the highest risk for progression to Barrett's esophagus, and 6 percent of patients with GERD are likely to progress to diagnosis of Barrett's esophagus at five years.

Progression to Barrett's esophagus is most likely to occur in patients with the presence of erosive esophagitis at initiation of PPI therapy, and PPIs promote Barrett's esophagus in some patients. That 6 percent of patients with GERD are likely to progress to Barrett's esophagus at five years is not a minor issue. GERD affects upwards of 20 percent of the adult population of the United States. A conservative estimate of the number of U.S. adults who have GERD would be 55 million, implying that more than 660,000 Americans per year are progressing to Barrett's esophagus. This is an enormous healthcare problem and helps explain why esophageal adenocarcinoma is now epidemic.

Meet Dr. Sharona Ross

Sharona Ross, MD, FACS is a board-certified advanced foregut (Upper GI) and Hepato-Pancreato-Biliary (HPB) surgeon specializing in robotic and single incision laparoscopic operations. She's renowned as a leader and innovator in the development of robotic surgery in the United States with the goal of offering patients robotic complex abdominal operations for esophageal, stomach, small bowel and pancreatic cancers, as well as laparo-endoscopic single site (LESS) surgery, which she continues to perfect through innovative techniques and instrumentation.

Dr. Ross is a Professor of Surgery at the University of Central Florida College of Medicine, the Director of Minimally Invasive and Robotic Surgery and Surgical Endoscopy at AdventHealth Tampa, the Director of the Center for Digestive Disorders and Pancreatic Cancer and the Director of the Advanced GI and HPB Surgery Fellowship at the Digestive Health Institute, which trains new surgeons to master minimally invasive and robotic complex surgery.

Dr. Ross is meritoriously named a Patient Preferred Surgeon Representing the State of Florida for 2020, 2021, and 2023. She was also recognized by Continental Who's Who as a Top Surgeon in the field of Gastroenterology in acknowledgment for her role as an advanced Foregut and HPB surgeon with the Digestive Health Institute at AdventHealth Tampa.

We're Here for You.

If you have a question, concern or just need someone to talk to, please let us know. Our team of compassionate and experienced attending surgeon, ARNPs and nurses are here to help you, whenever and however you need us.

Sharona Ross, MD, FACS

Sandy Freeman, ARNP

Alexis Crews
Surgical Coordinator

Dana Manzi, ARNP

Latisha Mills, MA

Notes:

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