Diagnostic methods and therapeutic options for gastroesophageal reflux: Review

Abdullah Bandar Almashouf, Meshal Abdulhameed Alolyan, Haifa Abdullah Abalkhail, Abdullah Fahad Alshareef

Abstract:

Gastroesophageal reflux disease happens when the quantity of gastric juice that refluxes into the esophagus exceeds the normal limitation, creating symptoms with or without connected esophageal mucosal injury. The spectrum of clinical presentations attributed to GERD has expanded from regular esophageal symptoms of heartburn and regurgitation, to an assortment of extraesophageal indications including respiratory and laryngeal symptoms. The purpose of this review is to discuss the current approach to the diagnosis and treatment of gastroesophageal reflux disease and we also highlight the surgical management. PubMed and Embase were searched for eligible studies that discussing the gastroesophageal reflux, diagnosis and management approaches up to November 2017, search strategy used MeSH／terms and free text words, and included sub-searches related to the index test, target condition, study population and publication type. Lifestyle changes are a key element in the management of GERD and should be incorporated into all therapy stages. Modifications consist of reducing fat intake, stopping smoking, reducing alcohol consumption, reducing weight, preventing recumbency for three hours postprandially and not consuming large meals and specific types of food. In addition to life-style changes, patients with mild signs frequently need periodic drug

therapy for symptom relief. This is generally achieved via the as-needed use of antacids, alginic acid (an element of antacid products such as Gaviscon) or over-the-counter histamine H2-receptor blockers. Surgery might be considered in patients that fail clinical therapy or establish complications of GERD. Patients could fail medical treatment due to noncompliance, failure to afford medications, relapse of symptoms soon after drug is quit or relapse of symptoms regardless of continual use of medication.

Introduction:

Gastroesophageal reflux disease (GERD), recognized as a scientific entity only in the mid-1930s, is currently one of the most common upper gastrointestinal disease in the Western nations, with 10-20 of the populace experiencing weekly symptoms [1].Its prevalence is also increasing in the Far East (Japan) and other locations in Asia [2]. This may be associated with enhanced fat consumption in the diet, and the broadening percentage of obese people [3].

The disease is defined by a broad spectrum of clinical symptoms and disorders [4]. According to the Montreal meaning and category of the illness [5], GERD is a condition which establishes when the reflux of stomach components triggers troublesome symptoms and/or problems. The condition includes esophageal and extra-esophageal syndromes. The esophageal syndromes consist of the symptomatic syndromes, that is, the normal reflux syndrome and the reflux chest pain disorder, and the syndromes with esophageal injury, that is, reflux esophagitis, reflux stricture, Barrett's esophagus (BE) and esophageal adenocarcinoma. The extra-esophageal syndromes are breathing conditions, such as chronic coughing, asthma, laryngitis, otitis media, mostly triggered by the reflux of gastric juice into the respiratory tract [6].

GERD is a chronic condition defined mainly by signs and symptoms of heartburn and acid regurgitation throughout everyday tasks. On top of that approximately 45% of the symptomatic GERD victims have nighttime symptoms (NTG), and patients with NTG have considerably higher odds of having modest or serious GERD [7].The aim of therapy for patients with GERD is to achieve symptomatic relief, avoidance of relapses and healing in patients with extreme esophagitis or difficult illness. These goals could now be accomplished with medication, such as proton-pump inhibitors (PPI), which are now the essential of medical therapy of GERD. On the other hand, antireflux surgical treatment, open or laparoscopic, has been successfully made use of for long-term control of the condition [8].

The purpose of this review is to discuss the current approach to the diagnosis and treatment of gastroesophageal reflux disease and we also highlight the surgical management.

Methodology:

PubMed and Embase were searched for eligible studies that discussing the gastroesophageal reflux, diagnosis and management approaches up to November 2017, search strategy used MeSH／terms and free text words, and included sub-searches related to the index test, target condition, study population and publication type. A methodological filter for the identification of relevant studies was added to increase the specificity of the search. Reference lists of all

retrieved concerned studies were checked for additional relevant studies for pathogenies and treatment of these two diseases.

