

The Accuracy of the Laryngopharyngeal Reflux Diagnosis: Utility of the Stroboscopic Exam

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Abstract

Objective. To determine the prevalence and also accuracy of the laryngopharyngeal reflux (LPR) referring diagnosis and to determine the most useful clinical tool in arriving at the final diagnosis in a tertiary laryngology practice.

Study Design. Case series with planned data collection.

Setting. Six tertiary academic laryngology practices.

Subjects and Methods. We collected referring diagnosis and demographic information, including age, sex, ethnicity, referring physician, and whether or not patients had prior flexible laryngoscopy for 1077 patients presenting with laryngologic complaints from January 2010 and June 2013. Final diagnosis after the referred laryngologist's examination and the key diagnostic test used was then recorded.

Results. Of 1077 patients, 132 had a singular referring diagnosis of LPR. Only 47 of 132 patients (35.6%) had LPR confirmed on final primary diagnosis. Transnasal flexible laryngoscopy confirmed this in 27 of 47 (57.4%) patients. Eighty-five of 132 (64.4%) had a different final diagnosis than LPR. Sixty-five of 85 (76.5%) of these alternative pathologies were diagnosed with the aid of laryngeal stroboscopy.

Conclusions. LPR appears to be an overused diagnosis for laryngologic complaints. For patients who have already had transnasal flexible laryngoscopic exams prior to their referral, laryngeal stroboscopy is the key diagnostic tool in arriving at the correct diagnosis.

Keywords

reflux, laryngopharyngeal reflux, stroboscopy, flexible laryngoscopy

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More than 50% of the patients with hoarseness have been presumed to have reflux-related disease.¹ Laryngopharyngeal reflux (LPR), which is the

reflux of gastric contents into the laryngopharynx, has also been reported in up to 10% of all patients presenting to an otolaryngologist's office.² Because of the prevalence of this disorder, primary care physicians have become comfortable treating LPR without the assistance of the specialist. A recent study showed that 64% of primary care physicians were willing to empirically treat hoarse patients for up to 6 weeks before referring them to a specialist for a more directed examination.^{3,4} However, there is concern that empiric treatment without proper examination may result in missed pathology. The issue is complicated by the fact that there is no pathognomonic symptom(s) or finding(s) for LPR, which makes its initial accurate diagnosis more difficult. Recent studies emphasizing the incorrect diagnosis of laryngopharyngeal reflux among otolaryngologists compared with dedicated laryngologists suggest that laryngeal pathology can be difficult to identify even with direct visualization.^{5,6}

The presumed typical symptoms of LPR consist of excessive throat clearing, cough, hoarseness, and globus pharyngeus, which are very nonspecific and may be caused by a host of other etiologies. The LPR diagnosis can be confirmed by the response of symptoms to empiric behavioral and medical therapy, endoscopic observation of mucosal injury, and demonstration of reflux by impedance and pH monitoring studies.⁷ Failure to respond to a 2- to 3-month

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trial of behavioral change and proton pump inhibitors necessitates the development of a new differential diagnosis and possible use of studies to objectively measure reflux.

Accurate diagnosis of laryngeal pathology improves with more sophisticated visualization as the treatment for various disorders can be vastly different.^{8,9} For example, the hoarse patient may need an oncologic resection for cancer, a microflap excision for a cyst, laser ablation for a polyp, a proton pump inhibitor for reflux, voice therapy for muscle tension dysphonia, or a whole range of other therapies.

The dedicated laryngologist is directly referred patients from many different specialties, including multiple medical specialties and other otolaryngologists. We sought to compare the accuracy of the primary referring diagnosis of LPR from all referring physicians with their final diagnosis. Furthermore, we aimed to determine the specific diagnostic test that was key in determining the correct diagnosis.

Methods

Institutional review board approval was obtained from all study sites. We collected prospective de-identified data comparing referring diagnosis with final diagnosis on all consecutive patients presenting with laryngologic complaints to a total of 6 tertiary laryngology practices. The data collected included referring diagnosis, additional referring diagnosis, referring physician's medical subspecialty, final diagnosis, additional final diagnosis, key diagnostic test and additional key diagnostic test used, and the use of prior laryngoscopy prior to the referral. Other demographic information obtained included age, sex, ethnicity, and study site location.

