

# Diagnostic Yield of Prolonged Wireless pH vs 24-hour pH-Impedance Monitoring for Evaluation of Chronic Laryngeal Symptoms



**Swathi Eluri, MD, MSCR**

*Senior Associate Consultant, Mayo Clinic Florida, Jacksonville, FL; and Adjunct Assistant Professor of Medicine, University of North Carolina School of Medicine, Chapel Hill, NC*

Dr Swathi Eluri  
Associate Editor

This summary reviews Krause AJ, Greytak M, Kaizer MA, et al. Diagnostic yield of ambulatory reflux monitoring systems for evaluation of chronic laryngeal symptoms. *Am J Gastroenterol.* 2024 1;119(4):627-634.

Correspondence to Swathi Eluri, MD, MSCR, Associate Editor. Email: [EBGI@gi.org](mailto:EBGI@gi.org)

Keywords: Laryngopharyngeal reflux, GERD, Bravo, 24-hr impedance monitoring

## STRUCTURED ABSTRACT

**Question:** Is the diagnostic yield for abnormal gastroesophageal reflux comparable between ambulatory reflux monitoring systems in patients with chronic laryngeal symptoms?

**Design:** Multicenter, international, cross-sectional study (**Figure 1**).

**Setting:** Five laryngopharyngeal reflux (LPR) referral centers (4 centers in the United States and 1 center in Taiwan) between March 2018-May 2023.

**Patients:** Adult patients with chronic laryngeal symptoms, including cough, globus, dysphonia, throat clearing, and sore throat, who had undergone ambula-

tory reflux monitoring off proton pump inhibitor (PPI) therapy, with or without concomitant esophageal symptoms such as heartburn, regurgitation, or noncardiac chest pain. Patients with prior foregut surgery were excluded.

**Interventions/Exposure:** The intervention was ambulatory reflux monitoring systems in 1 of 2 24-hour pH-impedance monitoring configurations: 1) prolonged wireless single pH capsule (Bravo; Medtronic, Minneapolis, MN) or 2) multichannel intraluminal impedance with a single distal pH catheter (MII-pH) and hypopharyngeal-esophageal multichannel intraluminal impedance-pH (HEMII-pH) (Medtronic or Diversatek Healthcare, Milwaukee, WI).

**Outcome:** The primary outcome was presence or absence of abnormal gastroesophageal reflux (GER+ or GER-) as defined per Lyon consensus criteria. For multichannel intraluminal impedance with a single distal pH catheter, GER+ was total distal esophageal acid exposure time (AET) of at least 6% with esophageal pH < 4.0 and/or at least 80 reflux events/24 hour period. For prolonged wireless reflux monitoring, GER+ was defined as 2 days or more of AET of at least 6% with esophageal pH < 4.0. Those not meeting gastroesophageal reflux disease (GERD) criteria per these definitions were categorized as GER-.

**Data Analysis:** Demographic and clinical data were compared between subjects undergoing 24-hour pH-impedance and wireless monitoring. Secondary analyses were performed to assess diagnostic agreement/disagreement between the 2 pH monitoring systems for the 15 patients who underwent both tests and to compare patients with and without concomitant esophageal symptoms.

