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# Evaluation of GERD Diagnosis, Management, and Outcomes

**Mada Bejad G. Almutairi[1], Salem Muaedh Alsulaimi[2], Rayan Ali I Alghamdi[2], Khalid Abdullah Alrehaili[2], Sohaib Aziz Habhab[2], Abdulrahman Mohsen Althagafi[2], Faisal Ali Alghamdi[3], Naif Abdulaziz Meighrbl[3], Waleed Mohammed Alsuhaymi[3], Mohammed Saeed Al_Yahya[4]**

[1]Almaarefa College, [2]Umm Al-Qura University, [3]University of Jeddah, [4]King Khalid University

## ABSTRACT

**Background:** Gastroesophageal Reflux Disease (GERD) is a condition which develops when the reflux of gastric content causes troublesome symptoms or complications. GERD is arguably the most common disease encountered by the gastroenterologist. It is equally likely that the primary care providers will find that complaints related to reflux disease constitute a large proportion of their practice.(1) GERD condition can present with different presentations and the response to the intervention significantly differs from patient to patient. As a result reviewing the new literatures done in this field will help in providing a better outcomes for the patients.

**Objective:** Treating patients with GERD is difficult and needs different approaches. In this paper, we reviewed the major and the latest studies regarding GERD symptomatology, risk factors, diagnosis and management.

**Method:** A comprehensive search was done using biomedical databases; Medline, and PubMed, for studies concerned with assessment of GERD. Keywords used in our search through the databases were as; "GERD Pathophysiology", "GERD Classification", and "GERD Management".

**Conclusion:** GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms such as heartburn, regurgitation, and sleep disturbance. GERD can be diagnosed by various measures such as GERD Questionnaire, PH Monitoring, and Upper Endoscopy. Initially GERD can be managed by simple life modification measures, then physicians can add Protons Pump Inhibitors (PPIs), and Histamine 2 Receptor Blocker (H2RBs). In case of PPIs and H2RBs failure in reliving GERD symptoms physicians may go for anti-reflux surgical interventions.

**Keywords:** GERD, Diagnosis, Management, Outcomes.

## INTRODUCTION

GERD is defined as heartburn, acid regurgitation, or both, at least once a week. These troublesome symptoms are caused by the movement of gastric contents into the esophagus.

GERD represents a common disorder, particularly in the Western world (about 10%-20% in Western countries and under 5% in Asia) and its prevalence appears to be increasing. The incidence rate, reported by two longitudinal studies was 4.5 and 5.4/1000 people per year, respectively. In Saudi Arabia, ***Alsuwat et al.*** [2] found that the prevalence of GERD is suspected to be around 25% of the population, which means it is slightly higher than Western countries and much higher than countries of East Asia.

## OBJECTIVE

In this review our aims are: 1) Discussing the pathogenesis that stands behind GERD development. 2) Discussing the various methods of GERD diagnosis, and management 3) Providing a paper that analyzed the recent literatures done in this field.

## METHODOLOGY

### Sample

We performed comprehensive search using biomedical databases; Medline, and PubMed, for studies concerned with evaluation of GERD published in English language. Keywords used in our search through the databases were as; "GERD Pathophysiology", "GERD Classification", and "GERD Management". More relevant articles were recruited from references lists scanning of each included study.

### Analysis

No software was used, the data were extracted based on specific form that contain title of the study, name of the author, objective, summary, results, and outcomes. Double revision of each member's outcomes was applied to ensure the validity and minimize the errors.

## PATHOPHYSIOLOGY

Normal gastric acid has a pH of 1.5 to 3.5 (similar to lemon juice) secreted by the stomach's parietal cells in response to histamine, acetylcholine, and gastrin. All three of these substances coordinate hydrogen ion generation; however, histamine represents the dominant route and plays an important role in current GERD management strategies.

