

# The role of pH-impedance monitoring in swallowing disorders

Francois Bobin<sup>a</sup> and Jerome R. Lechien<sup>a,b,c,d</sup>

## **Purpose of review**

To review the current evidence about the usefulness and the place of pH study in the management of patients with swallowing disorders.

#### **Recent findings**

Gastroesophageal reflux disease (GERD) and laryngopharyngeal reflux (LPR) are found in approximately 30% of patients with esophageal or oropharyngeal dysphagia. Patients with suspected GERD may benefit from gastrointestinal endoscopy and proton pump inhibitors according to guidelines. The diagnosis of LPR in patients with oropharyngeal dysphagia is more controversial because there are no gold standard and diagnostic guidelines. The clinical diagnosis based on empirical therapeutic trial is a reasonable first-line strategy, but many dysphagic patients should not respond to treatment. These patients require hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring (HEMII-pH), which is the most effective examination providing important information on GERD and LPR features. At the HEMII-pH, GERD patients often report upright (daytime) and supine (nighttime) liquid acid esophageal events with significant esophageal distal acid exposure time. LPR patients have more frequently upright (daytime) gaseous weakly acid or nonacid pharyngeal reflux events without distal esophageal acid exposure abnormalities in many times. The features of reflux at the HEMII-pH may indicate a personalized treatment for dysphagic patients combining proton pump inhibitors, alginate/magaldrate or gastroprokinetic in cases of esophageal dysmotility.

#### Summary

GERD and LPR are prevalent causes of dysphagia. The large number of reflux patients who do not respond to empirical treatment makes important the awareness of otolaryngologists about pH-impedance monitoring indication, features, and interpretation.

#### **Keywords**

dysphagia, gastroesophageal, head neck surgery, impedance, laryngitis, laryngopharyngeal, otolaryngology, pH study, reflux, swallowing

# **INTRODUCTION**

Dysphagia is an increasingly frequent disorder defined as the difficulty in transferring food from the mouth to the stomach [1]. Dysphagia may be classified into esophageal and oropharyngeal dysphagia according to the location of the dysfunction. In otolaryngology, physicians are frequently faced with patients with oropharyngeal dysphagia that is related to abnormalities in the physiology of swallowing in the upper gastrointestinal tract [1,2<sup>••</sup>]. The management of swallowing disorders is an important issue because persistent dysphagia may be associated with malnutrition, dehydration, aspiration pneumonia, bronchospasm, choking, and death [3<sup>•</sup>,4]. Laryngopharyngeal reflux (LPR), gastroesophageal reflux disease (GERD) and some associated disorders are common causes of dysphagia

[5]. Depending on the type of reflux (GERD versus LPR), patients may report findings of esophageal and/or oropharyngeal dysphagia. The GERD diagnosis is easily made regarding typical symptoms,

Curr Opin Otolaryngol Head Neck Surg 2022, 28:000-000 DOI:10.1097/MOO.00000000000841

1068-9508 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

www.co-otolaryngology.com

<sup>&</sup>lt;sup>a</sup>Polyclinic of Poitiers, Elsan Hospital, Poitiers, France, <sup>b</sup>Department of Anatomy and Experimental Oncology, Mons School of Medicine, UMONS Research Institute for Health Sciences and Technology, University of Mons (UMons), Mons, <sup>c</sup>Department of Otolaryngology-Head and Neck Surgery, EpiCURA Hospital, Baudour, Belgium and <sup>d</sup>Department of Otolaryngology-Head and Neck Surgery, Foch Hospital, Paris Saclay University, Paris, France

Correspondence to Jerome R. Lechien, MD, PhD, MS, Department of Otolaryngology-Head and Neck Surgery, EpiCURA Hospital, Rue L. Cathy, Baudour, Belgium. Tel: +32 65 37 35 84; e-mail: Jerome.Lechien@umons.ac.be

# **KEY POINTS**

- About 30% of patients with esophageal dysphagia reported reflux disease.
- The diagnosis of gastroesophageal reflux disease (GERD) is standardized, and the usefulness of gastrointestinal endoscopy is demonstrated.
- The laryngopharyngeal reflux (LPR) clinical diagnosis based on empirical therapeutic trial is considered as a reasonable first-line strategy, but many patients with swallowing disorder and suspicion of reflux should not respond to treatment. These patients require pH study to confirm the reflux diagnosis.
- Hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring (HEMII-pH) appears to be the most effective examination because it provides important information on GERD and LPR features.
- Most patients with GERD have upright(daytime)/supine (nighttime) liquid acid esophageal events with an esophageal distal acid exposure time >6% of testing according to Lyon consensus.
- LPR patients have more frequently upright(daytime) gaseous weakly acid or nonacid HREs, while the distal esophageal acid exposure time may be normal.
- The features of reflux at the HEMII-pH may indicate a personalized treatment for dysphagic patients.

consensus and guidelines, but the LPR diagnosis remains complicated because nonspecificity of both symptoms and signs and the lack of a gold standard examination for the diagnosis [5,6]. To date, the pH study is commonly considered as the most effective approach to demonstrate the occurrence of GERD or hypopharyngeal reflux events (HRE) and, therefore, may support the diagnosis [7,8]. In the present review, we aimed to summarize the current evidence about the usefulness and the place of pH study in the management of patients with swallowing disorders.

### **EPIDEMIOLOGY**

The prevalence of dysphagia in the general population was estimated to 13.4% and may range from 7.3% to 64.2% according to populations and diseases [2<sup>••</sup>]. Elderly patients reported higher rates of dysphagia than younger adults. The prevalence of dysphagia significantly increased over the past decades regarding the worldwide population aging [2<sup>••</sup>,9]. Based on age, several comorbidities may be associated with a high prevalence of dysphagia, including dementia, Parkinson disease, head and neck cancer and stroke [2<sup>••</sup>,10]. Swallowing disorders are a substantial cause of mortality, with more than 60 000 deaths resulting from swallowing disorder complications according to the U.S. Agency for Healthcare Policy and Research [11]. The annual cost of dysphagia to the U.S. healthcare system is between \$4 and \$7 billion [12], whereas it may overall reach  $\in$ 10.5 billion in UK [13]. Irrespective to the types and the causes of dysphagia, the global cost and burden trend to increase in Western countries [14].

