The utility of oropharyngeal pHmetry in the diagnosis and treatment of laryngopharyngeal reflux

Original Article

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Article received on April 25, 2024.
Accepted for publication on January 20, 2025.

Abstract

Introduction: Laryngopharyngeal reflux is a chronic illness with variable and unspecific symptoms, representing up to 10% of otolaryngology appointments. Its diagnosis and treatment are controversial, with high rates of treatment failure. Oropharyngeal pHmetry is an objective diagnosis method that measures both liquid and gaseous pH variations in the oropharynx, having previously demonstrated a higher diagnosis value than esophageal pHmetry.
Methods: Prospective observational study. Thirty patients who were observed in otolaryngology appointments between May 2022 and May 2023 were referred to the study (observed by an otolaryngologist who suspected of laryngopharyngeal reflux and referred the patients). Patients fulfilled Reflux Symptom Index and Voice-Handicap Index-10, were submitted to flexible nasofibrolaryngoscopy with posterior fulfillment of the Reflux Finding Score and oropharyngeal pHmetry. Posteriorly, underwent treatment of 3 months with protein pump inhibitors (esomeprazol 40mg twice daily). Response to treatment was defined as an improvement of at least 5 points in the reflux symptom index. Based on the obtained results and literature review, we propose a protocol of diagnostic and treatment approach for laryngopharyngeal reflux. RESULTS: 28 patients were included in the study, 75% female, aged μ=53,5 years and body mass index μ=28.6. Regarding pHmetry, 63% had acid reflux (15% slight, 37% moderate e 11% severe), 26% had non-acid reflux and 11% had normal pHmetry. After 3 months of proton-pump inhibitors 50% of patients had no significant improvement in their symptoms. Oropharyngeal pHmetry predicted treatment response in 26 out of 28 patients (93%). The correlation of acid events with symptom events had a significant correlation with proton-pump inhibitor response ($p<0.01$), as well as Ryan score positivity ($p<0.01$). In patients responsive to treatment, the average of reflux symptom index improvement was 13,7 points. Reflux Symptom Index, Reflux Finding Score and Body Mass Index had a statistically significant correlation with the severity of acid reflux (slight, moderate or severe) but not with the type of reflux (acid vs non-acid).

Conclusions: This study demonstrates that oropharyngeal pHmetry is an effective method for differentiating acid and non-acid Laryngopharyngeal reflux, effectively predicting proton-pump inhibitor treatment response, being useful from the moment of diagnosis or in treatment adjustment for proton-pump inhibitor refractory patients.
Keywords: pharyngolaryngeal reflux; oropharyngeal pHmetry; reflux protocol; reflux diagnosis; reflux treatment; acid reflux; non-acid reflux.

Introduction

Laryngopharyngeal reflux (LPR) is the retrograde movement of gastrointestinal gases or liquids of varying pH, which affects the mucosa of the upper aerodigestive tract. It is often associated with gastroesophageal reflux disease (GERD)[1]. It is a chronic condition characterized by variable and nonspecific symptoms, including dysphonia, chronic cough, globus pharyngeus, odynophagia, throat clearing, burning sensation, and dysphagia[2].

Approximately 10% of otolaryngology visits are estimated to be related to LPR symptoms[3]. Histopathological damage to the laryngeal and oropharyngeal tissues primarily results from the action of pepsin rather than gastric acid per se[3]. Gastric acid, pepsin, bile salts, and pancreatic proteolytic enzymes induce chronic inflammation of the laryngeal structures, metaplasia of the epithelium to squamous epithelium, and reversible hypertrophy of mucous glands[3], and may continue to cause mucosal injury even during treatment with proton pump inhibitors (PPIs). Despite extensive research, controversy remains regarding the epidemiology, clinical presentation, diagnosis, and treatment of LPR. Currently, both subjective and objective diagnostic tools can be used; however, no standardized protocol has been established[3].

Among the currently available subjective (symptom-based) diagnostic tools, the most widely used is the Reflux Symptom Index (RSI)[4]; however, parameters such as sex and sociocultural factors can significantly influence its results[5]. An RSI score higher than 13 is considered indicative of LPR. More recently, the Reflux Symptom Score 12 (RSS-12) has been validated for the Portuguese population[6]. This simplified version of the original Reflux Symptom Score (RSS)[1,2] considers not only the severity but also the frequency of symptoms and includes additional associated symptoms not evaluated by the RSI. Another widely used tool is the Voice Handicap Index (VHI), which was designed to assess vocal symptoms but lacks items specific to LPR[7]. This questionnaire is frequently used to measure the vocal handicap perceived by patients with dysphonia. All three scales, the RSI, VHI, and RSS-12, have been validated for use in the European Portuguese language[6–8].

The most commonly used endoscopic scoring system is the Reflux Finding Score (RFS), which correlates laryngoscopic findings with the diagnosis of LPR. Other scoring systems include the Reflux Sign Assessment (RSA)[9] and Warsaw scale[3].