**Funding:** National Institutes of Health.

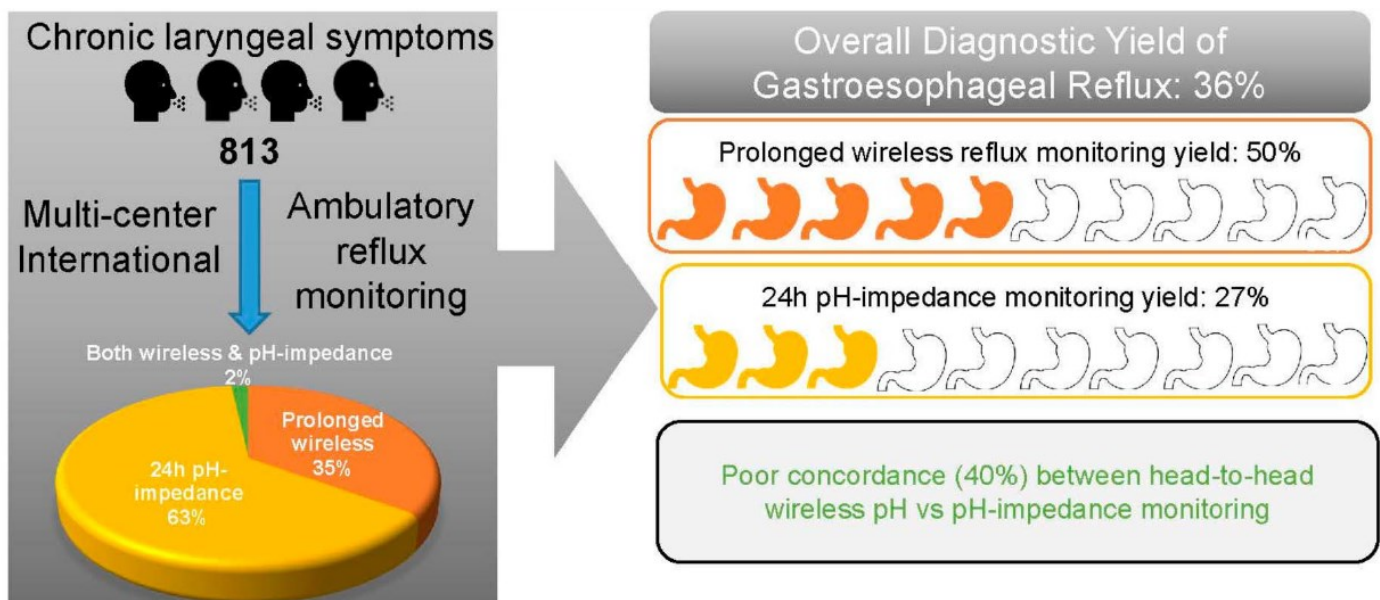
**Results:** Among 813 study patients, demographic data included mean age 53 (SD-16 years); 37% male; 36% with hiatal hernia; 72% with concurrent GERD symptoms (in addition to laryngeal symptoms), and mean body mass index-27. Among study patients, the most common laryngeal symptoms were throat clearing (69%), cough (67%), globus sensation (67%), voice hoarseness (57%), and sore throat (28%). Demographic data were similar between groups getting wireless pH monitoring and 24-hour impedance monitoring except patients getting 24-hour pH impedance monitoring were significantly older (54.0 vs 50.6 years,  $P < 0.01$ ).

Overall, diagnostic yield for GER+ was significantly higher for wireless pH monitoring compared with 24-hour impedance monitoring: 50% (148/296) vs 27%

(145/532);  $P < 0.01$ . Total AET was significantly higher on wireless pH monitoring compared with 24-hour pH-impedance monitoring (6.4% [SD 4.9] vs 3.6% [SD 5.3];  $P < 0.01$ ). The first day of AET on wireless pH monitoring was significantly higher than total AET on 24-hour pH-impedance monitoring (6.7 [SD 6.6] vs 3.6 [SD 5.3],  $P < 0.01$ ), with 45% being GER+ on day 1 of wireless monitoring compared to 20% on 24-hour pH-impedance testing when strictly using the criteria of AET of at least 6%. When adding at least 80 reflux events per 24 hours on pH-impedance testing, the diagnostic yield increased from 20% to 27% for wireless monitoring.

Among the 15 patients who underwent both wireless pH vs 24-hour pH-impedance monitoring, there was diagnostic agreement between studies for only 6 (40%) patients. Among 5 patients with a positive wireless pH monitoring study but negative or inconclusive 24-hour pH-impedance study, AET was abnormal on 2 or more days of wireless pH monitoring.

Only 28% (226/813) of the sample had isolated laryngeal symptoms. For patients with isolated laryngeal symptoms, the diagnostic yield of GER+ remained higher



**Figure 1.** Visual abstract showing the multicenter, international, cross-sectional study.

## COMMENTARY

### *Why Is This Important?*

LPR is a common condition leading to GI referrals. Historically, LPR has been diagnosed based on clinical symptoms of chronic cough, hoarseness, or throat clearing, and most gastroenterologists are quite familiar with patients referred by otolaryngologists who have reported seeing erythema or edema on laryngoscopy among patients with these symptoms and then told patients that their symptoms are due to acid reflux. Two important points should be emphasized here. First, we've known for over 20 years that the inter-rater reliability of this assessment is quite poor (i.e., multiple otolaryngologists can look at the same images of laryngeal folds and provide quite variable assessments about presence or severity of edema and erythema).<sup>1</sup> Second, more than 60% of LPR patients do not have pathologic acid reflux on objective pH monitoring. Therefore, when patients with chronic cough, hoarseness, or throat clearing, etc., but without GERD symptoms are referred for LPR treatment based on laryngoscopic images, we must educate the patient that their symptoms may not be due to acid reflux, especially if they have already failed to improve with PPIs. Given this dilemma, recent guidelines have moved towards endorsing ambulatory reflux monitoring in those with isolated chronic laryngeal symptoms to measure pathologic acid exposure, abnormal reflux events, and correlation between patient symptoms and reflux events. However, it is unclear if

the diagnostic yield between the 2 ambulatory reflux monitoring systems that are available are comparable, specifically in those with chronic laryngeal symptoms. Understanding whether one method of ambulatory pH monitoring provides results that are more diagnostic in this specific population can have significant clinical utility and implications.