# **ETIOLOGIES OF DYSPHAGIA**

The causes and the types of dysphagia (esophageal versus oropharyngeal) varied across age populations. The patient history, comorbidities and lifestyle, as well as the clinical course of dysphagia and associated-symptoms (intermittent or progressive) may help the physician to clarify the cause of the swallowing disorder. According to the medical history, the otolaryngologist may perform nasofiberoptic, transnasal esophagoscopy or fiberoptic endoscopic evaluation of swallowing (FEES) inoffice for the diagnosis [15<sup>••</sup>].

In oropharyngeal dysphagia, the most common causes included laryngopharyngeal reflux; laryngeal nerve injury; some medications; neurodegenerative conditions; cricopharyngeal muscle dysfunction; Zenker's diverticulum; cervical web; myositis; and histories of head and neck radiation or surgery [15<sup>••</sup>,16,17,18<sup>•</sup>]. The main etiologies of esophageal dysphagia are gastroesophageal reflux disease; some medications; eosinophilic or pill esophagitis; peptic stricture; cancer; achalasia and sclerodermia [15<sup>••</sup>,16,17,18<sup>•</sup>].

Reflux diseases were considered as the most prevalent conditions associated with dysphagia in many population-based or swallowing center investigations [19–22,23<sup>••</sup>]. Hoy et al. [22] evaluated 100 patients presenting in swallowing clinic and they observed that the most prevalent causes of oropharyngeal dysphagia were reflux (27%), radiation history (14%) and cricopharyngeal muscle dysfunction (11%). In 2020, Adkins et al. [23<sup>•••</sup>] investigated the swallowing disorder prevalence in 31 129 individuals. Among them, 16.1% reported dysphagia with the following most prevalent causes: reflux (30.9%), eosinophilic esophagitis (8.0%) and esophageal structure (4.5%) [23<sup>•••</sup>]. These study findings corroborated those of the population-based survey of Almario et al. [24] who reported in 71 812 U.S. individuals that the most common symptoms associated with dysphagia were heartburn/reflux, bloating, abdominal pain, diarrhea, and constipation. The estimation of the prevalence of LPR in patients with oropharyngeal dysphagia is however difficult because most authors did not confirm the LPR

2 www.co-otolaryngology.com

diagnosis through the identification of hypopharyngeal reflux events (HRE) at the hypopharyngealesophageal multichannel intraluminal impedancepH monitoring (HEMII-pH). About clinical presentation, dysphagia (and 'difficulties to swallow') was reported as one of the most prevalent symptoms in LPR patients in the largest cohort-study [25<sup>•</sup>,26,27]. Because there is no correlation between symptoms and findings, the anatomical origin of dysphagia in LPR patients remains unclear [5]. LPR patients with dysphagia may have tongue tonsil hypertrophy, edema of the retrocricoid or the laryngeal posterior commissure but the anatomical study of findings associated with dysphagia requires future large cohort studies [5,25<sup>•</sup>].

In sum, according to the recent literature findings [22,23<sup>••</sup>,24], reflux diseases appear to be prevalent conditions in the dysphagia origins.

# DIAGNOSIS OF REFLUX AND PLACE OF pH STUDY

# **Empirical therapeutic trial**

The confirmation of the reflux diagnosis in patients with dysphagia may differ from GERD to LPR patients [5]. As reported in Fig. 1, patients with esophageal dysphagia and GERD symptoms may benefit from gastrointestinal (GI) endoscopy to detect and treat esophagitis, Barrett disease or *Helicobacter pylori* infection. The GI endoscopy (and manometry) may detect another condition that may contribute to esophageal dysphagia, such as eosinophilic esophagitis, esophageal stricture or achalasia. The management of GERD is standardized and reported in recent guidelines [28–30].

The management of LPR patients remains controversial because there is no gold standard for the diagnosis. Currently, most otolaryngologists consider symptoms and nasofiberoptic findings for the baseline evaluation and they confirm the diagnosis after a positive response to a 3-month empirical therapeutic trial [31]. The 'positive' response consists of symptom improvement but it is subjective and the definition may substantially vary from one study to another [5,32]. For this reason, it is recommended to use validated patient-reported outcome questionnaires (e.g. reflux symptom index > 13 [33] or reflux *symptom score* > 13 [34]) and clinical instruments (e.g. reflux finding score > 7 [35] or reflux sign assessment > 14[36]) to improve the clinical diagnostic accuracy and therapeutic response evaluation [37].

A recent review reported that 57% of patients exhibit improvement or relief of LPR symptoms after 3-month proton pump inhibitors (PPIs), which remains a low therapeutic success rate [38]. The reasons of nonresponse to empirical treatment include the use of inadequate treatment (i.e. PPIs in nonacid reflux), the chronic course of some LPR clinical presentations, the lack of adherence of patient to diet or medication, the inappropriate intake of medication, and the existence of differential diagnoses [38,39,40<sup>•</sup>,41]. Some differential diagnoses of reflux-like symptoms are described in Table 1.

Moreover, the nonspecificity of symptoms and findings makes uncertain the clinical diagnostic and, consequently, the use of antireflux empirical therapeutic trial may be inconsistent and costly [42<sup>•</sup>]. The HEMII-pH is indicated in nonresponder patients for two main reasons. First, the HEMII-pH is the most reliable tool to detect HRE and, therefore, confirm the diagnosis [43<sup>•</sup>]. Second, HEMII-pH may provide useful information about the presence of GERD and/or LPR; the type (acid, weakly acid, versus nonacid); the composition (gaseous, liquid, *versus* gaseous/liquid); and the position of patient when reflux events occur (upright versus supine) [44\*\*,45]. To date, most otolaryngologists used twice daily PPIs for the empirical treatment [46<sup>•</sup>,47] even though most HREs are weakly or nonacid [44\*\*,48,49]. The consideration of the reflux features is important to prescribe a more personalized treatment consisting of a combination of PPIs, alginate or magaldrate [45].