For more precise diagnosis, methods such as esophageal pH monitoring, esophageal manometry, oropharyngeal pH monitoring, and salivary pepsin detection have been proposed. Esophageal manometry evaluates the movement and contractile strength of the esophageal sphincters and body using electrodes, while esophageal pH monitoring measures pH levels at the esophageal sphincters (distal, proximal, or both). These objective tests are typically used to diagnose GERD and may indirectly indicate LPR due to their frequent association. However, they are not diagnostic for LPR itself, as GERD and LPR are distinct clinical entities that may occur independently. Moreover, the reliability of proximal esophageal pH measurements may be compromised if the electrode becomes completely dry. Consequently, oropharyngeal pH monitoring was developed as an objective diagnostic method for LPR, capable of detecting both liquid and gaseous pH changes. Several studies have demonstrated that oropharyngeal pH monitoring has a higher positive predictive value for LPR diagnosis than esophageal pH monitoring[10]. Multichannel intraluminal impedance with pH monitoring

(MII-pH) is considered a more comprehensive diagnostic method than traditional pH monitoring, although it has a lower sensitivity[11]. It is also significantly more invasive and costly. Nonetheless, multiple studies have demonstrated a strong correlation between MII-pH and pH monitoring findings[10,12,13]. Salivary pepsin detection is another promising diagnostic method. However, its sensitivity and specificity appear to vary depending on the technique used (enzyme immunoassay, enzyme linked immunosorbent assay, Western blot)[14]. Moreover, this method is costly and not widely available in Portugal. A meta-analysis has revealed that its sensitivity and specificity are approximately 64% and 68%, respectively[1]. Given these considerations, each diagnostic tool has certain advantages and limitations. However, oropharyngeal pH monitoring stands out as a promising, simple, objective, minimally invasive, and outpatient-friendly diagnostic approach.

Empirical therapy with PPIs remains the primary pharmacological treatment of LPR. Clinically, response to PPI treatment is often used as a confirmatory diagnostic indicator. However, treatment response does not provide guidance for managing non-responders, approximately 40% of patients, which includes individuals with non-acid LPR or those without LPR[1,15].

This study aimed to evaluate the predictive value of oropharyngeal pH monitoring for therapeutic response to PPI treatment.

Based on a review of the literature and findings of this study, we have also propose a diagnostic and therapeutic protocol for the management of patients with suspected LPR, aiming to promote a more standardized approach.

Materials and Methods

This protocol of this prospective observational study was approved by the Research Ethics Committee of the Almada-Seixal Local Health Unit (ULSAS). All participants provided written informed consent. Patients were referred to the study from the ULSAS otorhinolaryngology outpatient clinic between May 2022 and May 2023, the period during which the study was conducted. Referral occurred after evaluation by an otorhinolaryngologist who suspected the presence of LPR based on the medical history and targeted physical examination, including flexible fiberoptic nasolaryngoscopy, Referred patients were evaluated by the research team and completed the RSI and 10-item VHI (VHI-10) questionnaires at the initial evaluation. During this first visit, the patients also underwent flexible fiberoptic nasolaryngoscopy and the research team completed the RFS. Subsequently, an oropharyngeal pH probe was placed for 24-h monitoring. Prior to insertion, the probe was calibrated using pH 4 and 7 solutions, as recommended by the manufacturer. The probe was introduced through the more patent nasal fossa and positioned at the level of the uvula, and the placement was adjusted to avoid the sensation of a foreign body.

The next day, the probe was removed, and patients were instructed to implement dietary modifications and begin treatment with esomeprazole 40 mg approximately 30 min before breakfast and dinner.

After 3 months, patients were re-evaluated. They again completed the RSI and VHI-10 questionnaires and underwent repeat flexible fiberoptic nasolaryngoscopy, with a new RFS score recorded by the research team. A therapeutic response was defined as an improvement of ≥5 points in the RSI score[11]. The exclusion criteria were patients under 18 years of age and those with an identifiable alternative cause of dysphonia unrelated to LPR, such as vocal nodules, polyps, cysts, or sulci. Patients were instructed to discontinue PPI therapy at least eight days prior to pH monitoring. Patients who were unable to tolerate probe placement or who failed to adhere to PPI therapy for a minimum of three months were excluded. The data were analyzed using the IBM SPSS® software version 29.0.0. 0. To develop a diagnostic and therapeutic protocol for LPR, a literature review was conducted using the PubMed® database to identify original