Lower esophageal sphincter (LES) is located at the juncture of the stomach and the esophagus. When LES pressure is lower than intragastric pressure, LES become lax. Subsequently, acid contents can easily reflux into the esophagus. This will be leading to the mentioned troublesome symptoms (esophageal and extra esophageal) depending on the severity. Transient LES relaxation (TLESR) occurs largely in the postprandial period,



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the increasing frequency of TLESR after a meal attributed to gastric distention. Not surprisingly and particularly in GERD patients, reflux with increases in intra-abdominal pressure and free reflux through an abnormal low-pressure sphincter make up the remainder of the episodes. Normally, the distal esophagus passes through the diaphragmatic hiatus that is usually formed by the right crus of the diaphragm. As a result, the diaphragm can function as an "external sphincter" by compressing the gastroesophageal junction; this compression increases LES pressure which will work as an anti-reflux mechanism. In the presence of a hiatus hernia, the diaphragmatic sphincter is distanced from the gastroesophageal junction and therefore loses its ability to function as an anti-reflux mechanism(3).

## CLASSIFICATION

An International Consensus Group in 2006 developed a classification of GERD [4] and called it The Montreal Classification (figure 1). This classification provides a basis for universally accepted terminology that bridges cultures and countries and may simplify disease management, allow collaborative research, and make studies more generalizable, assisting patients, physicians, and regulatory agencies.

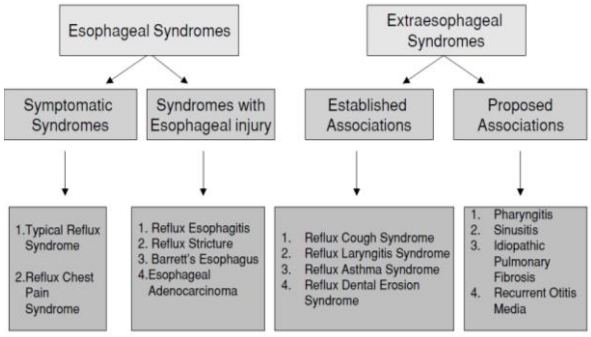


**Figure (1):** The Montreal Definition and Classification of GERD Syndromes.

## RISK FACTORS

***Festi et al.*** [5] showed a sufficient evidence to support the relationship between being obese/overweight and GERD, expressed as specific symptoms and endoscopic features. In addition, it is been found that controlled weight loss (by diet or surgery) is able to induce a significant improvement in GERD symptoms and/or in GERD clinical-endoscopic manifestations. They also focused on dietary habits and its relation to the incidence of GERD.(5) In **Jarosz *et al.*** [6] paper, it is been suggested that patients should be recommended to eat more than three small meals a day and eat dinner and supper at appropriate times instead of one to two big meal in the evening. It had been shown that dietary habits changing is one of the most effective methods of treatment of GERD. The evidence showed that incorrect dietary habits and the absence of regular physical activity represent important risk factors for the development of the so-called "non-communicable diseases". Moderate physical activity seems beneficial regarding the prevention of GERD, while vigorous activity may be dangerous in predisposed individuals.

As GERD was shown to be very common in Saudi Arabia **Alsuwat *et al.*** [2] another study **Alkhathami *et al.*** [7] was conducted to find the risk factors that are present among GERD patients in Saudi Arabia. The observed statistically significant characteristics and behaviors of participants with GERD were positive family history (39.3%), obese (body mass index > 30 kg/m2) (39.4%), not performing weekly regular physical activities ≥ 30 min (31.1%) and smoking (39.3%). GERD was commonly noticed in participants on analgesics (38.4%), not taking fibers (37.4%), drinking tea (33.4%), eating greasy (31.2%) and fast food (32.7%), and these were statistically significant with GERD ($P \leq 0.05$).[7]

## SYMPTOMS

In Saudi Arabia, a large study **Almadi *et al.*** [8] was done using GerdQ about the prevalence of symptoms among GERD patients[8] .It had been found that only 37.27% of patients did not experience any heartburn, while the remainder (62.73%) had one or more episodes of heartburn per week and 17.48% had four to seven episodes per week. There was an increase in the frequency in heartburn episodes in smokers. There was also an increased episode of regurgitation, sleep disturbance, and use of antacids in those with more frequent heartburn episodes. Furthermore, sleep disturbance secondary to heartburn occurred at least once per week in 48.59% of those surveyed, while 12.77% had four to seven episodes of sleep disturbance per week. Regurgitation of food content at least once a week was reported by 60.87%; also, 13.69% of those surveyed reported four to seven episodes of regurgitation in a week. Nausea was reported to occur at a frequency of at least once a week by 75.13%. Epigastric discomfort was common with 77.15% experiencing it at least once a week and 35.14% experiencing it 4-7 times a week. The use of antacid medications at least once a week was reported by 31.48% of those surveyed and it was used by 9.60% at least 4-7 times per week.