In sum, the clinical diagnosis based on empirical therapeutic trial is currently considered as a reasonable first-line strategy, but many patients with swallowing disorder and suspicion of reflux should not respond to treatment and may require objective examination to confirm the reflux diagnosis.

# Types, indications, and limits of pH study

Many types of pH studies are commonly used worldwide in the management of patients with swallowing disorder and suspected reflux, including single, dual, triple-probe pH monitoring, hypopharyngeal/ esophageal multichannel intraluminal impedancepH monitoring, Bravo pH monitoring, and oropharyngeal pH monitoring. According to the characteristics of the devices (number and positions of pH/ impedance sensors, etc.), the information provided by the pH study may vary. From a practical standpoint, the pH study is usually performed over a 24-h period. Patients may report inconvenience, but the tolerance is usually adequate [50]. The difficulties related to the placement of the pharyngeal sensor(s) and the probe movements during swallowing are both considered as the main weaknesses of the pH study [50,51]. Moreover, it was long time suggested that drying of the pharyngeal sensors may lead to pseudoreflux and false positive results but this finding was poorly demonstrated [51].

1068-9508 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.



**FIGURE 1.** Management of dysphagic patients with a suspicion of reflux. \*The presence of GERD/digestive symptoms may lead to the proposition of GI endoscopy to patients. Note that elderly patients may have GI endoscopy abnormalities, such as GERD, and no symptom. FEES, fiberoptic endoscopic evaluation of swallowing; GERD, gastroesophageal reflux disease; GI, gastrointestinal; HEMII-pH, hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring; HRE, hypopharyngeal reflux event; LPR, laryngopharyngeal reflux; NF, nasofiberoptic examination; RFS, reflux finding scopre; RSA, reflux sign assessment; RSI, reflux symptom index; RSS, reflux symptom score.

# Single, dual- or triple-probe esophageal pH monitoring

Single esophageal probe pH monitoring is commonly used in gastroenterology for the GERD diagnosis that is based on distal esophageal acid exposure. Dual-probe pH monitoring (with the proximal sensor placed in upper esophagus or pharynx) was developed for LPR and was used in the first study differentiating LPR from GERD [52]. When the reflux is suspected as the main cause of the patient

Table 1. Differential diagnoses of reflux disease symptoms in dysphagic patients

Reported differential diagnoses of symptoms of reflux and swallowing disorders.				
Esophageal disorders	Ear, nose, and throat disorders			
Hypertonicity of upper esophageal sphincter	Infections			
Eosinophilic esophagitis	Chronic rhinosinusitis			
Zenker diverticulum	Mycosis			
Esophageal sclerodermia	Recurrent angina			
Esophageal candidosis	Tuberculosis			
Heterotopic esophageal gastric mucosa	Rheumatologic/auto-immune disorders			
Neoplasia	Rheumatic arthritis			
Hypertensive lower esophageal sphincter	Sjogren's syndroma			
Achalasia	Laryngeal sarcoÿdosis			
Esophageal spasm	Amyloÿdosis			
Absent peristaltism	Granulomatosis with polyangiitis			
Hypercontractile esophagus	Fibromyalgia			
Gastroparesis	Allergic pharyngolaryngitis			
Esophageal myositis	Laryngeal musculoskeletal disorders			
Postradiation mucositis	Muscle tension dysphonia			
Pill esophagitis	Cervical osteophytes			
Extrinsic compression (i.e. mediastinum/lung/thyroid)	Benign or malign tumors			
Rumination	Anatomical disorders			
	Size & shape of the epiglottis			
Neurological and psychological disorders	Tongue tonsil hypertrophy or cyst			
Neurodegenerative diseases	Uvula hypertrophy			
Vagus, glossopharyngeal nerve disorders	Retroverted epiglottis			
Stress, depression, anxiety and related muscle tension	Traumatic			
Drugs	Laryngeal fracture			
Anticholinergic (salivary hypofunction)	Upper aerodigestive tract injury			
	Other			
Lung disorders	Aging voice			
COPD and intake of inhaled corticosteroids	Upper aerodigestive tract neoplasia			
	Tobacco/alcohol induced pharyngitis			
	Thyroid disease (nodules, goiter, etc.)			

These differential diagnoses may be investigated in patients who do not respond to 3-month empirical therapeutic trial based on a combination of proton pump inhibitors and alginate/magaldrate.

dysphagia, practitioners have to keep in mind that LPR may occur without abnormal distal esophageal acid exposure. Indeed, Murris *et al.* [51] reported that 24% of patients with LPR findings (>1 HRE) had normal acid exposure in the low esophagus. They also reported that 68% of distal-to-proximal esophageal reflux events reached pharynx [51]. The lack of association between distal esophageal and pharyngeal acid events was supported by the study of Postma *et al.* [53] who found that 38% of LPR patients (>1 HRE) had normal esophageal acid exposure times. The pH-impedance monitoring differences between GERD and LPR are summarized in Table 2. The accuracy of single, dual- or triple-probe pH studies without impedance ring is called into question regarding the inability of devices to detect weakly acid or nonacid reflux events [5].