Figure 1
Oropharyngeal pH probe in place

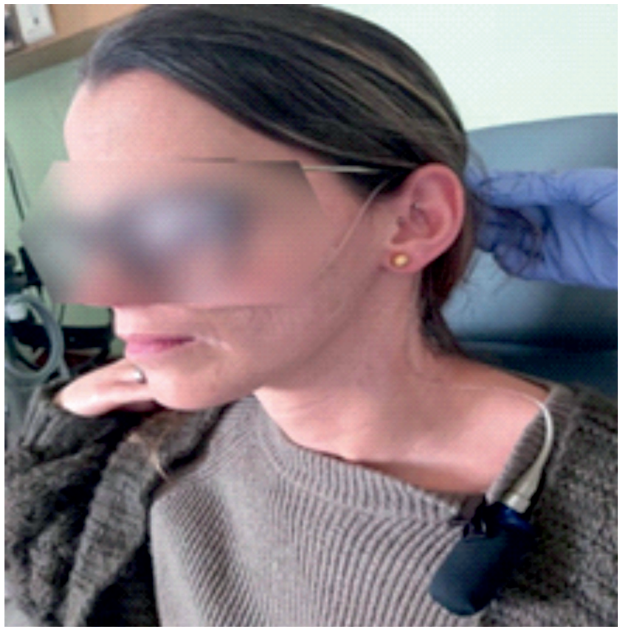
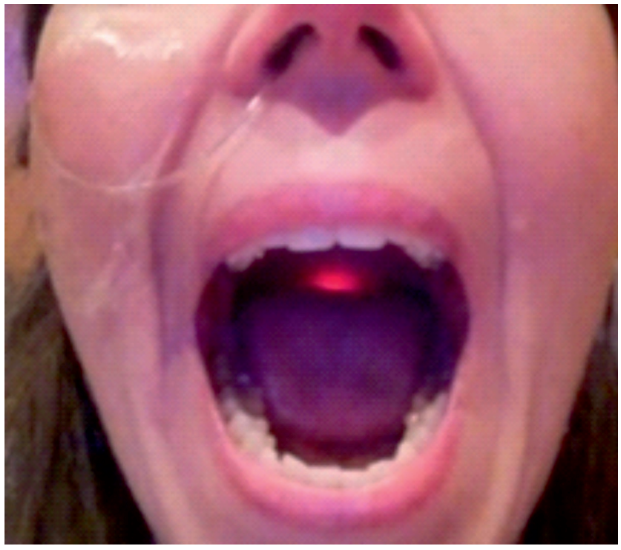


Figure 2
Positioning of the oropharyngeal pH probe



research articles on the topic. The following keywords were used: *"Laryngopharyngeal OR Pharyngolaryngeal reflux," "Laryngopharyngeal OR Pharyngolaryngeal reflux AND treatment," "laryngopharyngeal OR pharyngolaryngeal AND diagnosis," "extra-esophageal reflux AND diagnosis OR treatment," "Supraesophageal Gastric Reflux," and "Non-acid reflux."*

Results and Discussion

A total of 28 patients were included in this study (one patient was excluded due to intolerance to pH probe placement, and one probe was lost due to technical issues). Patients who participated in the study did not report any technical difficulties or significant discomfort during the procedure. Of the included patients, 75% were women and 25% were men, with an average age of 53.5 years. The age distribution is illustrated in Figure 3.

A high prevalence of individuals with excess weight was observed, with 69% patients classified as overweight or obese. The distribution of body mass index (BMI) classifications is shown in Figure 4.

The responses to the initial assessment questionnaires showed an RSI score of 21.25 (range: 5–37) and average VHI-10 score of 8.93. Statistically significant correlations were found between the RSI and VHI-10 (Spearman's test, $p < 0.01$), BMI and RSI (Pearson's test, $p < 0.01$), and BMI and VHI-10 (Spearman's test, $p < 0.01$).

All patients underwent flexible fiberoptic nasolaryngoscopy, which was recorded and later evaluated using the RFS by two blinded evaluators, one general otolaryngologist and one laryngologist. The final RFS score was calculated as the average of both evaluations. The average RFS score was 9.73. Statistically significant correlations were confirmed between the RFS and RSI (Pearson's test, $p < 0.01$), VHI-10 (Spearman's test, $p < 0.05$), and BMI (Pearson's test, $p < 0.05$).

The pH monitoring data were analyzed by the first two authors, following the manufacturer's guidelines. This test provides 24-h pH measurement graphs and enables evaluation of the acid exposure time, number and duration of acid reflux events, and their association with meals, supine/lying position, and time of the day (daytime/nighttime). It also records patient-reported symptoms, which are marked using predefined buttons during the monitoring period, and calculates the Ryan score, a quantitative measure available only in patients with moderate–severe acid reflux. Oropharyngeal pH monitoring also enables