Further statistical calculations were done on those patients just presenting with a referral of LPR and no other primary or secondary diagnosis. Categorical variables were summarized using frequency tables, and age was summarized using median with interquartile range (IQR). Associations between categorical factors and the diagnosis accuracy were examined using χ^2 tests, while t test was used for age. The sensitivity, specificity, predictive value positive, and predictive value negative were also calculated from a 2-by-2 contingency table to measure the accuracy of diagnosis.

Results

The study yielded 1077 patients over all 6 laryngology practices. Patients' median age was 56.0 years, with an IQR of 43.0 to 68.0. Females were more predominant at 58.2% of the study population. Overall, 74.4% of patients were white, 17.9% African American, and 5.6% Hispanic. The referring physicians sent 132 patients with a referral diagnosis of LPR. **Table 1** describes the study population further.

In this population, 143 patients were referred with a primary diagnosis of LPR, and 9 other patients were referred with an additional diagnosis of LPR; overall, 152 were referred with some type of diagnosis of LPR. In particular, 132 patients presented with a singular referring diagnosis of LPR, which made up 12.3% of referrals, not including those

Table 1. Population Characteristics.^a

Demographic	Value
No. of patients	1077
Age, y	
Median	57
IQR	43.0-68.0
Sex, No. (%)	
Male	450 (41.8)
Female	627 (58.2)
Ethnicity, No. (%)	
White	801 (74.4)
African American	193 (17.9)
Hispanic	60 (5.6)
Other	23 (2.1)
Referral of only LPR, No. (%)	132 (12.3)
Confirmed	47 (35.6)
Refuted	85 (64.4)

IQR, interquartile range; LPR, laryngopharyngeal reflux.

^aThis table describes the total study population.

with other significant pathology. Among these 132 patients, median age was 53.0 years (IQR, 42.0-64.0 years), and 59.1% (78/132) of these patients were female. LPR was confirmed as the primary diagnosis in only 35.6% (47/132) of patients, with 1 more patient secondarily diagnosed with LPR after muscle tension dysphonia (MTD). The different study sites that saw more than 1 patient with LPR varied considerably in their percentage agreeing with the referral diagnosis (0%-66.7%). The other most prevalent final diagnoses that described >5% of this subgroup were MTD, vocal fold polyp/nodules, unilateral vocal fold paresis, sulcus, and bilateral vocal fold atrophy. A complete list of final diagnoses for these patients referred with a singular referral LPR diagnosis can be seen in **Table 2**.

Of the 47 patients who were confirmed to have LPR during their referral, 51.1% (24/47) were female, and the median age was 55.0 years (IQR, 44.0-63.0 years). The referring doctor was most likely to be an otolaryngologist (57.5%, 27/47), followed by a primary care physician (27.7%, 13/47). Twenty-eight of 47 (59.6%) patients had a prior laryngoscopy. Transnasal flexible laryngoscopy (TFL) was the crucial diagnostic test used to confirm LPR in 27 of 47, followed by stroboscopy (8/47) and history (7/47).

Of the 85 patients who had their referral diagnosis of LPR changed, 63.5% (54/85) were female, and the median age was 52.0 years (IQR, 40.0-64.0 years). The referring doctor was most likely to be an otolaryngologist (78.8%, 67/85), followed by a primary care physician (5.9%, 5/85). Seventy-three of 85 patients (85.9%) had a prior laryngoscopy. Stroboscopy was considered the key test to establish the final diagnosis in 76.5% (65/85) patients, followed by TFL (16.5%, 14/85) and history (2.4%, 2/85).