Discussion:

- **Diagnosis**

The medical diagnosis of GERD is generally made by a combination of medical signs, feedback to acid suppression, in addition to objective testing with upper endoscopy and esophageal pH monitoring. For example, the mix of moderate to severe normal symptoms and endoscopic changes (abrasive esophagitis or Barrett's esophagus) are very details (97%) for GERD (verified with pH screening) [9].However, a well-taken history alone could prove extremely valuable in the diagnosis, especially in the setup of heartburn and acid regurgitation which have a really high specificity (89% and 95%, respectively), albeit reduced sensitivity (38% and 6%) for GERD [11].This could allow one making a presumptive diagnosis and begin empiric treatment, therefore avoiding a comprehensive and expensive evaluation in every patient providing with uncomplicated symptoms [10].Extra screening could be essential, nonetheless, for those that do not respond to acid suppression, those that have alarm symptoms (e.g., dysphagia, odynophagia, iron shortage anemia, weight-loss, and so on) and those who have struggled with the illness for a prolonged period of time because of concern for Barrett's esophagus [12].The reasoning for pursuing additional screening consists of verification of GERD in addition to assessment of GERD associated complications or alternative medical diagnoses (Table 1).

Table 1. Diagnostic Testing for gastroesophageal reflux disease

Diagnostic test	Indication
PPI trial	Classic GERD symptoms with no alarm symptoms.
Esophageal pH monitoring	Refractory symptoms where GERD diagnosis is in question, pre-operative evaluation for non-erosive disease
Upper endoscopy	Alarm symptoms (*e.g.*, dysphagia), PPI unresponsive patients, high risk for Barrett's esophagus
Barium esophagram	Evaluation of dysphagia, otherwise not recommended for GERD evaluation
Esophageal manometry	Prior to anti-reflux surgery to rule out esophageal dysmotility (*e.g.*, achalasia, scleroderma), otherwise not recommended for GERD evaluation

GERD: Gastroesophageal reflux disease; PPI: Proton pump inhibitor.

Empirical therapy

As mentioned above, those with a history suggestive of uncomplicated GERD manifesting in typical signs of heartburn and/or regurgitation can be provided empiric treatment (see treatment area). Normal signs and symptoms that are responsive to acid suppression deal added proof for pathologic esophageal acid exposure and it is reasonable to presume a medical diagnosis of GERD in patients that reply to appropriate treatment [12].On the other hand, regular symptoms that do not enhance warrant further assessment to demonstrate the presence of GERD and assess for an alternative diagnosis. Furthermore, patients with atypical signs or non-cardiac chest pain as their primary issue need to likewise be considered for additional analysis examination before empiric treatment. It needs to be remembered that a minority of patients on also high dose proton pump inhibition will certainly continue to have objective proof of pathologic esophageal acid direct exposure on ambulatory pH surveillance [13], likely an outcome of medication non-compliance or PPI resistance.

Ambulatory pH monitoring

Ambulatory reflux monitoring is the only technique enabling direct measurement of esophageal acid exposure, reflux episode frequency and association in between signs and reflux episodes. It is commonly utilized to assess patients with consistent signs and symptoms despite medical therapy, specifically those without endoscopic proof of GERD, in order to validate the medical diagnosis. It could also be employed to monitor the control of reflux in those on treatment with relentless signs and symptoms [12] and is additionally suggested in endoscopy unfavorable patients prior to undergoing anti-reflux surgical procedure in order to confirm the diagnosis.

Reflux monitoring is generally done using either a cordless capsule or a transnasal catheter (pH alone or integrated pH-impedance) with the patient either on or off acid suppression. Though there is no consistent consensus concerning one of the most ideal method, each has its benefits and drawbacks. For either research, diet plan and activity ought to stay the same in order to capture an accurate depiction of everyday esophageal acid exposure.

Wireless capsule reduces patient discomfort, permits longer recording time, and could enhance accuracy by permitting the patient to return to typical activities without the visibility of a transnasal catheter. The test includes endoscopic or transnasal placement of a radiotelemetry pH sensing capsule to the mucosa of the distal esophagus. The capsule (traditionally positioned 6 centimeters over the squamocolumnar junction) measures pH and sends the information through a radiofrequency signal to a small receiver clipped into the patient's belt [14].Unlike with conventional catheter-based systems, this strategy allows the patient to return to typical task without the conspicuous existence of a transnasal catheter and also enables extra recording time (normally 48 h compared to 24 h recording with catheter-based surveillance). One more benefit of wireless capsule is the fixed placement of the capsule on the esophageal wall in contrast to

catheter-based systems where migration because of ingesting or talking has been revealed to occur [15].Potential negative aspects include additional expense due to endoscopic placement (as nasal passage can be difficult as a result of dimension of capsule), early detachment in a minority of patients, patient discomfort which might call for elimination using repeat endoscopy, along with overdiagnosis of GERD because of ingestion of acidic foods [16].There is likewise some information suggesting a raised number of reflux episodes during the initial 6 hour duration following propofol management [17].