## DIAGNOSIS

### *GERD Q*

Specific questionnaires have been developed for the diagnosis of GERD. GerdQ that was developed by **Jones *et al.*** [11] is the most frequently used (figure 3). GerdQ can be used to diagnose GERD with an accuracy similar to that of the gastroenterologist and to assess the relative impact of the disease on patients' lives and to assist in choice of treatment. In addition, it can be used to measure response to treatment over time because it assists in the selection of suitable treatment based on response measurement.

**Table (1):** GerdQ questions.

| | Question | Frequency score (points) for symptom | | | |
|---|---|---|---|---|---|
| | | **0 day** | **1 day** | **2–3 days** | **4–7 days** |
| 1- | How often did you have a burning feeling behind your breastbone (heartburn)? | 0 | 1 | 2 | 3 |
| 2- | How often did you have stomach contents (liquid or food) moving upwards to your throat or mouth (regurgitation)? | 0 | 1 | 2 | 3 |
| 3- | How often did you have a pain in the centre of the upper stomach? | 3 | 2 | 1 | 0 |
| 4- | How often did you have nausea? | 3 | 2 | 1 | 0 |
| 5- | How often did you have difficulty getting a good night's sleep because of your heartburn and/or regurgitation? | 0 | 1 | 2 | 3 |
| 6- | How often did you take additional medication for your heartburn and/or regurgitation, other than what the physician told you to take? (such as Tums, Rolaids, Maalox?) | 0 | 1 | 2 | 3 |

Measuring GerdQ is done adding the point values for each corresponding answer. Total score of 0 to 2 points means 0% likelihood of GERD; 3 to 7 points means 50% likelihood; 8 to 10 points means 79% likelihood; 11 to 18 points means 89% likelihood.

### *Endoscopy*

Endoscopy has revolutionized the diagnosis and management of gastrointestinal illness. However, inappropriate use has the potential to add cost with no benefit. The American College of Physicians in 2012 published "Best Practice Advice" regarding EGD for GERD **Shaheen *et al.*** [12]. They suggested that upper endoscopy in the setting of GERD symptoms is useful only in a few, well-circumscribed situations. Avoidance of repetitive, low-yield endoscopy that has little effect on clinical management or health outcomes will improve patient care and reduce costs.

**Table (2): ACP Best Practice Advice.**

| |
|---|
| Best Practice Advice 1:<br>Upper endoscopy is indicated in men and women with heartburn and alarm symptoms:<br>▪ Dysphagia<br>▪ Bleeding<br>▪ Anemia<br>▪ Weight loss<br>▪ Recurrent vomiting |
| Best Practice Advice 2<br>Upper endoscopy is indicated in men and women with:<br>▪ Typical GERD symptoms that persist despite a therapeutic trial of 4 to 8 weeks of twice-daily PPI therapy.<br>▪ Severe erosive esophagitis after a 2-month course of PPI therapy to assess healing and rule out Barrett esophagus. Recurrent endoscopy after this follow-up examination is not indicated in the absence of Barrett esophagus.<br>▪ History of esophageal stricture who have recurrent symptoms of dysphagia. |
| Best Practice Advice 3<br>Upper endoscopy may be indicated:<br>▪ In men older than 50 years with chronic GERD symptoms (symptoms for more than 5 years) and additional risk factors (nocturnal reflux symptoms, hiatal hernia, elevated body mass index, tobacco use, and intra-abdominal distribution of fat) to detect esophageal adenocarcinoma and Barrett esophagus.<br>▪ For surveillance evaluation in men and women with a history of Barrett esophagus. In men and women with Barrett esophagus and no dysplasia, surveillance examinations should occur at intervals no more frequently than 3 to 5 years. More frequent intervals are indicated in patients with Barrett esophagus and dysplasia. |