# Multichannel intraluminal impedance-pH monitoring

Multichannel intraluminal impedance-pH monitoring (MII-pH) is available with or without pharyngeal impedance sensors. MII-pH is indicated in GERD patients with a suspicion of nonacid distal reflux, in which bile acids may be involved in the development of esophageal lesions [54<sup>\*</sup>,55]. Interestingly,

1068-9508 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

Impedance-pH monitoring features	GERD	LPR
Distal esophageal reflux	Mostly acid	Normal in 30–50%
	Frequent events	
	Mostly liquid	
	Upright and supine	
	Increased in supine position	
	Mostly postmeal time	
	Lyon & DeMeester criteria	
Proximal esophageal/pharyngeal events	Infrequent	>1 events (HEMII-pH)
	If present: mostly acid	Weakly/nonacid events
		Mostly gaseous events
		Upright and daytime
		Outside the postmeal time
Contributing factors	Supine position	Hiatal hernia (resistance to treatment)
	Hiatal hernia	LES and UES insufficiencies
	LES insufficiency	
Correlation between symptoms-events	Frequently significant	Rarely significant

Table 2. Features of gastroesophageal reflux disease and laryngopharyngeal reflux patients at the pH-impedance monitoring

GERD, gastroesophageal reflux disease; HEMII-pH, hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring; L/UES, lower/upper esophageal sphincter; LPR, laryngopharyngeal reflux.

two studies using pH-impedance monitoring reported the back flow of gastroduodenal content into the pharynx, and measurable bile acids in the saliva [56,57]. The detection of bile acids in the saliva supports the potential occurrence of duodenogastric reflux events in LPR patients even if this though was never studied. According to the high prevalence of LPR in GERD patients, and the involvement of both GERD and LPR in the development of swallowing disorders, the use of HEMII-pH makes sense rather than the MII-pH without pharyngeal sensors [5]. Indeed, the HEMII-pH provides useful information about GERD and LPR [5].

To date, there are no international guidelines establishing normative data for HRE at the HEMIIpH (diagnostic criteria). A few studies investigated the HEMII-pH findings in healthy individuals (Table 3) [58<sup>••</sup>,59,60–73]. Kim *et al.* [74] observed that the consideration of  $\geq 1$  HRE was associated with sensitivity and specificity of 76.0% and 81.5%, respectively, whereas others reported a normal range of 1-10 HREs [58<sup>••</sup>,68]. The diagnosis criteria may vary regarding the type of pH study device used. The findings of a recent systematic review suggested that the 95th percentile thresholds were 10–73 events for proximal esophageal reflux event, 0-10 for HREs, and 40-128 for events with pH <6.0 on oropharyngeal pH monitoring [58<sup>•••</sup>]. The findings of this review suggested that the differences between studies (e.g. impedance/pH sensor placements or configurations; definition of reflux event; definition of composition) make difficult the establishment of consensual normative criteria for LPR diagnostic. The device differences in the detection sensitivity of HRE should be particularly important between HEMII-pH and oropharyngeal pH monitoring (cf. below).

# Profiles of reflux patients at the hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring

The profile of LPR patients at the HEMII-pH was investigated recently in few studies [43<sup>•</sup>,44<sup>••</sup>,48,49,75]. In 2021, we observed that 74% of HREs occurred outside 1-h postmeal times, whereas 20.5% and 5.5% events occurred during the 1-h postmeal and nighttime, respectively (Fig. 2) [44<sup>••</sup>]. In another study, authors found that more than 44.5% of patients reported weakly acid or nonacid LPR [75], which were defined according to the ratio of number of acid HREs (pH < 4.0)/numberof nonacid (pH  $\geq$  4.0) HREs through the 24-h testing period. Patients with a ratio of acid/nonacid HREs <0.5 were considered as individuals with nonacid LPR, while those with a ratio between 0.5 and 2.0 had weakly acid LPR [75]. HREs occurred upright and daytime in 59% of cases [44<sup>••</sup>,75]. In practice, the pH of the reflux event may increase from the distal to the proximal esophagus and pharynx. Sikavi et al. [76] observed that the occurrence of

References	Device	Sample features	PRE/HRE event features	Results
Shay, 2004 [70]	24-h MII-pH	N=60 HIs	Total/upright/supine PRE (median)	8/7/0
			Acid/weakly acid/nonacid (median)	5/2/0
Zentilin, 2006 [71]	24-h MII-pH	N=25 HIs	Proximal events (median)	15
			Upright/supine ratio	94%
Xiao, 2009 [60]	24-h MII-pH	N=70 Hls	Total/upright/supine PRE (median)	8/8/0
			Acid/weakly acid/nonacid (median)	6/2/0
Wang, 2011 [59]	24-h HEMII-pH	N=37 HIs	Total/upright/supine PRE (median)	6/6/0
			Acid/weakly acid/nonacid (median)	1/0/1
			Total/upright/supine HRE (median)	0/0/0
Норро, 2012 [61]	24-h HEMII-pH	N = 40 HIs	Total/upright/supine HRE (median)	0/0/0
Desjardin, 2013 [62]	24-h HEMII-pH	N = 45 HIs	PRE events pH <4; pH <5 (number)	1/1
			HRE events pH <4; pH <5 (number)	1/1
JettÕ, 2014 [72]	24-h MII-pH	N = 142 HIs	Total/acid/nonacid PRE (mean)	24/15/9
Kawamura, 2016 [73]	24-h MII-pH	N=42 HIs	Total/upright/supine PRE (median)	16/35/1
			Acid/weakly acid/nonacid (median)	7/8/17
Hou, 2020 [64]	24-h HEMII-pH	N=38 HIs	Total/acid/nonacid HRE	0/0/0
Chen, 2020 [8]	24-h MII-pH	N = 25 HIs	PRE information	NP
Doo, 2020 [65]	24-h HEMII-pH	N=21 HIs	PRE/HRE information	NP
Sun, 2009 [66]	Oropharyngeal pH metry	N = 20 HIs	HRE-pH <4; pH <5 (median)	0/0
			Upright/Recumbent HRE pH <4	0/0
			Upright/Recumbent HRE pH<6	1/3
Ayazi, 2009 [68]	Oropharyngeal pH metry	N = 55 HIs	HRE-pH <4; <5; <5.5 (median)	0/0/0
			HRE-pH <6; <6.5 (median)	1/10
Chheda, 2009 [69]	Oropharyngeal pH metry	N = 20 HIs	HRE-pH <4; <4.5; <5; <5.5 (median)	0/0/0/1
Feng, 2014 [63]	Oropharyngeal pH metry	N=29 HIs	HRE (median/mean/number)	NP
Yadlapati, 2016 [67]	Oropharyngeal pH metry	N = 18 HIs	Abnormal % time pH <5/5.5 (mean)	0/3

