Diagnosis of Reflux and Place of pH Study

Subjects: Otorhinolaryngology

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Laryngopharyngeal reflux (LPR) is an inflammatory condition of the upper aerodigestive tract tissues related to direct and indirect effect of gastroduodenal content reflux, which induces morphological changes in the upper aerodigestive tract. The demonstration of pharyngeal reflux events through pH study is an important step in the management of LPR because this is the most effective approach to objective the back flow of gastric content into the pharynx.

Keywords: larynx ; laryngitis ; laryngopharyngeal ; reflux ; otolaryngology ; head neck surgery ; gastroesophageal reflux ; pH impedance ; monitoring

1. Clinical Diagnosis and Importance of pH Study

To date, most physicians consider patient symptoms and nasofibroscopic findings for the LPR check-up and confirm the diagnosis through symptom improvement after 1- to 3-month empirical therapeutic trial [1]. The use of patient-reported outcome questionnaires (e.g., reflux symptom index > 13 [2] or reflux symptom score > 13 [3]) and clinical instruments (e.g., reflux finding score > 7 [4] or reflux sign assessment > 14 [5]) improves the clinical diagnostic accuracy [6][7]. However, the clinical approach is limited for many reasons. First, the non-specificity of symptoms and findings makes uncertain the clinical diagnostic, and the prescription of empirical treatment may be inconsistent and costly [8]. Second, the empirical therapeutic success remains uncertain, with 57% of patients reporting improvement or relief of symptoms [8]. The use of inadequate treatment, the chronic course of some LPR disease presentations, and the patient adherence are all factors that may underly the low empirical therapeutic success rate [8]. According to recent reviews [8][9], most authors used proton pump inhibitors (PPIs) for the empirical treatment, even though most hypopharyngeal reflux events (HREs) are weakly or nonacid at the hypopharyngeal-esophageal multichannel intraluminal impedance–pH monitoring (HEMII-pH) [10][11][12]. The use of PPIs with alginate or magaldrate makes further sense [8], but this combination remains infrequently used [13][14]. The low success rate of empirical treatment may result from the clinical course of some LPR diseases. Indeed, LPR may be acute (30%), recurrent (40%), or chronic (30%) disease [15]. Patients with chronic course reported low therapeutic response rates for unknown reasons [15][16]. Another issue that may underly the difficulty to reach adequate therapeutic success rate is the lack of adherence of patients to treatment regimen [17]. In practice, many patients did not experience heartburn or gastroesophageal reflux disease (GERD)-related symptoms and may doubt the reflux (LPR) diagnosis, which may strengthen the poor therapeutic adherence.

2. Place, Indications, and Features of pH Study

To date, there is no objective tool considered as the gold standard for the LPR diagnostic. According to the characteristics of the device (impedance ring, placement of sensors, etc.), the pH study may be considered as the most reliable tool to demonstrate the back flow of gastric content into the pharynx. This approach is associated with advantages and disadvantages that may be considered in the decision of physician to propose pH study to the patients.

The pH study is usually performed over a 24-h period, which may be associated with patient inconvenience despite adequate tolerance [18]. Most patients tolerate the examination (>95%) [18]. The catheter insertion may be associated with significant pain, and the pH probe may cause belching and coughing during the early part of the monitored period, especially in patients with esophageal or laryngopharyngeal mucosa hypersensitivity [18][19]. The pharyngeal probe placement difficulties and movements are both points that were frequently considered as weaknesses of the technique, leading to probe movement and false-positive diagnostic [18][20]. From a theoretical standpoint, it has for a long time been suggested that drying of the hypopharyngeal sensors led to pseudoreflux and false positive, but in practice, this was not really demonstrated [20].

The main advantage of pH study is the identification of HREs and their following features: composition (gaseous, liquid versus mixed), types (acid, weakly acid, versus nonacid), and the position of occurrence (upright versus supine). The identification of the LPR features may lead to a more personalized treatment considering the usefulness of PPIs

(acid/weakly acid versus alkaline reflux) as well as the time of medication intake (daytime, nighttime or 24-h reflux) [21]. In other words, pH study may be useful for the therapeutic strategy.