### *Key Study Points*

Diagnostic yield for GER+ was significantly higher for wireless pH monitoring compared with 24-hour impedance monitoring: 50% (148/296) vs 27% (145/532);  $P < 0.01$ .

### *Caution*

Given that this study was performed at expert LPR referral centers, there are likely some limitations in the generalizability of these results. Data regarding PPI response is also not available and may have provided some nuances to results regarding the yield between the 2 modalities. Most importantly, when comparing the diagnostic yield of 2 different tests, then all patients should undergo both diagnostic tests and the results should be compared to an appropriate "gold standard." Unfortunately, only a handful of patients had both modalities of testing performed and no potential gold standard that included information about PPI response was provided.



### *My Practice*

In my clinical practice, in those presenting with chronic laryngeal symptoms, I almost always perform upfront pH testing off PPI therapy. However, there may be some situations such as patient preference to not pursue pH testing or lack of access to pH testing that may warrant an empiric trial of acid suppression to see if there is a symptom response. Recent studies have also shown significant response with potassium competitive acid blockers (PCABs) in patients with non-erosive reflux disease,<sup>2</sup> and is a potential alternative in those who have previously failed PPI therapy and do not want to pursue objective pH testing. Alternately an empiric trial with a PCAB as the first line could also be considered, given that it is a more potent acid suppressor than PPIs.

It's surprising that the diagnostic yield for gastroesophageal reflux was so much lower with 24-hour impedance monitoring versus wireless pH monitoring even when just looking at the first 24 hours of results. This is one possible hypothesis: patients undergoing 24-hour pH impedance monitoring may systematically alter their diet and activity leading to fewer reflux events. Certainly, many of our patients undergoing 24-hour pH impedance monitoring report eating smaller meals, being less active, or even sleeping in a semi-recumbent position because of the discomfort associated with having a catheter running from their nostril through their oropharynx and into the esophagus.

Ultimately, these study results will change my practice. Previously, I typically preferred 24-hour pH impedance monitoring over wireless pH monitoring, given the lack of data supporting one testing modality over the other. The reason for this is the ability for the 24-hour pH impedance monitoring to provide information regarding reflux events in the proximal esophagus.<sup>3</sup> However, as outlined in this article, some studies have shown no difference in proximal reflux between those with esophageal symptoms and those with chronic laryngeal symptoms.<sup>4</sup> Data is also limited on the significance of non-acid reflux and distal mean nocturnal baseline impedance (2 parameters with increased diagnostic yield using 24-hour pH impedance testing) in those with extraesophageal and atypical GERD symptoms. Since the findings from this study suggest that wireless pH monitoring is the preferred testing method for GERD in patients with chronic reflux symptoms, I will likely adopt this diagnostic method into my practice when seeing patients with laryngeal symptoms.

### *For Future Research*

Future prospective studies comparing both pH monitoring modalities in a head-to-head manner would be valuable. Further assessment of additional reflux monitoring metrics such as proximal acid exposure and reflux, nonacidic reflux events, and mean nocturnal baseline impedance in patients with chronic laryngeal symptoms will also add to the limited literature in this area and help

guide diagnostic and therapeutic pathways in this group.

### *Conflict of Interest*

No potential conflict of interest

## REFERENCES

1. Branski RC, Bhattacharyya N, Shapiro J. The reliability of the assessment of endoscopic laryngeal findings associated with laryngopharyngeal reflux disease. *Laryngoscope*. 2002;112:1019–1024.
2. Fass R, Vaezi M, Sharma P, et al. Randomised clinical trial: Efficacy and safety of on-demand vonoprazan versus placebo for non-erosive reflux disease. *Aliment Pharmacol Ther*. 2023;58(10):1016-1027.
3. Chen JW, Vela MF, Peterson KA, et al. AGA clinical practice update on the diagnosis and management of extraesophageal gastroesophageal reflux disease: Expert review. *Clin Gastroenterol Hepatol* 2023;21(6):1414–21.e3.
4. Zikos TA, Triadafilopoulos G, Kamal A, et al. Baseline impedance via manometry and ambulatory reflux testing are not equivalent when utilized in the evaluation of potential extraesophageal gastroesophageal reflux disease. *J Thorac Dis* 2020;12(10):5628–38.