Figure 3
Age distribution of patients

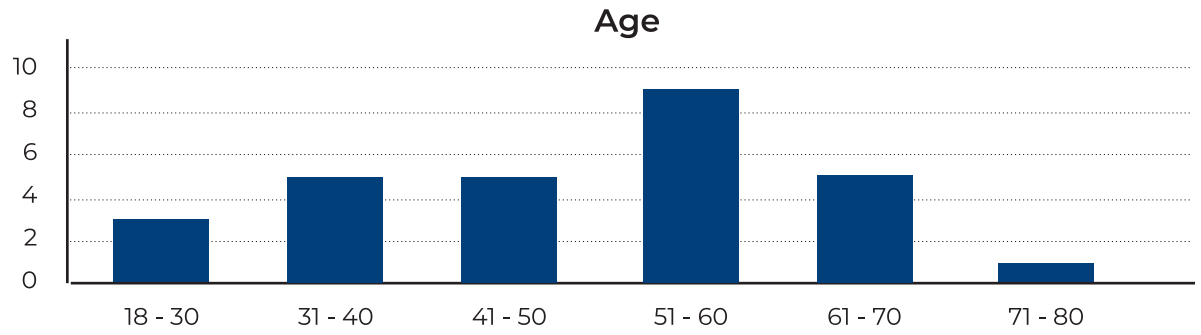
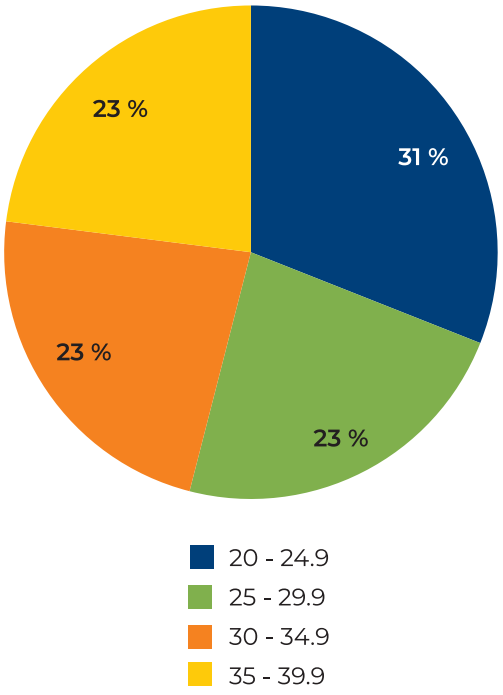


Figure 4
Body mass index) of patients



graphical qualitative observation of non-acid reflux, though it does not quantify the number or duration of non-acid reflux episodes. Figure 5 shows examples of pH monitoring graphs (A – normal; B – acid reflux; and C – non-acid reflux). Acid reflux was classified as mild, moderate, or severe based on the number, duration, and pH of reflux events, as well as the Ryan score, according to the manufacturer's instructions. Results were classified as normal pH (11%), acid reflux (63%; further classified as mild [15%] mild, moderate [37%], and severe [11%]), and non-acid reflux (26%). A summary of these results is shown in Figure 6. A statistically significant relationship was observed between BMI and degree of acid reflux (Spearman's test, $p < 0.01$) but not between BMI and type of reflux (acid/non-acid, Spearman's test, $p > 0.05$). Similarly, RSI and RFS scores were significantly correlated with the severity of acid reflux (Spearman's test, $p < 0.05$) but not with the reflux type (Spearman's test, $p > 0.05$). No statistically significant association was found between the VHI-10 scores and pH monitoring results. A statistically significant correlation was identified between symptom-reflux events and response to PPI therapy ($p < 0.01$), and between symptom-reflux events and a positive Ryan score ($p < 0.01$).

After 3 months of PPI treatment, patients repeated the RSI and VHI-10 questionnaires and underwent a second flexible fiberoptic nasolaryngoscopy with RFS evaluation. In this follow-up, the average RSI was 16.44 (decrease of 4.82 points from baseline), VHI-10 was 8.29 (decrease of 0.64), and RFS was 9.08 (decrease of 0.65). In 50% patients, the RSI improvement was less than five points. No statistically significant correlations were found between the treatment response and changes in the VHI-10 and RFS scores. Laryngoscopic findings tend to resolve more slowly than symptoms, which may explain the limited improvement in RFS scores[15,16]. PPI response was significantly associated with the presence of symptom-reflux event correlation in pH monitoring (Spearman's test, $p < 0.01$), number of events with pH < 6.0 (Spearman's test, $p < 0.01$), total acid exposure time

Figure 5
Examples of oropharyngeal pH monitoring results

(Spearman's test, $p < 0.05$), and number of events with pH < 6.5 (Spearman's test, $p< 0.05$). In patients who responded to PPI therapy, the average RSI improvement was 13.7 points. Figure 7 illustrates RSI improvement based on the reflux classification, showing that patients with mild–moderate reflux experienced the greatest therapeutic benefit after 3 months.

Patients with severe acid reflux may have shown less improvement than the others due to the need for a longer treatment period or potential need for adjunctive therapy. None of the patients with normal or non-acid reflux results reported significant symptom improvement after three months of treatment. In contrast, only two patients with acid reflux failed to show an RSI improvement greater than five points. These findings suggest that pH monitoring could predict the PPI response in 26 out of 28 patients (93%), and the presence of symptom-reflux correlation and number of reflux events with pH < 6.0 are the strongest predictors of treatment response in patients with acid reflux. While evaluating patients with suspected LPR, it is essential to rule out confounders such as allergies, chronic laryngitis due to exposure to irritants (tobacco, chemical agents, pollutants, pollens, or previous chemotherapy or radiotherapy), and masses or other lesions observed on pharyngolaryngoscopy that may mimic LPR symptoms[1]. Daily water intake should be assessed, as inadequate hydration compromises the mucosal integrity of the upper aerodigestive tract[1,15]. For symptom characterization and therapeutic monitoring,