Upper endoscopy

Upper endoscopy is the primary technique utilized in the evaluation of the esophageal mucosa in patients with GERD and permits biopsies of concerning lesions (e.g., Barrett's metaplasia, strictures or masses). It is important though to recognize that there are limitations with the use of upper endoscopy in the medical diagnosis of GERD. As an example, while an endoscopy revealing esophagitis or Barrett's esophagus essentially confirms the diagnosis of GERD (high specificity), a normal endoscopy does not shoot down the medical diagnosis. Actually, most patients with normal signs and symptoms of GERD will have no endoscopic evidence of GERD on esophagogastroduodenoscopy. As a result, an upper endoscopy is not needed for the medical diagnosis and is mostly done for examination of GERD connected difficulties and alternate medical diagnoses along with for placement of wireless capsule pH probes. Patients with several risk factors for esophageal adenocarcinoma (age 50 years or older, male sex, white race, chronic GERD, hiatal hernia, elevated BMI, and intra-abdominal circulation of body fat) ought to get screening endoscopy for Barrett's esophagus [18].

Barium esophagram

Barium esophagram was once advised as a screening examination for GERD, but is no longer part of the diagnostic assessment. A 1996 research study of 125 patients compared barium esophagram to esophageal pH monitoring to assess the accuracy of barium testing as a predictor of unusual esophageal acid exposure. A significantly better degree of abnormal esophageal acid direct exposure happened in patients that had a hiatal hernia or spontaneous reflux on barium radiography. Nonetheless, the level of sensitivity and specificity of barium radiography for abnormal levels of acid reflux were insufficient and consequently this examination is no longer advised in the diagnosis of GERD [19]. On the other hand, it is often utilized in the evaluation of difficulties connected to GERD (e.g., peptic stricture) along with in the evaluation of dysphagia in the post anti-reflux surgical treatment patient, together with endoscopic evaluation.

Esophageal manometry

Esophageal manometry is most helpful for the assessment of dysmotility and has just restricted utility in the analysis of GERD. Although disturbance of the anti-reflux barrier (gastroesophageal junction) and disorder of esophageal peristalsis prevail in GERD patients, these searchings for are not analysis and as a result there is no manometric pattern which is pathognomonic for reflux [20].The role of manometry in the assessment of GERD remains minimal to preoperative screening for exclusion of considerable motility problems such as achalasia or scleroderma (clear contraindications to anti-reflux surgery) as well as for aiding in proper positioning of transnasal pH probes. Or else, this test is not recommended for the medical diagnosis of GERD.

- ### Treatment

GERD is a chronic disease that typically requires long term management in the form of lifestyle modification, medical therapy and, for a subset of patients, surgical therapy.

Lifestyle changes

Lifestyle and diet regimen change typically have included weight-loss, head of bed elevation, avoidance of nighttime dishes, and elimination of trigger foods such as chocolate, high levels of caffeine and alcohol. A 2006 methodical testimonial of 16 randomized trials reviewed the impact of lifestyle measures on GERD and concluded that only weight loss and elevation of the head of the bed boosted esophageal pH and/or GERD signs and symptoms [21].A 2006 organized review and meta-analysis recommended a favorable association in between increasing BMI and the presence of GERD within the United States and potentially within other countries too [22].Interestingly, BMI was located to be associated with signs of GERD in both typical weight and overweight females as well as moderate weight gain amongst those of normal weight was discovered to trigger or intensify signs [23].Consequently, weight-loss is suggested for GERD patients that are overweight or that have had current weight gain.

Medical therapy

The mainstay of therapy of GERD is acid suppression which can be accomplished with numerous courses of medicines including antacids, histamine-receptor villains (H2RAs) or proton-pump inhibitors (PPIs). Researches have revealed extra total healing of erosive esophagitis and heartburn relief with PPIs vs H2RA and this result takes place nearly two times as fast (recovery rate and heartburn relief of 11.7%/ wk and 11.5%/ wk vs5.9%/ wk and 6.4%/ wk in the PPI and H2RA teams, respectively) [24].Additionally, studies show that ERD is more difficult to treat with H2RA as compared to PPIs [25] and patients with ERD have the tendency to have a higher symptom action to PPIs compared to their NERD counterparts [26].Therefore, it is recommended to treat abrasive reflux disease with upkeep PPI therapy at the lowest efficient dosage as most

will certainly regression after discontinuation of treatment [27].As a whole, PPIs are felt to be similarly reliable and patients need to be advised to take these medicines 30-60 minutes prior to dishes; the exception to this is dexlansoprazole which can be taken irrespective of food intake.