***PH Study***

The routine performance of intragastric pH measurement in the proximal esophagus or the hypopharynx is not recommended in the evaluation of GERD patients. However, in patients with typical or extraesophageal symptoms of GERD and negative endoscopy that do not respond to PPI therapy, the ambulatory 24 to 48 h measuring of esophageal pH (pH study) is indicated. It is used to confirm the presence of pathologic reflux in patients that are candidates for anti-reflux surgery with no evidence of esophageal mucosal lesions at endoscopy. Acid-blocking medications must be stopped at least 7 days before the study[(13)].

***Barium Study***

Most frequently used diagnostic tools to detect GERD are endoscopy and ambulatory pH-impedance measurements, but barium esophagograms are also still occasionally used. Fluoroscopy can be used to observe the occurrence of spontaneous or provoked gastro-esophageal reflux after drinking a barium suspension.[(14)] Gastro-esophageal reflux can be provoked by maneuvers such as straight leg raises, coughing, Valsalva maneuver, and a water siphon test. The value of barium esophagograms as diagnostic tool for detecting GERD is controversial. Many studies showed substantially poorer performance rates. **Saleh *et al.*** [14] conducted a study regarding barium study and found that the presence or absence of reflux during barium esophagography is not a predictor of the frequency of gastro-esophageal reflux and does not have any value for the diagnosis of GERD.

## COMPLICATIONS

***Extra-Esophageal:***

Beside asthma and post-nasal drip, GERD has been confirmed to be one of the main three causes of chronic cough, accounting around 20% of cases. So, **Eherer** [16] did a review investigating the extraesophageal consequences of GERD. The suggested hypothesis behind the association between GERD related cough is irritation of the upper respiratory tract with or without micro aspiration but this is still controversial. The American College of Chest Physicians suggested that GERD-related cough typically occurs during daytime, in the upright position and is non-productive.

Chronic laryngitis is persistent inflammation of the larynx caused by either external irritation from smoking, alcohol, or intrinsic factors such as asthma and GERD. It is estimated that 50−60% of chronic laryngitis and difficult-to-treat sore throat may be related to GERD. Reflux of gastroduodenal contents in a patient with chronic laryngitis is often referred to as laryngopharyngeal reflux (LPR), where presenting symptoms typically include dysphonia, globus pharyngeus (sensation of lump in throat), mild dysphagia, hoarseness, chronic cough, and nonproductive throat clearing.

Asthmatic patients whose symptoms are getting worse after meals, and or patients who do not respond to anti-asthmatic therapy should be suspected of having GERD-related asthma. Similarly, patients who have GERD symptoms before the onset of asthma symptoms should be considered to have reflux induced asthma. So, one should be cautious to delineate the subgroup of asthmatic patients who may benefit from acid suppressive medication or surgical fundoplication.

Sometimes, GERD is not only irritant to the upper airway, it can cause injury as well. According to **Vaezi *et. al.*** [9] chronic laryngitis and difficult-to-treat sore throat are associated with acid reflux in as many as 60% of patients. Laryngitis can cause troublesome symptoms such as hoarseness, throat clearing, cough, throat pain, and voice fatigue [9].

**Naik and Vaezi**[10] developed an algorithm for diagnosis and treatment of extra-esophageal reflux symptoms (figure 2).