Figure 6
Reflux classification based on oropharyngeal pH monitoring

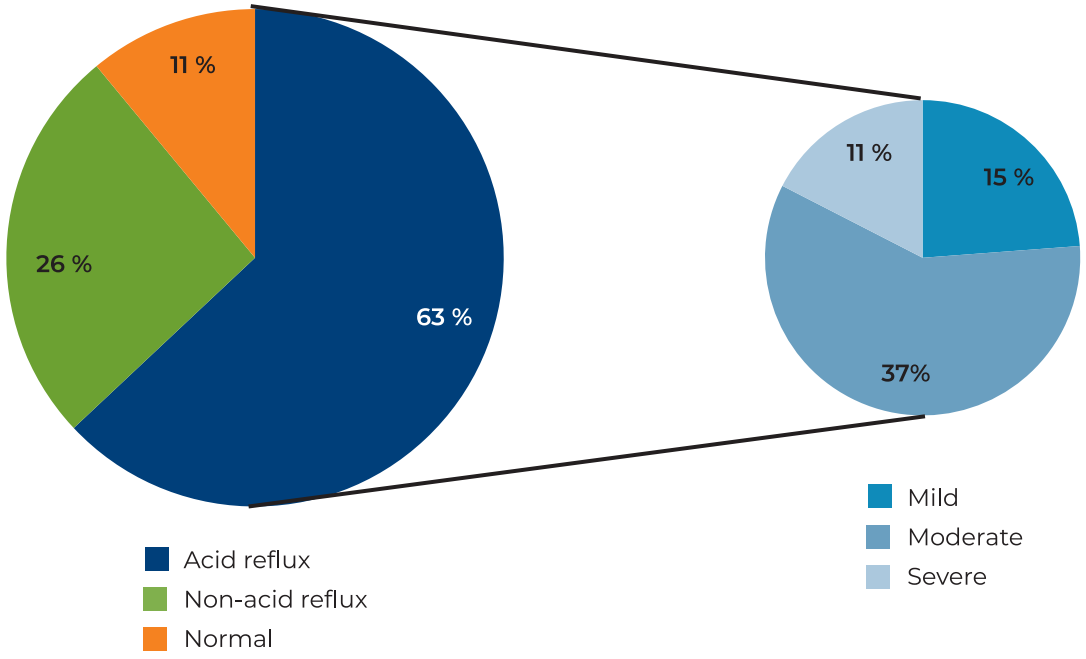
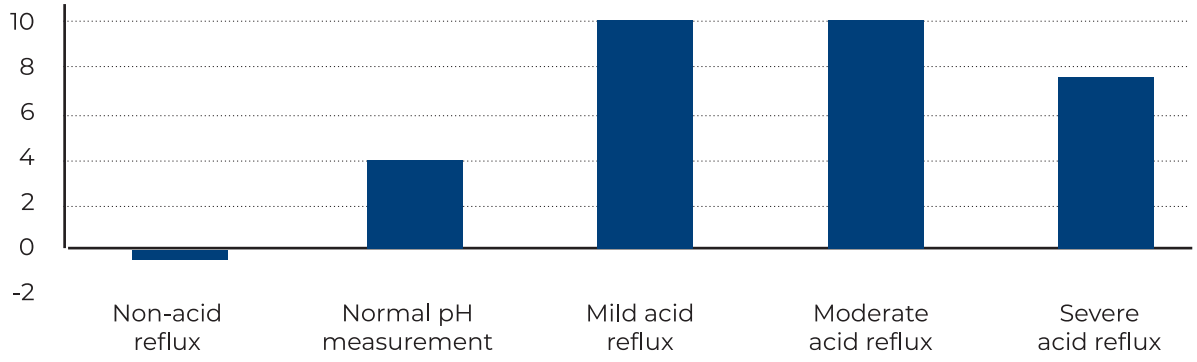


Figure 7
Average Reflux Symptom Index improvement by the reflux type and severity on oropharyngeal pH monitoring



we recommend the Portuguese versions of the RSI and RSS-12 questionnaires, along with the VHI in patients with significant dysphonia[6–8]. It is also crucial to inquire about concurrent dysphagia; when present, a formal swallowing assessment should be conducted to evaluate the risk of aspiration[1]. The most common objective findings associated with LPR include posterior commissure hypertrophy and erythema of the arytenoid, oropharynx, and anterior tonsillar pillar. To standardize the clinical findings, Belafsky developed the RFS in 2001, which focuses on laryngeal signs; however, it has low interobserver reproducibility. Lechien later introduced the RSA, a 16-item tool that evaluates both laryngeal and extra-laryngeal signs associated with LPR, such as erythema of the anterior pillar, uvula, posterior pillars, and coated tongue. Among the complementary diagnostic tools, oropharyngeal pH monitoring or MII-pH monitoring is recommended for patients with moderate to severe LPR symptoms. This cost-effective approach enables therapeutic adjustments based on the reflux profile (acidic, non-acidic,