To examine the factors associated with diagnostic accuracy, we compared the group of 47 patients who were

Table 2. Final Diagnosis by Laryngologist of Those Referred With LPR.^a

Final Diagnosis	No. of Patients	% of Total
Laryngopharyngeal reflux	47	35.6
Hyperfunction or MTD	14	10.6
Vocal fold polyp or nodules	13	9.8
Sulcus or scar	12	9.1
Unilateral vocal fold paresis	8	6.1
Bilateral atrophy	6	4.5
Vocal fold cyst or pseudocyst	5	3.8
Dystonia	4	3.0
Other	4	3.0
Reinke's edema	3	2.3
Bilateral vocal fold paresis	3	2.3
Leukoplakia	2	1.5
RRP	2	1.5
Unspecified vocal fold paresis	2	1.5
Central nervous system	1	0.8
Cricopharyngeal dysfunction	1	0.8
Laryngeal neoplasm	1	0.8
No answer	1	0.8
Normal exam	1	0.8
Rheumatologic	1	0.8
Unilateral vocal fold paralysis	1	0.8
Total	132	

LPR, laryngopharyngeal reflux; MTD, muscle tension dysphonia; RRP, recurrent respiratory papillomatosis.

^aBreakdown of final diagnosis when patients were referred for LPR.

confirmed to have LPR during their referral with the group of 85 patients who had their singular referral diagnosis of LPR changed. Neither sex ($P = .17$) nor age ($P = .72$) was significantly associated with diagnostic accuracy. Interestingly, referrals from otolaryngologists were significantly more likely to have their diagnosis changed ($P = .009$), while referrals by primary care physicians were significantly more likely to keep their LPR diagnosis ($P < .001$). In addition, 73 of 85 patients with their singular referral LPR diagnosis changed had a prior laryngoscopy, a significantly higher percentage than the confirmed LPR group ($P < .001$), including 97% (65/67) of those referred by otolaryngologists. Moreover, while stroboscopy was crucial in confirming the diagnosis in some patients due to the lack of other findings, it was much more significantly used in its ability to suggest another diagnosis to the laryngologist ($P < .001$). In addition, stroboscopy was relied on to change the diagnosis in 83.1% (54/65) of the patients referred from another otolaryngologist. Other diagnostic tests used to establish the final diagnosis were history ($n = 2$), laryngeal electromyography (EMG) ($n = 1$), manometry ($n = 1$), direct laryngoscopic examination under general anesthesia ($n = 1$), TFL ($n = 14$), and transnasal esophagoscopy (TNE) ($n = 1$).

Only 12 patients had a non-reflux-related diagnosis that was eventually changed to LPR on the final diagnosis. A

Table 3. Referring Diagnosis in Patients With a Final Diagnosis of Laryngopharyngeal Reflux (LPR).^a

Referral Diagnosis	No. of Patients
Globus	2
Other	2
Sulcus or scar	1
Vocal fold cyst or pseudocyst	1
Vocal fold granuloma	1
Bilateral vocal fold paresis	1
Unilateral vocal fold paresis	1
Vocal fold polyp or nodules	2
Zenker's diverticulum	1
Total	12

^aReferring diagnosis when final diagnosis by the laryngologist was only LPR.

breakdown of referral diagnoses in this group is listed in **Table 3**. Six of 12 of these patients were referred from other otolaryngologists, and 4 of 6 were referred from their primary care physician.

Finally, we investigated the accuracy of the LPR referring diagnosis by summarizing outcomes from all 1077 patients. The referral diagnosis (either primarily or additionally diagnosed with LPR) was compared directly with the final diagnosis (either primary or additional). The sensitivity of the referral diagnosis compared with the laryngologist's final diagnosis was 72.84%, and the specificity was 90.66%. The positive predictive value of the referral diagnosis was 38.82%, and the negative predictive value was 97.62%.

Discussion

Laryngopharyngeal reflux is one of the most commonly made diagnoses for patients with a wide array of general laryngologic complaints. The most common symptoms that these patients possess are hoarseness, globus pharyngeus, dysphagia, cough, chronic throat clearing, and sore throat.¹⁰ Diagnosis of LPR is often made based on symptoms/laryngeal findings along with response to empiric treatment, but the gold standard consists of 24-hour double-probe pH monitoring. However, physical exam findings are not always helpful as limited evidence has been found for each mucosal finding in LPR.¹¹ Pseudosulcus vocalis, ventricular obliteration, and granulomas have been shown in some studies to be more associated with proven pharyngeal reflux. In addition, in those symptomatic from LPR, pseudosulcus vocalis, interarytenoid thickening, and Reinke's edema have been more prevalent. Due to the paucity of objective laryngeal findings and the nonspecific symptoms, it is not hard to imagine discrepancy in the diagnosis of LPR.