To date, there are no consensus for the indications of HEMII-pH. According to a recent survey, most otolaryngologists do not prescribe pH study and prefer to refer patients to the gastroenterologist for the following reasons: patient inconvenience (59.4%), lack of understanding of interpretation (49.2%), lack of meaningfulness (42.8%), lack of skills to interpret the results (35.4%), and the suspected high cost of the approach (35.1%). Among aware otolaryngologists, HEMII-pH was mainly proposed to resistant patients for an empirical therapeutic trial [13][14].

3. Single, Dual-, or Triple-Probe Esophageal pH Monitoring

The consideration of LPR as a different condition than GERD appeared in the nineties with the work of Jamie Koufman [16][22]. In 1991, Jamie Koufman estimated the LPR incidence at 10% of outpatients presenting to otolaryngology departments with extra-esophageal manifestations of GERD [16]. In this study, 62% of individuals had abnormal esophageal pH studies considering acid GERD criteria, and 30% reported documented acid reflux events in both esophagus and pharynx. This study was perhaps the first important research differentiating LPR from GERD, but the dual-probe pH study device only focused on acid HRE.

Triple-probe hypopharyngeal-esophageal pH monitoring was used in many studies over the two last decades considering the LPR diagnostic when pharyngeal drop in pH value <4 occurred immediately after distal and proximal esophageal acid exposure [20][23][24]. The use of triple-probe pH study provided new information in LPR physiology about the role of upper esophageal sphincter (UES). Initially, Murris et al. observed that 24% of LPR patients may have acid HRE but normal acid exposure in the low esophagus [20]. These authors also reported that only 68% of proximal esophageal reflux events reached pharynx [20]. The lack of association between distal esophageal and pharyngeal acid events was corroborated by Postma et al. who observed that 38% of LPR patients (>1 pharyngeal acid event) had normal esophageal acid exposure times [25]. Interestingly, Harrel et al. observed that adding a hypopharyngeal pH sensor in pH study increased the detection of abnormal pH values and supported the diagnosis of LPR more often than traditional dual-sensor esophageal monitoring [23]. Nowadays, the accuracy of single, dual-, or triple-probe pH-study devices is called into question regarding the lack of correlation between distal/proximal esophageal events and HREs and the lack of consideration of weakly acid or nonacid HREs [10][11][12][26].

4. Multichannel Intraluminal Impedance–pH Monitoring

The recent literature dedicated to MII-pH without pharyngeal sensor was not reviewed because only HEMII-pH may detect HRE. To date, there is no international consensus guidelines determining HRE threshold for the LPR diagnosis. In a recent study, Kim et al. observed that the consideration of ≥1 HRE at the HEMIII-pH was associated with sensitivity and specificity of 76.0% and 81.5%, respectively [27]. According to the type of pH-impedance monitoring used for the diagnosis, the diagnosis criteria may vary. Many differences across studies make difficult the establishment of consensual normative criteria for LPR on ambulatory reflux monitoring, e.g., impedance/pH sensor placements or configurations, definition of HRE, definition of composition (gas, liquid, mixed), or type (acid/weakly acid/nonacid) events [26][28][29][30][31][32][33][34][35][36][37][38][39][40][41][42]. These differences may involve the various devices available on the market. Thus, in a recent systematic review including the pH study findings of 720 healthy individuals, authors observed that the 95th percentile thresholds were 0 to 10 HREs for HEMII-pH and 40 to 128 for events with pH < 6.0 on oropharyngeal pH monitoring, respectively [26]. These differences between HEMII-pH and oropharyngeal pH monitoring may be related to different sensitivities and precisions of pH study devices in the HRE detection.