or alkaline; daytime/upright position vs. nighttime/laying position) and relationship to meals, allowing for the incorporation of agents such as sucralfate or alginate before meals[1]. Esophagogastroduodenoscopy (EGD) is not recommended for diagnosing LPR, as a normal EGD does not exclude the condition[1,15]. However, gastroenterology referral and potential EGD should be considered in patients with chronic symptoms and age over 50 years (asymptomatic esophagitis or Barrett's metaplasia may be present)[1], a family history of upper gastrointestinal malignancy, severe symptoms, non-cardiac chest pain, gastrointestinal bleeding, hypersalivation, or weight loss (to exclude esophageal lesions, motility disorders, Zenker's diverticulum, or other gastrointestinal pathologies). Referral is also indicated for patients who remain symptomatic despite optimal treatment with PPI or alginate, after exclusion of alternative diagnoses or confirmation of LPR through pH monitoring or MII-pH[15,17]. Salivary pepsin detection using the Peptest® may be a useful alternative in patients with inconclusive results, intolerance, or unavailability of standard diagnostic tools.

LPR treatment involves lifestyle modifications, complementary therapy, and, in selected cases, surgical intervention[1,15,18].

Educating patients about LPR enhances treatment adherence and outcomes. A study by Pisegna et al. found that approximately 63% of patients did not take their prescribed medication when not adequately informed about the disease[19].

Regarding lifestyle modifications, obesity is a major risk factor in the pathophysiology of GERD and LPR, as increased intra-abdominal pressure raises the pressure of the lower esophageal sphincter (LES) and reflux events. Therefore, weight loss is recommended for all overweight patients. Other recommended modifications include elevating the head of the bed; avoiding the supine position postprandially; quitting smoking; increasing dietary fiber and protein intake; and avoiding alcohol, refined sugars, acidic foods, fatty foods, spicy foods, fried foods, chocolate, and carbonated beverages, especially in the evening[15,17]. Adequate hydration (more than 1.5 L/day) is also important. Stress and anxiety, which can promote autonomic dysfunction and LES[1] relaxation, should be considered in therapeutic planning. An anti-reflux diet is cost-effective and should be recommended to all patients, particularly those with mild symptoms[15].

The pharmacological options for LPR include PPIs, potassium-competitive acid blockers (P-CABs), H_2 receptor antagonists (H2RAs), alginates, prokinetic agents, and baclofen to inhibit LES relaxation[15]. Table 1 summarizes the mechanisms of action and recommended dosages.

The use of PPIs in LPR remains controversial[15] due to their high failure rate (30–40%) and lack of consistent evidence demonstrating superiority over placebo[15]. Nevertheless, they remain the first-line therapy due to their availability and low cost. Chronic PPI use may increase the risk of gastric neoplasms and acute nephritis; thus, clinicians must monitor for adverse effects and drug interactions, particularly in older patients[20], who may require longer treatment durations (6 months versus 3 months) for symptom relief[20]. This high failure rate may be due to misdiagnosis (PPIs are ineffective in non-acid reflux[21], where acidity is not the underlying cause and PPIs do not reduce reflux events) or interindividual pharmacokinetic variability due to CYP2C19 genetic polymorphisms[15]. PPIs have a delayed onset of pharmacological action and often require multiple doses to achieve optimal acid suppression and symptom relief. Furthermore, they may not provide consistent 24-h acid suppression[15,17]. The standard therapeutic dose remains controversial, with variable efficacy between once-daily and twice-daily regimens[15]. In case of symptom improvement, dose tapering to the minimum effective level is highly recommended[17].

P-CABs, such as vonoprazan, reversibly inhibit the H^+/K^+- ATPase proton pump by competing with potassium ions, resulting in nearly

complete acid suppression from the first dose. The recommended dose of vonoprazan is 20 mg once daily, independent of meals, which simplifies its use compared with PPIs[8]. This medication is not yet available in Portugal.

H2RAs were the first drugs used to treat GERD and are now considered second-line therapy. They have a shorter action duration (4–8 h) and provide less effective acid suppression than PPIs. However, nighttime H2RA supplementation in patients already on twice-daily PPIs may improve acid control in selected cases.

Alginates, naturally derived from seaweed, expand upon contact with the gastric fluid to form a gel-like barrier that reduces reflux events regardless of the pH[2]. Alginates are suspected to inhibit pepsin activity[15]. Various studies have suggested that alginates are as effective as PPIs, particularly for non-acidic and mixed reflux[22]. The recommended dose is 10–20 mL after meals and/or at bedtime. No significant adverse effects have been reported.

Prokinetic agents, such as mosapride, bromopride, cisapride, domperidone, and metoclopramide, may enhance gastric emptying and increase the basal LES pressure. The recommended dosage is one tablet three times daily before meals.

Baclofen inhibits LES relaxation, potentially reducing the number and duration of both acid and non-acid events. However, due to limited evidence and potential central nervous system side effects, its routine use in LPR is not currently recommended[15]. It may be considered in refractory disease, defined as persistent symptoms despite optimized medical therapy (including twice-daily PPI for at least 8 weeks) and objective evidence of reflux in MII-pH or pH monitoring[23].