One very interesting finding in the study was the high rate at which the referral laryngologist disagreed with a referring otolaryngologist who had already performed a TFL. One possible explanation is the amount of experience in visualizing subtle laryngeal findings. In addition, laryngologists at tertiary

centers tend to have higher resolution distal chip flexible laryngoscopes and rigid laryngoscopes combined with stroboscopy that provide for enhanced image quality over that seen in the typical otolaryngologist's office. Finally, general otolaryngologists could also have a higher rate of non-LPR diagnoses because they referred their patients after first treating for LPR and did not notice symptoms or laryngeal findings improving in a presentation that was atypical, in comparison to primary care physicians who would refer based off of symptoms alone.

LPR and gastroesophageal reflux disease (GERD) have been shown to be commonly interlinked. The diagnosis of GERD relies on a combination of objective testing with endoscopy, ambulatory reflux monitoring, response to anti-secretory therapy, and symptom presentation.¹² In a population of patients with endoscopically proven GERD, the prevalence of LPR symptoms reported on a questionnaire correlated significantly with the severity of GERD findings.¹³ However, that study did not examine the larynx as part of their protocol.

Primary care providers have been found on previous surveys to empirically treat their patients with dysphonia for greater than 6 weeks, with 85% giving a reflux medication and 54.2% giving an antihistamine.⁴ The biggest risk of delayed referral to the laryngologist consists of a delay in the diagnosis and treatment of laryngeal cancer or precancerous lesions such as leukoplakia. Our study showed roughly 2% of patients originally thought to have LPR had leukoplakia, and only 1% had an actual neoplasm on the vocal folds. A much larger percentage of patients had a benign mucosal lesion (18%), vocal fold paresis/paralysis (11%), or MTD (11%). All of these disorders require additional therapy and do not benefit from the use of proton pump inhibitors. In a similar study at a single institution that looked at laryngeal pathology in those patients originally diagnosed with LPR, they found that benign mucosal lesions, vocal fold paresis, and MTD made up 29%, 29%, and 14% of these patients, respectively.⁵ These patients therefore would not necessarily get any clinical benefit from treatment of LPR.

In a 2009 Clinical Practice Guideline on hoarseness, the panel recommended that a clinician not prescribe antireflux medications for patients with hoarseness without signs or symptoms of GERD.¹⁴ The panel only offered an option of prescribing antireflux medication for patients with hoarseness along with signs of chronic laryngitis. In light of these guidelines and the findings of our study, a patient with hoarseness without symptoms of GERD and those with significant quality-of-life changes from their voice should be referred to a specialist for visualization of their larynx.

A recent study of 259 patients presenting with complaints of hoarseness to a laryngologist had similar findings to our study.¹⁵ They found that patients most likely to have their diagnosis modified were those initially diagnosed with edema, LPR, infection or allergy, MTD, and behavioral disorders. In addition, the diagnoses of scar, sulcus, atrophy, and paresis were more likely to be overlooked on the initial referring diagnosis.

Table 4. Percentage of Patients With Laryngopharyngeal Reflux (LPR) Confirmed on Their Final Diagnosis per Study Site.^a

Study Site	No. of LPR Confirmed Patients	Total No. of LPR Referred Patients	% Confirmed LPR
1	1	1	100
2	17	29	58.6
3	18	70	25.7
4	0	13	0
5	7	13	53.8
6	4	6	66.7
Total	47	132	35.6

^aThis table describes the different study sites and their number and rate of confirmation for referred cases with singular LPR diagnosis.

In another recent national database study looking at the change in diagnosis codes following stroboscopic exams and treatment differences following the referral to a laryngologist, chronic laryngitis was changed to another diagnosis 56.4% of the time for 436 patients.¹⁶ Proton pump inhibitor use, a surrogate marker for LPR prevalence, was discontinued in 44.5% of patients who were taking it and started in 23.9% of patients who had not been taking it. All patients in their study received a stroboscopic exam within 90 days of a flexible laryngoscopic exam, which served as the study's definition of a specialty voice evaluation.