The profiles of LPR patients at the HEMII-pH were studied in few studies. It was found in a recent study that 74% of HREs occurred outside 1-h post-meal times, while 20.5% and 5.5% occurred during the 1-h post meal and nighttime, respectively [12]. LPR was nonacid or weakly acid in more than half patients, and they had only upright and daytime HREs in 59% of cases [12]. The findings of this study corroborated those summarized in the systematic review of the Young Otolaryngologists of the International Federation of Otorhinolaryngological Societies [26]. The occurrence of daytime, upright, and gaseous HREs involved esophageal dysmotility, especially transient relaxations of the lower and upper esophageal sphincters. Thus, Sikavi et al. observed that LPR patients (with or without coexisting motility disorder) had reduced proximal esophageal contractibility at the high-resolution manometry, which significantly predicted increased of HREs [43]. The same team reported in another publication that 43.3% of patients with LPR at the HEMII-pH had abnormal findings at the high-resolution manometry, with the ineffective esophageal motility being the most common diagnosis [44]. Interestingly, recent findings reported that most HREs are weakly or nonacid [27][30][45][46], which supports the consideration of alginate or magaldrate in the therapeutic strategy [21][46]. Moreover, in practice, the pH of the reflux event

may increase from the distal to the proximal esophagus. The mechanisms underlying this increase of pH remain unknown and would involve the bicarbonate secretion into the esophagus mucosa.

5. Oropharyngeal pH Monitoring

Oropharyngeal pH monitoring (Restech Dx–pH monitoring) was specifically developed for the diagnosis of LPR [37]. As for HEMII-pH studies, there are several diagnostic criteria in the literature [26]m but many authors agreed to consider a positive Ryan score (upright score ≥ 9.41 or supine score ≥ 6.8) for the presence of LPR [35][37][38][47][48]. Ryan score is calculated according to three components: the percent time pH < 5.5 upright or <5.0 supine; the number of episodes in which the pH dropped below threshold; and the duration of the longest episode. The low consideration of HRE with pH > 7.0 in the Ryan score is a controversial issue because many studies demonstrated that there are significant proportions of HREs with pH > 7 in LPR patients [12][26][27]. At alkaline pH, the bile salts and some potential other enzymes may injury the laryngopharyngeal mucosa. Interestingly, Vance et al. compared the diagnostic utility of HEMII-pH study versus oropharyngeal pH monitoring in patients who benefited from both examinations throughout the same 24-h period [49]. These authors reported that oropharyngeal pH monitoring (Restech®) detected more percent time/total HREs in supine and upright positions and longer event times compared with HEMII-pH. Moreover, HEMII-pH testing was able to detect more HREs of pH < 4 than oropharyngeal pH monitoring [49]. Vance et al. observed that oropharyngeal pH monitoring correlated better with total patient symptom scores including cough, heartburn, burping, and throat clearing compared with HEMII-pH. The findings of Vance et al. do not corroborate those of Weitzendorfer et al. who observed that elevated Dx-pH measurements did not show significant correlation with either pH–impedance monitoring features, RSI, RFS, and saliva pepsin measurements [50]. However, irrespective to the pH study device, the correlation between pH study, symptoms, and findings remains controversial according to many studies that could not demonstrate an apparent relationship between the intensity of symptoms and the magnitude and patterns of hypopharyngeal reflux events [6][51]. This lack of correlation may be related to various patient profiles of mucosa sensitivity and microbiome differences [52]. In sum, the usefulness of oropharyngeal pH monitoring needs to be demonstrated in future controlled studies.

6. Placement and Technical Point

The placement of the pH study probe is commonly performed by an experienced nurse or physician who needs to be aware about potential complications, including probe kink or pulmonary placement [53]. In HEMII-pH, the distal sensor is usually placed 5 cm above the upper margin of the lower esophageal sphincter to avoid displacement into the stomach during swallowing, when the esophagus is shortened [20]. The pharyngeal sensor is placed 1–2 cm above the UES, but this position may change from one study to another [26]. In oropharyngeal pH monitoring, the pharyngeal sensor is placed in the oropharynx cavity. The control of the HEMII-pH probe placement may be done with chest radiography, nasofibroscopy, or pH control in the distal sensor (stomach). Importantly, the analysis of HEMII-pH needs to be performed by experienced otolaryngologist or gastroenterologist because automated analysis was found to be associated with a tendency of excessive reflux measurement when compared with manual analysis [54].

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