The combination of hyaluronic acid and chondroitin sulfate in poloxamer 407 forms a macromolecular complex that protects the mucosa against acid injury and promotes healing and mucosal regeneration (owing to anti-inflammatory effect of chondroitin sulfate and regenerative effect of hyaluronic acid)[24]. It has been proposed as an adjunct therapy to PPIs or monotherapy in patients unresponsive to PPIs. However, no studies have specifically evaluated its efficacy in LPR. Palmieri et al. reported significant improvement in GERD symptom scores with poloxamer 407, although an objective reflux assessment was not conducted[25]. Simone et al. conducted an experimental study in pigs, and reported reduced esophageal mucosa permeability to acid following exposure to the compound, suggesting a potential protective effect against structural mucosal lesions[24].

Speech therapy and rehabilitation techniques – The diaphragm plays a key role in reflux and can be trained through specific maneuvers and breathing exercises aimed at optimizing reflux management. Laryngeal rehabilitation therapy for patients with chronic cough associated with GERD has demonstrated significant improvement, including a documented increase in the LES pressure measured by manometry after eight weeks of treatment[17]. Despite limited evidence supporting its efficacy in patients with LPR, speech therapy should be considered, particularly for patients with refractory symptoms, prominent cough, dysphonia, or significant dysphagia[17].

Devices designed for external compression of the upper esophageal sphincter (UES) function by applying targeted pressure over the cricoid cartilage, thereby increasing the intraluminal esophageal pressure by 20–30 mmHg and reinforcing the UES barrier. Some studies have suggested that combining PPI therapy with UES compression results in greater symptom improvement than PPI monotherapy[15]. These devices are intended for nighttime use, are noninvasive, generally well tolerated, and may represent a valuable strategy for patients with significant nocturnal reflux[15].

Surgical treatment – Anti-reflux surgery may be indicated in patients not responding to PPI therapy. Laparoscopic anti-reflux surgery (LARS) is the most recommended procedure and is widely recognized as an effective intervention for GERD. Although its role in LPR management has not been fully investigated,

evidence suggests that LARS may be effective and safe in patients who demonstrate a favorable response to PPIs or exhibit objective findings consistent with GERD[17]. According to the Society of American Gastrointestinal and Endoscopic Surgeons, anti-reflux surgery is recommended for patients who (1) cannot tolerate or adhere to pharmacologic therapy; (2) present with significant extra-esophageal symptoms, such as dysphagia, asthma, or chronic cough; or (3) exhibit peptic structural changes indicative of GERD[18].

In summary, empirical therapy of LPR should include lifestyle modifications, PPI therapy, and alginate supplementation to increase treatment efficacy across all types of LPR[1,15]. For patients who remain symptomatic despite treatment, adjunctive pharmacologic strategies may be used following diagnostic confirmation of the reflux type and therapeutic adjustments based on pH or MII-pH monitoring. In selected cases, external UES compression devices or surgical intervention may be considered. The diagnostic and therapeutic approach for LPR is illustrated in Figure 8.