In 1991, Sataloff et al¹⁷ described the usefulness of the stroboscopic exam in the evaluation of professional voice patients. In 377 stroboscopies of the larynx, 18% of the time it changed their preprocedure diagnosis, and 47% of the time it modified the diagnosis. The next year in 1992, Casiano et al¹⁸ corroborated the findings and showed that the use of stroboscopy was able to change their primary diagnosis in 19% of their patients who had already received a full otolaryngologic examination. While our study collected data on the use of prior laryngoscopy, the previous use of stroboscopy was not obtained. However, stroboscopy has been validated in other studies in its ability to assist in the diagnosis of difficult pathologies before operative evaluation such as sulcus vocalis, submucosal cysts, and pseudocysts.¹⁹ In our study, stroboscopy was critical in the diagnosis in 8 of the confirmed 47 LPR cases, whereas it was critical in finding another pathology in 65 of the 85 patients with another final diagnosis that was not LPR. Thus, stroboscopy appears to be invaluable in its ability to identify other pathology when LPR is suggested as the referral diagnosis.

Our study has several limitations. While the diagnosis was recorded as well as the diagnostic test used, no objective information was recorded in terms of examination or study findings to more objectively classify patients with LPR. In addition, no method was used to establish interrater reliability for diagnosis across institutions. As such, there was a wide range of LPR confirmation on tertiary referral, ranging from 0% to 100% (Table 4 and Table 5). In

Table 5. Percentage of Patients With LPR Confirmed on Their Final Diagnosis per Study Site (ENT vs Primary Care).^a

Study Site	ENT			Primary Care		
	No. of LPR Confirmed	Total No. of LPR Referred	% Confirmed LPR	No. of LPR Confirmed	Total No. of LPR Referred	% Confirmed LPR
1	1	1	100.0	0	0	NA
2	6	11	54.5	10	13	76.9
3	13	56	23.2	1	3	33.3
4	0	12	0.0	0	0	NA
5	5	11	45.5	0	0	NA
6	2	3	66.7	2	2	100.0
Total	27	94	28.7	13	18	72.2

ENT, ear, nose, and throat; LPR, laryngopharyngeal reflux; NA, not applicable.

^aThis table shows those patients who had their singular referral diagnosis of LPR confirmed compared between otolaryngologists and primary care referrers.

addition, while the symptoms of LPR typically resolve with treatment in 2 to 3 months and the laryngoscopic findings abate around 6 months, it is still possible that the referred patient could have already improved with therapy for LPR before being seen by the laryngologist. On top of that, our study fails to catch all of the patients who were successfully treated with empiric LPR therapy and never even reached the attention of a laryngologist. Finally, prior stroboscopy was not recorded, which would have been able to yield some information as to the utilization rate and effectiveness of the technology in other otolaryngologists' offices.

Laryngopharyngeal reflux has been shown to be a common diagnosis in the laryngologist's practice and makes up a considerable portion of referring diagnoses from primary care providers as well as other otolaryngologists. However, this diagnosis appears to be overused even when patients have been seen by an otolaryngologist before and have had a flexible laryngoscopic examination of their larynx. The careful use of stroboscopy can help visualize other pathologies mimicking the common symptoms attributed to LPR. Therefore, patients nonresponsive to antireflux therapy should warrant a timely referral for direct visualization of their larynx, which should include stroboscopy.

Author Contributions

Mark A. Fritz, analysis, interpretation, drafting, final approval; **Michael J. Persky**, analysis, interpretation, drafting, final approval; **Yixin Fang**, analysis, interpretation, drafting, final approval; **C. Blake Simpson**, concept, acquisition, interpretation, drafting, final approval; **Milan R. Amin**, concept, acquisition, interpretation, drafting, final approval; **Lee M. Akst**, concept, acquisition, interpretation, drafting, final approval; **Gregory N. Postma**, concept, acquisition, interpretation, drafting, final approval.

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