Table 3. Normative values (median/mean/number of positive individuals) for pH-impedance study or oropharyngeal pHmonitoring

(HE)MII-pH, (hypopharyngeal-esophageal) multichannel intraluminal impedance-pH monitoring; HIs, healthy individuals; HRE, hypopharyngeal reflux events; N, number; NP, not provided; PRE, proximal esophageal reflux events.

daytime, upright and gaseous HREs was commonly associated with transient relaxations of the lower and upper esophageal sphincters. In another recent study, these authors reported that 43.3% of patients with >1 HREs reported abnormal findings at the high-resolution manometry; the most common abnormality being the ineffective esophageal motility, whereas most patients having reduced proximal esophageal contractibility [77]. The findings of these recent studies support the observations of studies conducted over the past decade [61,74]. Regarding GERD, the patient profile at the HEMII-pH is mostly characterized by upright(daytime)/supine(nighttime) liquid acid esophageal events, with an esophageal distal acid exposure time >6% of testing according to Lyon consensus [29].

According to the upright and weakly/nonacid profile of LPR patients, the use of twice daily PPIs for the empirical therapeutic trial in dysphagic patients with a suspicion of LPR may be put into question. Indeed, the second PPI intake (before dinner) was proposed to reduce the acid stomach production during the evening and the night [77]. Moreover, PPIs do not change the number and duration of reflux events. PPIs only increase the pH of reflux events (that are already weakly acid in pharynx), whereas alginate or magaldrate reduce the number of reflux events; acting on acid, weakly acid and nonacid esophageal and hypopharyngeal reflux events [78]. Thus, practitioners may consider more frequently the combination of PPIs with alginate or magaldrate, or alginate/magaldrate only in the

1068-9508 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.



**FIGURE 2.** pH-impedance profiles of patients with different types of refluxes. Most LPR patients have daytime and upright HRE at the HEMII-pH (a). Patients with GERD commonly have daytime and nighttime reflux events (b). GERD, gastroesophageal reflux disease; HEMII-pH, hypopharyngeal esophageal multichannel intraluminal impedance-pH monitoring; LPR, laryngopharyngeal reflux.

empirical therapeutic trial. Alginate and magaldrate may be also used in the post-HEMII-pH personalized treatment of patients with swallowing disorder [42<sup>•</sup>,45]. Patients with esophageal dysmotility and reflux may also benefit from gastroprokinetic, but the identification of motility disorders requires high-resolution manometry examination.

# **Oropharyngeal pH monitoring**

Oropharyngeal pH monitoring (Restech Dx-pH monitoring) was developed for the diagnosis of LPR [68]. To date, a positive Ryan score (upright score  $\geq$  9.41 or supine score  $\geq$  6.8) is considered as relevant for the LPR diagnosis. Ryan score is calculated considering the following components: the percentage 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 [66,68,69]. The accuracy of Ryan score

was however controversial because the score does not consider events with pH > 7, which are frequent in LPR patients. Vance et al. [79"] compared both diagnostic approaches in 77 patients who benefited from HEMII-pH and oropharyngeal pH monitoring throughout the same 24-h period. The comparison between HEMII-pH and oropharyngeal pH monitoring revealed that oropharyngeal pH monitoring detected more percentage time/total pharyngeal reflux events in supine and upright positions and longer event times than HEMII-pH; whereas HEMIIpH testing was able to detect more events of pH<4 than oropharyngeal pH monitoring [79<sup>•</sup>]. Moreover, oropharyngeal pH monitoring correlated better with total patient symptom scores including cough, heartburn, burping, and throat clearing, than HEMII-pH [79<sup>•</sup>]. In practice, the main weakness of oropharyngeal pH monitoring is the lack of information about esophageal findings and GERD. The limitation is important because patients with severe GERD have a higher probability to have severe LPR and both esophageal and oropharyngeal dysphagia [75].

## Placement and technical point

The distal sensor of HEMII-pH is usually placed 5 cm above the lower esophageal sphincter and the pharyngeal sensor is placed 1-2 cm above the upper esophageal sphincter [58<sup>••</sup>]. The placement of the probe (and the hypopharyngeal sensors) may be controlled with chest radiography, nasofibroscopy, or through a high-resolution manometry. The placement of the pH-study probe may be difficult in patients with swallowing disorder because it requires the need of swallow the probe. The analysis of HEMII-pH tracing may be automated but Kang *et al.* [80] found that the automated analysis was associated with a tendency of excessive reflux meas-urement when compared with manual analysis by experienced practitioners.

#### CONCLUSION

Gastroesophageal reflux disease and laryngopharyngeal reflux are both prevalent causes of esophageal and oropharyngeal dysphagia. The large number of reflux patients who do not respond to empirical treatment makes important the awareness of otolaryngologists about pH-impedance monitoring. HEMII-pH is probably the most relevant pH study for patients with swallowing disorder because it provides useful information about esophageal (GERD) and pharyngeal (LPR) reflux events and may indicate a personalized treatment using PPIs, alginate or magaldrate.

#### Acknowledgements

None.

**Financial support and sponsorship** 

None.

## **Conflicts of interest**

There are no conflicts of interest.

#### REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- of special interest
- of outstanding interest
- Suntrup-Krueger S, Muhle P, Kampe I, et al. Effect of capsaicinoids on neurophysiological, biochemical, and mechanical parameters of swallowing function. Neurotherapeutics 2021; 18:1360–1370.

 Rajati F, Ahmadi N, Naghibzadeh ZA, Kazeminia M. The global prevalence of oropharyngeal dysphagia in different populations: a systematic review and meta-analysis. J Transl Med 2022; 20:175.

This study summarized the last epidemiological (prevalence/incidence) data about dysphagia.

 Banda KJ, Chu H, Kang XL, et al. Prevalence of dysphagia and risk of pneumonia and mortality in acute stroke patients: a meta-analysis. BMC Geriatr 2022; 22:420.