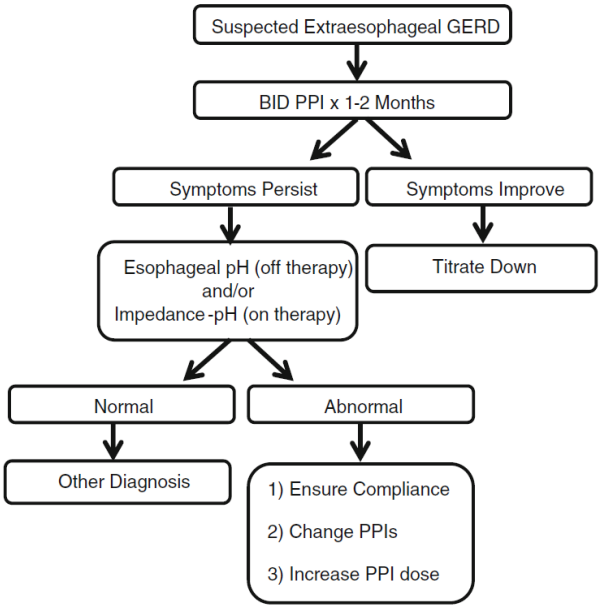


**Figure (2):** (Naik et Vaezi)'s algorithm for diagnosis and treatment of extra-esophageal reflux symptoms.

***Esophageal***

Barrett Esophagus:

Barrett esophagus was first described in 1950 as a metaplastic change of the distal esophagus from normal squamous cell epithelium to columnar epithelium. This metaplasia most often occurs in response to chronic exposure to chronic GERD. According to **Ronkainen *et al.***[13], the prevalence of Barrett esophagus in the general population is around 1%. Risk factors include chronic reflux symptoms, smoking, white race, male sex, increasing age (particularly older than 50 years), hiatal hernia, and obesity. Patients with GERD who have alarm signs should undergo endoscopy. Screening may be considered in patients with multiple risk factors for Barrett esophagus. **Zimmerman** [17] published a review of different American protocols regarding Barrett esophagus and formulate an algorithm for endoscopic surveillance in patients with Barrett esophagus and chronic symptoms of gastroesophageal reflux disease (figure 4).

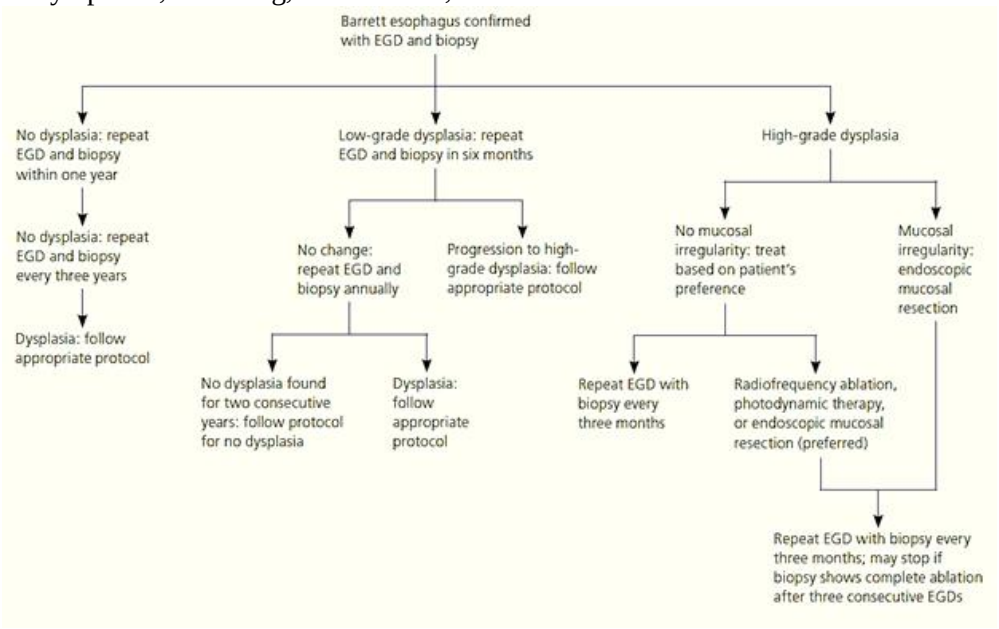


**Figure (4):** Algorithm for endoscopic surveillance in patients with Barrett esophagus.

## MANAGEMENT

There are two general management strategies to GERD: "step-up" and "step-down" approaches. The "step-up" approach begins with lifestyle management and dietary measures, gradually "stepping up" to medications (including types and doses) as needed. Conversely, the "step-down" approach begins with potent acid-suppressive agents (that is, proton pump inhibitors) to achieve rapid symptom relief, then gradually decreases until the minimal therapy is found for managing the individual's symptoms. Either approach is considered acceptable; thus, symptom severity and patient preferences should guide initial management choice.