If signs and symptoms linger after efforts at optimizing clinical treatment, an evaluation for non-GERD etiologies ought to be taken on. An upper endoscopy needs to be executed following and might disclose an abnormality such as consistent abrasive esophagitis, eosinophilic esophagitis, or Barrett's esophagus in roughly 10% of patients in whom empiric PPI treatment falls short [28] The finding of esophagitis would certainly sustain the medical diagnosis of GERD and factor to disagreement or failing of clinical treatment. Many times, the esophagus will show up endoscopically typical and these patients ought to be additional examined with pH surveillance to verify or refute the medical diagnosis of GERD. Verifying pathologic acid reflux with a positive sign correlation would show PPI failing and need for rise of clinical treatment or factor to consider of surgical choices. The absence of GERD in a patient with normal heartburn symptoms would certainly suggest a medical diagnosis of practical heartburn.

Surgical therapy

Surgical therapy is another therapy alternative for long-lasting therapy in patients with GERD and has become extra enticing considering that the introduction of laparoscopic anti-reflux surgical treatment. Indications for anti-reflux surgical treatment, which normally consist of laparoscopic fundoplication or bariatric surgery, consist of unwillingness to stay on lifelong clinical therapy, intolerance of medical therapy, medically refractory signs and symptoms with proof of GERD on endoscopy or pH surveillance, or GERD in the setting of a large hiatal hernia (Table 2).

Table 2.Indications for anti-reflux surgery.

Unwillingness to remain on lifelong medical therapy
Intolerance of medical therapy
Medically refractory symptoms with objective evidence of GERD
GERD in the setting of a large hiatal hernia
Medically refractory GERD in the setting of morbid obesity

The short and medium term outcomes of laparoscopic anti-reflux surgery are quite excellent in regards to enhancing the typical signs and symptoms of GERD [29]. Nevertheless, in the long-term it appears these results may reduce. Throughout a follow-up period of 10 to 13 years, one study contrasting long-term end results in clinical and medical therapies for GERD located that 62% of surgical patients took anti-reflux medications often, as compared to 92% of medical patients. Anti-reflux surgical procedure can be really effective yet should not be advised with the assumption that patients will certainly no longer take anti-secretory medicines [30].

Complications from anti-reflux surgery consist of dysphagia of adequate seriousness to need esophageal dilation in about 6% of patients treated with fundoplication surgical procedure [31] along with a significant rise in flatulence and lack of ability to belch (gas bloat syndrome). This possibility for difficulties underscores the importance of carefully picking patients for anti-reflux surgery in order to maximize end results.

Conclusion:

Gastroesophageal reflux disease happens when the quantity of gastric juice that refluxes into the esophagus exceeds the normal limitation, creating symptoms with or without connected esophageal mucosal injury. The spectrum of clinical presentations attributed to GERD has

expanded from regular esophageal symptoms of heartburn and regurgitation, to an assortment of extraesophageal indications including respiratory and laryngeal symptoms. Lifestyle changes are a key element in the management of GERD and should be incorporated into all therapy stages. Modifications consist of reducing fat intake, stopping smoking, reducing alcohol consumption, reducing weight, preventing recumbency for three hours postprandially and not consuming large meals and specific types of food. In addition to life-style changes, patients with mild signs frequently need periodic drug therapy for symptom relief. This is generally achieved via the as-needed use of antacids, alginic acid (an element of antacid products such as Gaviscon) or over-the-counter histamine H2-receptor blockers. Surgery might be considered in patients that fail clinical therapy or establish complications of GERD. Patients could fail medical treatment due to noncompliance, failure to afford medications, relapse of symptoms soon after drug is quit or relapse of symptoms regardless of continual use of medication. Possible complicating factors consist of big hiatal hernia, Barrett's esophagus, severe esophagitis, recurrent esophageal strictures and severe pulmonary symptoms. Surgical intervention has been revealed to give long-lasting relief of symptoms in patients with GERD.

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