This study summarized the last epidemiological (comorbidities and risks) data about dysphagia.

- Gupte T, Knack A, Cramer JD. Mortality from aspiration pneumonia: incidence, trends, and risk factors. Dysphagia 2022. doi: 10.1007/s00455-022-10412w.
- Lechien JR, Akst LM, Hamdan AL, *et al.* Evaluation and management of laryngopharyngeal reflux disease: state of the art review. Otolaryngol Head Neck Surg 2019; 160:762–782.
- Lechien JR, Saussez S, Karkos PD. Laryngopharyngeal reflux disease: clinical presentation, diagnosis and therapeutic challenges in 2018. Curr Opin Otolaryngol Head Neck Surg 2018; 26:392–402.
- Snow G, Dhar SI, Akst LM. How to understand and treat laryngopharyngeal reflux. Gastroenterol Clin North Am 2021; 50:871–884.
- Chen S, Liang M, Zhang M, *et al.* A study of proximal esophageal baseline impedance in identifying and predicting laryngopharyngeal reflux. J Gastroenterol Hepatol 2020; 35:1509–1514.
- Nieto K, Ang D, Liu H. Dysphagia among geriatric trauma patients: a population-based study. PLoS One 2022; 17:e0262623.
- Lechien JR, Cavelier G, Thill MP, et al. Validity and reliability of the French version of Eating Assessment Tool (EAT-10). Eur Arch Otorhinolaryngol 2019; 276:1727-1736.
- American Speech-Language-Hearing Association. Adult dysphagia (practice portal). Available at: www.asha.org/Practice-Portal/Clinical-Topics/Adult-Dysphagia/ [Accessed May, 12, 2022].
- Patel DA, Krishnaswami S, Steger E, et al. Economic and survival burden of dysphagia among inpatients in the United States. Dis Esophagus 2018; 31:1-7.
- 13. Elia M, Stratton R, Russel C, et al. The cost of disease- related malnutrition in the UK and economic considerations for the use of oral nutritional supplements (ONS) in adults. Redditch: Health Economic Group of the British Association for Parenteral and Enteral Nutrition (BAPEN); 2005.
- Attrill S, White S, Murray J, et al. Impact of oropharyngeal dysphagia on healthcare cost and length of stay in hospital: a systematic review. BMC Health Serv Res 2018; 18:594.
- **15.** Schindler A, Baijens LWJ, Geneid A, Pizzorni N. Phoniatricians and otorhinolaryngologists approaching oropharyngeal dysphagia: an update on FEES.
- Eur Arch Otorhinolaryngol 2022; 279:2727-2742. This study summarized the last clinical and in office approaches for oropharyngeal
- dysphagia.
  Roden DF, Altman KW. Causes of dysphagia among different age groups: a systematic review of the literature. Otolaryngol Clin North Am 2013; 46:965–987.
- McCarty EB, Chao TN. Dysphagia and swallowing disorders. Med Clin North Am 2021; 105:939–954.
- 18. Chheda NN. Upper esophageal dysphagia. Surg Clin North Am 2022;
  102:199-207.
- This study summarized the last clinical and physiological findings of upper esophageal sphincter functioning.
- Cho SY, Choung RS, Saito YA, et al. Prevalence and risk factors for dysphagia: a USA community study. Neurogastroenterol Motil 2015; 27:212-219.
- Cook IJ, Kahrilas PJ. AGA technical review on management of oropharyngeal dysphagia. Gastroenterology 1999; 116:455–478.
- Talley NJ, Weaver AL, Zinsmeister AR, Melton LJ 3rd. Onset and disappearance of gastrointestinal symptoms and functional gastrointestinal disorders. Am J Epidemiol 1992; 136:165–177.
- Hoy M, Domer A, Plowman EK, et al. Causes of dysphagia in a tertiary care swallowing center. Ann Otol Rhinol Laryngol 2012; 122:335–338.
- 23. Adkins C, Takakura W, Spiegel BMR, et al. Prevalence and characteristics of
- dysphagia based on a population-based survey. Clin Gastroenterol Hepatol 2020; 18:1970.e2-1979.e2.
- This study is a large population study assessing the prevalence of dysphagia in population.
- Almario CV, Ballal ML, Chey WD, et al. Burden of gastrointestinal symptoms in the united states: results of a nationally representative survey of over 71,000 Americans. Am J Gastroenterol 2018; 113:1701–1710.
- 25. Lechien JR, Bobin F, Muls V, *et al.* Changes of laryngeal and extralaryngeal symptoms and findings in laryngopharyngeal reflux patients. Laryngoscope 2021; 131:1332–1342.
- This study reported all symptoms and findings of LPR patients, including dysphagia.
- Lee YS, Choi SH, Son YI, et al. Prospective, observational study using rabeprazole in 455 patients with laryngopharyngeal reflux disease. Eur Arch Otorhinolaryngol 2011; 268:863–869.

1068-9508 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.