***Lifestyle***

Lifestyle modification, with some dietary recommendations are major issues in prevention or treatment, and suitable modification is generally recommended as the first step in treating the disease. First, some of the bad habits should be stopped such as eating before bedtime or wearing tight clothes. Then, moderate physical activity should be encouraged because they showed some evidence of promising results in preventing and decreasing the prevalence of GERD. Weight loss is a major part of the treatment plan. The pathophysiology is LES relaxation and eating before bedtime, wearing tight clothes, and obesity tend to exacerbate these problem resulting in the reflux consequences. In variables case-control studies, elevation of the head of the bed, left lateral decubitus position and weight loss have been associated with improvement in patients with GERD [16].

***Medicinal Therapy***

- Proton Pump Inhibitors

PPIs have been the mainstay of GERD management since omeprazole was introduced 1989 and continue to be one of the top selling

medication classes. PPIs suppress gastric acid by inhibiting the H+-K+-ATPase (proton pump) in the gastric parietal cells. PPIs are most effective when administered 1 hour prior to the first meal of the day. PPIs should be dosed at the lowest effective dose, and a discontinuation trial should be considered after 3 months [18].

PPIs can be a diagnostic test as well. A reduction in symptom severity by at least 50% after a short (usually 2 weeks) PPI course (PPI test) is considered indicative of GERD. However, the PPI test might also be positive in peptic ulcer disease and functional dyspepsia. So, it is used but it has poor specificity. Despite the superiority of PPIs over the H2RAs, questions continue regarding their safety. Gastric acid suppression can result in hypergastrinemia and trophic mutations in the stomach mucosa, changes that have been associated with gastric polyps, gastric cancer, gastric carcinoids, and colorectal cancer in animal studies. van **Soest *et. al.*** [19] paper showed no association between PPI use and the risk of colorectal cancer using data of 457,024 persons with long-term history of PPIs use. On the other hand, the overuse of PPIs has also led to tremendous costs. In addition, inappropriate use of PPIs can contribute to polypharmacy, which is the use of multiple medications, specifically those that are not indicated. Polypharmacy may result in reduced medication adherence, falls, cognitive impairment, functional impairment, delirium, and hospitalization, all of which increase morbidity and mortality.

- Alginates

Patients with non-erosive esophagitis (NERD) have a lower response rate to PPIs than patients with erosive esophagitis when gauged from relief of heartburn. Therefore, it is important to develop new treatment options. Sodium alginate reacts with gastric acid to rapidly produce a viscous gel-like raft of approximately neutral pH, which floats on top of the stomach contents and creates a physical barrier that prevents reflux into the esophagus. Unlike other agents, sodium alginate remains in the upper part of the stomach for at least 3 hours and effectively prevents the reflux of both acid and food residue into the esophagus following the intake of a reflux-provoking meal **Washington *et al.*** [20] and **Manabe *et al.*** [21] evaluated the efficacy of adding sodium alginate to basal PPI therapy for NERD. They found that treatment with omeprazole plus sodium alginate was effective for NERD over a period of 4 weeks. We speculate that long-term administration of sodium alginate might be useful for the treatment of NERD because sodium alginate acts directly on the mucosa of the esophagus, and this means that tolerance does not occur.

- Histamine 2 Receptor Antagonists

H2-receptor antagonists (H2RAs) work by blocking histamine (the dominant hormone in gastric acid production) and reducing pepsin output and gastric acid volume. Although the H2RAs are generally well-tolerated, they have been shown to increase the risk of drowsiness and falls in those 65 years and older, especially when combined with severe illness, cognitive impairment, or in those who are taking other anticholinergic medications. Cimetidine should be avoided in those 65 and older due to increased risk for delirium [22].