Conclusions

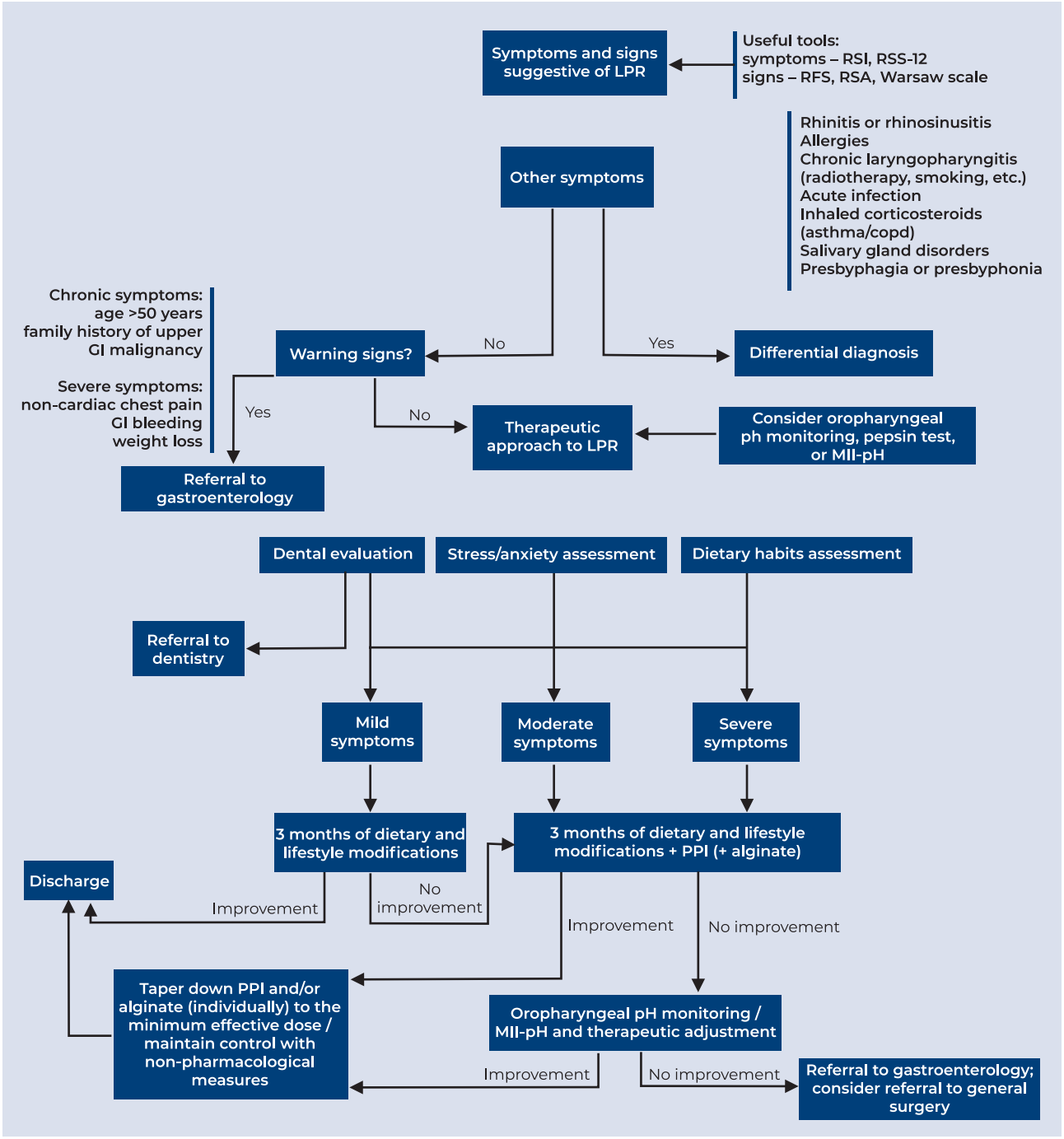
Clinical signs and symptoms demonstrate high sensitivity (approximately 90%) for the diagnosis of LPR and correlate with the degree of acid exposure. However, they cannot distinguish between acid and non-acid reflux. While acid reflux is the predominant form (63%), a significant proportion of patients (26%) experience non-acid reflux, an important distinction that can only be made through pH monitoring. Oropharyngeal pH monitoring is a minimally invasive and well-tolerated diagnostic method that shows a statistically significant correlation with response to PPI therapy, particularly regarding symptoms and acid reflux events detected on pH monitoring and the number of events with pH <6.0. Therefore, oropharyngeal pH monitoring can play a key role in predicting the PPI response and guiding therapeutic decisions in patients with LPR who are unresponsive to treatment.

Table 1
Pharmacotherapeutic options for LPR therapy (adapted from Lechien 2023[15])

Pharmacological class	Mechanism	Dose and frequency
PPIs	Form covalent bonds with H+/K+-ATPase, inactivating the proton pump	Standard dose, once or twice daily for 8–12 weeks
P-CABs	Inhibit H+/K+-ATPase through non-covalent competitive binding	Vonoprazan 20 mg once daily for 8–12 weeks
H2RAs	Selectively inhibit H2 receptors in the epithelial membrane of gastric cells	Variable dose regimens
Alginates	Form a viscous mechanical barrier that limits reflux into the esophageal mucosa	Gaviscon® one–two sachets/ tablets after meals and/or at bedtime
Prokinetic agents	Enhance gastric emptying and increase LES static pressure	Bromopride (Digesan®), domperidone, or metoclopramide three times daily before meals
Baclofen	Reduces transient LES relaxation and prevents both acidic and non-acidic reflux events	Not recommended for LPR
Hyaluronic acid + chondroitin sulfate	Provide a topical mechanical protective effect on the mucosa	Not specifically studied for LPR; consider in refractory GERD one sachet after meals and at bedtime

Abbreviations: LPR, laryngopharyngeal reflux; PPIs, proton pump inhibitors; P-CABs, potassium-competitive acid blockers; H2Ras, H2 receptor antagonists; LES, lower esophageal sphincter.

Figure 8
LPR diagnostic and therapeutic protocols



Abbreviations: LPR, laryngopharyngeal reflux; RSI, Reflux Symptom Index; RSS-12, Reflux Symptom Score 12; RFS, Reflux Finding Score; RSA, Reflux Sign Assessment; COPD, chronic obstructive pulmonary disease; GI, gastrointestinal; PPIs, proton pump inhibitors; MII-pH, Multichannel intraluminal impedance with pH monitoring.

Conflicts of interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

Data Confidentiality

The authors declare having followed the protocols used at their working center regarding patient data publication.

Protection of humans and animals

The authors declare that the procedures were followed according to the regulations established by the Clinical Research and Ethics Committee and the 2013 Helsinki Declaration of The World Medical Association.

Funding Sources

This work did not receive any contribution, funding, or scholarship.

Availability of scientific data

There are no datasets available, or publicity related to this work.

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