- Habermann W, Schmid C, Neumann K, et al. Reflux symptom index and reflux finding score in otolaryngologic practice. J Voice 2012; 26:e123-e127.
- Frazzoni M, Frazzoni L, Ribolsi M, et al. Applying Lyon Consensus criteria in the work-up of patients with proton pump inhibitory-refractory heartburn. Aliment Pharmacol Ther 2022; 55:1423–1430.
- Gyawali CP, Kahrilas PJ, Savarino E, et al. Modern diagnosis of GERD: the Lyon Consensus. Gut 2018; 67:1351–1362.
- Jung HK, Tae CH, Song KH, et al. 2020 Seoul Consensus on the diagnosis and management of gastroesophageal reflux disease. J Neurogastroenterol Motil 2021; 27:453–481.
- Ford CN. Evaluation and management of laryngopharyngeal reflux. JAMA 2005; 294:1534–1540.
- Lechien JR, Saussez S, Schindler A, et al. Clinical outcomes of laryngopharyngeal reflux treatment: a systematic review and meta-analysis. Laryngoscope 2019; 129:1174–1187.
- Belafsky PC, Postma GN, Koufman JA. Validity and reliability of the reflux symptom index (RSI). J Voice 2002; 16:274-277.
- Lechien JR, Bobin F, Muls V, et al. Validity and reliability of the reflux symptom score. Laryngoscope 2020; 130:E98–E107.
- Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). Laryngoscope 2001; 111:1313–1317.
- Lechien JR, Rodriguez Ruiz A, Dequanter D, et al. Validity and reliability of the reflux sign assessment. Ann Otol Rhinol Laryngol 2020; 129:313– 325.
- Francis DO, Patel DA, Sharda R, et al. Patient-reported outcome measures related to laryngopharyngeal reflux: a systematic review of instrument development and validation. Otolaryngol Head Neck Surg 2016; 155:923-935.
- Lechien JR, Muls V, Dapri G, et al. The management of suspected or confirmed laryngopharyngeal reflux patients with recalcitrant symptoms: a contemporary review. Clin Otolaryngol 2019; 44:784–800.
- Pisegna JM, Yang S, Purcell A, Rubio A. A mixed-methods study of patient views on reflux symptoms and medication routines. J Voice 2017; 31:381. e15-381.e25.
- 40. Verhasselt M, Rodriguez A, Dequanter D, Lechien JR. Chronic course,
  weaning, and awareness of patients with reflux toward proton pump inhibitor therapy. J Voice 2021. doi: 10.1016/j.jvoice.2021.03.002.
- This study identified the cause of nonadherence to medical treatment of LPR.
- Lechien JR, Hans S, Calvo-Henriquez C, et al. Laryngopharyngeal reflux may be acute, recurrent or chronic disease: preliminary observations. Eur Arch Otorhinolaryngol 2022. doi: 10.1007/s00405-022-07426-3.
- 42. Lechien JR, Bock JM, Carroll TL, Akst LM. Is empirical treatment a reasonable strategy for laryngopharyngeal reflux? A contemporary review. Clin Otolaryngol 2020; 45:450–458.
- This study summarized the current therapeutic findings of LPR.
- Suzuki T, Seki Y, Matsumura T, et al. Reflux-related extraesophageal symptoms until proven otherwise: a direct measurement of abnormal proximal exposure based on hypopharyngeal multichannel intraluminal impedance as a reliable indicator for successful treatment outcomes. J Neurogastroenterol
- Motil 2022; 28:69–77. This study is an important study in the understanding of the esophageal dysmotility
- and hypopharyngeal reflux events in LPR disease, leading to dysphagia. 44. Lechien JR, Bobin F, Dapri G, *et al.* Hypopharyngeal-esophageal impedance-
- pH monitoring profiles of laryngopharyngeal reflux patients. Laryngoscope 2021; 131:268–276.
- This study is an important study in the understanding of the esophageal dysmotility and hypopharyngeal reflux events in LPR disease, leading to dysphagia.
- 45. Lechien JR, Bobin F, Muls V, et al. The efficacy of a personalised treatment depending on the characteristics of reflux at multichannel intraluminal impedance-pH monitoring in patients with acid, nonacid and mixed laryngopharyngeal reflux. Clin Otolaryngol 2021; 46:602–613.
- 46. Lechien JR, Allen JE, Barillari MR, et al. Management of laryngopharyngeal reflux around the world: an international study. Laryngoscope 2021; 131: E1589-E1597.
- This study highlights the unawareness of otolaryngologist regarding pH-impedance monitoring.
- Lechien JR, Carroll TL, Allen JE, et al. Impact of subspecialty training on management of laryngopharyngeal reflux: results of a worldwide survey. Eur Arch Otorhinolaryngol 2021; 278:1933–1943.
- DeVore EK, Chan WW, Shin JJ, Carroll TL. Does the reflux symptom index predict increased pharyngeal events on HEMII-pH testing and correlate with general quality of life? J Voice 2021; 35:625-632.
- 49. Kim SI, Jeong SJ, Kwon OE, *et al.* 24-Hour multichannel intraluminal impedance-pH in proton pump inhibitor nonresponders vs responders in patients with laryngopharyngeal reflux. Otolaryngol Head Neck Surg 2022; 166:910-916.
- Jamieson JR, Stein HJ, DeMeester TR, et al. Ambulatory 24-h esophageal pH monitoring: normal values, optimal thresholds, specificity, sensitivity, and reproducibility. Am J Gastroenterol 1992; 87:1102–1111.
- Muderris T, Gokcan MK, Yorulmaz I. The clinical value of pharyngeal pH monitoring using a double-probe, triple-sensor catheter in patients with laryngopharyngeal reflux. Arch Otolaryngol Head Neck Surg 2009; 135:163-167.

- 52. Koufman JA. The otolaryngologic manifestations of gastroesophageal reflux disease (GERD): a clinical investigation of 225 patients using ambulatory 24-h pH monitoring and an experimental investigation of the role of acid and pepsin in the development of laryngeal injury. Laryngoscope 1991; 101 (Pt 2. Suppl 53):1 78.
- Postma GN. Ambulatory pH monitoring methodology. Ann Otol Rhinol Laryngol Suppl 2000; 184:10–14.
- 54. Savarino V, Marabotto E, Zentilin P, *et al.* Pharmacological management of gastro-esophageal reflux disease: an update of the state-of-the-art. Drug Des Dev Ther 2021; 15:1609-1621.

This study summarized the current therapeutic approaches of reflux and their physiological mechanisms.

- 55. de Bortoli N, Gyawali CP, Frazzoni M, et al. Bile reflux in patients with nerd is associated with more severe heartburn and lower values of mean nocturnal baseline impedance and chemical clearance. Neurogastroenterol Motil 2020; 32:e13919.
- 56. Sereg-Bahar M, Jerin A, Jansa R, *et al.* Pepsin and bile acids in saliva in patients with laryngopharyngeal reflux a prospective comparative study. Clin Otolaryngol 2015; 40:234–239.
- De Corso É, Baroni S, Salonna G, et al. Impact of bile acids on the severity of laryngo-pharyngeal reflux. Clin Otolaryngol 2021; 46:189–195.
- 58. Lechien JR, Chan WW, Akst LM, et al. Normative ambulatory reflux monitoring metrics for laryngopharyngeal reflux: a systematic review of 720 healthy individuals. Otolaryngol Head Neck Surg 2021; 166: 802-819

This systematic review summarized the current knowledge about the profile of pH impedance monitoring of healthy and reflux patients.