***Surgical Management***

Chronic GERD is an indication for anti-reflux surgical intervention. Failure of PPIs to heal the esophagitis, symptomatic hiatal hernia, and refractory reflux documented by pH testing can be reasons of chronic GERD. The main types of surgery are fundoplication and, for obese patients, gastric bypass. Fundoplication is the standard surgical treatment for GERD. The question of laparoscopic vs open surgery is no longer relevant [23]. Randomized studies and meta-analyses such as **Dallemagne and Perretta** [23] have shown that laparoscopic fundoplication should be preferred over the open alternative: efficacy is comparable but mortality is lower (0.04% vs 0.2%) and cosmesis is undoubtedly better. The fundoplication is now widely available in community hospitals, the length of stay ranges between 1 and 4 days, some operations are even performed as day surgery, and most patients return to normal activity within 2 weeks. Similar to younger patients, reflux patients older than 65 years of age can expect an excellent outcome in at least 90% of cases after laparoscopic surgery.(22) It was mentioned in **Frazzoni *et al.***[24] paper that laparoscopic fundoplication is highly effective in curing PPI-responsive GERD, long-term postoperative assessment consisting of symptom evaluation persistent relief of heartburn and regurgitation has

been reported in 90% and 80% of patients at 10-year and 20-year follow-up, respectively.

In a study about side effects and complications of fundoplication, it was mentioned that although long-term results with anti-reflux surgery are generally good, especially if performed by experienced surgeons, failures are unavoidable [25]. Most failures occur within the first 2 years of the initial operation. In large reviews, the most common symptoms are recurrent heartburn and/or dysphagia, with pain and bloating being less common. Late postoperative complications are much more common, but most resolve during 3–6 months after surgery. True failures after anti-reflux surgery are uncommon, usually occurring within the first 2 years after the initial operation. Reoperation rates range from 0%–15%, are associated with higher complications and mortality outcomes, and must be performed by experienced foregut surgeons [26].

To sum up the main aspects of GERD management, **Hershcovici and Fass** [27] in their paper developed an algorithm for refractory reflux and how to deal with different responses to PPIs treatment.

## CONCLUSION

GERD is a condition which develops when the reflux of gastric content causes troublesome symptoms such as heartburn, regurgitation, and sleep disturbance or complications such as chronic laryngitis, chronic cough and Barrett's esophagus. Regarding the first step of the approach, GerdQ questionnaire is a potentially useful tool for practitioners in diagnosing and managing GERD without initial endoscopy. Upper endoscopy is mostly indicated in men and women with alarm symptoms such as dysphagia, bleeding, anemia, weight loss or recurrent vomiting. Lifestyle modification is generally recommended as the first step in treating GERD. Also, weight loss is a major part of the treatment plan. PPIs is the mainstay of GERD medicinal therapy. Despite the superiority of PPIs over the H2RAs, questions continue regarding their safety. Failure of PPIs to heal the esophagitis, symptomatic hiatal hernia, and refractory reflux documented by pH testing can be reasons of chronic GERD. Chronic GERD is an indication for anti-reflux surgical intervention.

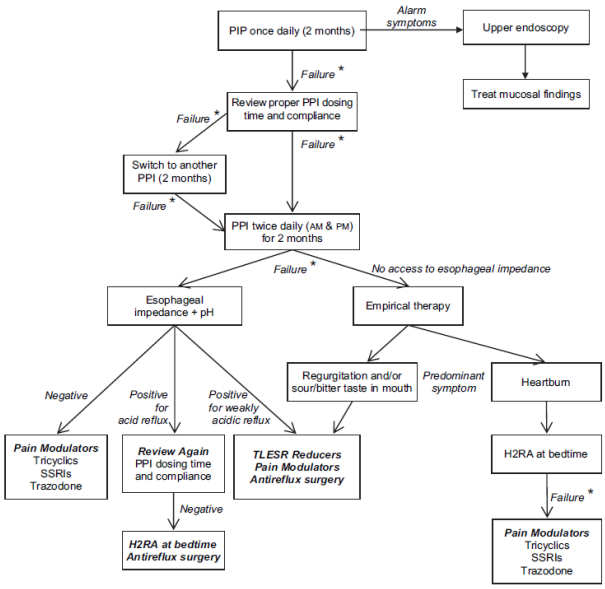


**Figure (3):** Algorithm for refractory reflux treatment.

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