- Wang AJ, Liang MJ, Jiang AY, et al. Gastroesophageal and laryngopharyngeal reflux detected by 24-h combined impedance and pH monitoring in healthy Chinese volunteers. J Dig Dis 2011; 12:173–180.
- 60. Xiao YL, Liu FQ, Li J, et al. Gastroesophageal and laryngopharyngeal reflux profiles in patients with obstructive sleep apnea/hypopnea syndrome as determined by combined multichannel intraluminal impedance-pH monitoring. Neurogastroenterol Motil 2012; 24:e258-e265.
- Hoppo T, Sanz AF, Nason KS, et al. How much pharyngeal exposure is 'normal'? Normative data for laryngopharyngeal reflux events using hypopharyngeal multichannel intraluminal impedance (HMII). J Gastrointest Surg 2012; 16:16-24; discussion 24-5.
- 62. Desjardin M, Roman S, des Varannes SB, et al. Pharyngeal pH alone is not reliable for the detection of pharyngeal reflux events: a study with oesophageal and pharyngeal pH-impedance monitoring. United Eur Gastroenterol J 2013; 1:438–444.
- Feng G, Wang J, Zhang L, Liu Y. A study to draw a normative database of laryngopharynx pH profile in Chinese. J Neurogastroenterol Motil 2014; 20:347-351.
- 64. Hou C, Chen M, Chen T, et al. Study on laryngopharyngeal and esophageal reflux characteristics using 24-h multichannel intraluminal impedance-pH monitoring in healthy volunteers. Eur Arch Otorhinolaryngol 2020; 277:2801–2811.
- Doo JG, Kim SI, Park JM, et al. Changes in pharyngeal baseline impedance in patients with laryngopharyngeal reflux. Otolaryngol Head Neck Surg 2020; 163:563–568.
- Sun G, Muddana S, Slaughter JC, et al. A new pH catheter for laryngopharyngeal reflux: normal values. Laryngoscope 2009; 119:1639–1643.
- 67. Yadlapati R, Adkins C, Jaiyeola ĎM, et al. Abilities of oropharyngeal pH tests and salivary pepsin analysis to discriminate between asymptomatic volunteers and subjects with symptoms of laryngeal irritation. Clin Gastroenterol Hepatol 2016; 14:535.e2–542.e2.
- Ayazi S, Lipham JC, Hagen JA, et al. A new technique for measurement of pharyngeal pH: normal values and discriminating pH threshold. J Gastrointest Surg 2009; 13:1422–1429.
- Chheda NN, Seybt MW, Schade RR, Postma GN. Normal values for pharyngeal pH monitoring. Ann Otol Rhinol Laryngol 2009; 118:166–171.
- Shay S, Tutuian R, Sifrim D, et al. Twenty-four hour ambulatory simultaneous impedance and pH monitoring: a multicenter report of normal values from 60 healthy volunteers. Am J Gastroenterol 2004; 99:1037–1043.
- Zentilin P, liritano E, Dulbecco P, *et al.* Normal values of 24-h ambulatory intraluminal impedance combined with pH-metry in subjects eating a Mediterranean diet. Dig Liver Dis 2006; 38:226-232.
- **72.** Jetté ME, Gaumnitz EA, Birchall MA, *et al.* Correlation between Reflux and multichannel intraluminal impedance pH monitoring in untreated volunteers. Laryngoscope 2014; 124:2345–2351.
- 73. Kawamura O, Kohata Y, Kawami N, et al. Liquid-containing refluxes and acid refluxes may be less frequent in the Japanese population than in other populations: normal values of 24- hour esophageal impedance and pH monitoring. J Neurogastroenterol Motil 2016; 22:620–629.
- 74. Kim SI, Jeong SJ, Kwon OE, et al. Pharyngeal reflux episodes in patients with suspected laryngopharyngeal reflux versus healthy subjects: a prospective cohort study. Eur Arch Otorhinolaryngol 2021; 278:3387–3392.
- Lechien JR, Bobin F, Muls V, et al. Gastroesophageal reflux in laryngopharyngeal reflux patients: clinical features and therapeutic response. Laryngoscope 2020; 130:E479–E489.

- 76. Sikavi DR, Cai JX, Leung R, et al. Impaired proximal esophageal contractility predicts pharyngeal reflux in patients with laryngopharyngeal reflux symptoms. Clin Transl Gastroenterol 2021; 12:e00408.
- Sikavi DR, Cai JX, Carroll TL, Chan WW. Prevalence and clinical significance of esophageal motility disorders in patients with laryngopharyngeal reflux symptoms. J Gastroenterol Hepatol 2021; 36:2076–2082.
- 78. Lechien JR, Mouawad F, Barillari MR, et al. Treatment of laryngopharyngeal reflux disease: a systematic review. World J Clin Cases 2019; 7:2995–3011.
- Vance D, Park J, Alnouri G, *et al.* Diagnosing laryngopharyngeal reflux: a
  comparison between 24-h pH-Impedance testing and pharyngeal probe (Restech) testing, with introduction of the Sataloff score. J Voice 2021. doi: 10.1016/j.jvoice.2021.04.002.
- This study compared pH-impedance monitoring with oropharyngeal pH monitoring.
  80. Kang HJ, Park JM, Choi SY, et al. Comparison between manual and automated analyses in multichannel intraluminal impedance: pH monitoring for laryngopharyngeal reflux. Otolaryngol Head Neck Surg 2022; 166:128-132.

1068-9508 Copyright © 2022 Wolters Kluwer Health, Inc. All rights reserved.