Original Article

The Utility of the Reflux Symptom Index for Diagnosis of Laryngopharyngeal Reflux in an Allergy Patient Population

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What is already known about this topic? Supraesophageal reflux disease (SERD)/laryngopharyngeal reflux (LPR) contributes to upper airway symptoms such as coughing, nonallergic rhinitis, postnasal drip, and asthma. The Reflux Symptom Index (RSI) is a tool used to determine the likelihood of SERD.

What does this article add to our knowledge? We show that an RSI score of 19 (as opposed to the original 13) better distinguishes SERD-related symptoms from other respiratory symptoms in an Allergy practice.

How does this study impact current management guidelines? The RSI is a simple tool that can be used easily in an allergy practice to aid in the diagnosis of SERD, and an abbreviated RSI may be even more appropriate.

BACKGROUND: Laryngopharyngeal reflux (LPR) is associated with asthma, vocal cord dysfunction, cough, postnasal drainage, and throat irritation. The Reflux Symptom Index (RSI) is a clinical tool to predict the presence of LPR, but a threshold RSI score has never been validated for the diagnosis of LPR in an allergic patient population.

OBJECTIVE: To identify the optimal threshold RSI score predictive of LPR in an allergy clinic population.

METHODS: The 9-question RSI questionnaire was administered to 84 patients in the Kaiser Permanente San Diego Allergy Department. The patient's allergist (who was blinded to the patient's RSI responses) was asked to determine whether the patient had symptoms consistent with LPR. Each subject's RSI score was then compared with a corresponding physician-based diagnosis. After determining the correlation between the subject's RSI score and physician-diagnosed LPR/supraesophageal reflux, a cutoff level above which LPR/supraesophageal reflux would be highly suspected was calculated on the basis of most optimal balance of sensitivity and specificity determined via a receiver-operating curve analysis.

RESULTS: Thirty of the 84 patients (36%) were diagnosed with LPR. The mean RSI score for the group without LPR was 18.3 ± 9.8 (out of 45 possible), while the LPR group's mean was 25.0 ± 8.3 ($P < .01$). The optimal RSI score cutoff was determined to be 19. An abbreviated questionnaire was also generated using 6 of the RSI questions found to be significantly different between patients with and without LPR.

CONCLUSIONS: An RSI score of 19 appears to represent the best threshold for predicting LPR in an allergy clinic patient population. © 2017 American Academy of Allergy, Asthma & Immunology (J Allergy Clin Immunol Pract 2017;■:■-■)

Key words: *GERD; Laryngopharyngeal reflux (LPR); Nonallergic rhinitis; Proton pump inhibitors; H2 blocker; Head-of-bed elevation; Reflux Symptom Index score*

BACKGROUND

Laryngopharyngeal reflux (LPR), also known as supraesophageal reflux (SERD), refers to the extraesophageal signs and symptoms that can develop from gastroesophageal reflux disease (GERD).[1,2] The pathophysiology involves reflux of gastric acidic and nonacidic components into the larynx and pharynx by traversing proximal to the upper esophageal sphincter.[3,4] LPR has been associated with various symptoms and conditions in the upper and lower respiratory tract, including asthma, vocal cord dysfunction, cough, postnasal drainage, and sinusitis.[3,5-8] In fact, the severity of LPR has been linked to the presence of asthma, and the presence of LPR has been demonstrated to correlate with difficult-to-treat asthma in children.[8,9]

The diagnosis of LPR may be made clinically on the basis of common signs and symptoms of the disease. However, confirmation of the diagnosis can also be made by demonstrating a positive response to empiric use of proton pump inhibitors (PPIs) or via overnight pH probe monitoring.[1,3] In addition, laryngoscopy has been used to both aid diagnosis and monitor response to therapy using a scoring system called the reflux finding score (RFS).[10,11] Treatment includes PPI therapy and/or

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Conflicts of interest: The authors declare that they have no relevant conflicts of interest.

Received for publication December 23, 2016; revised April 17, 2017; accepted for publication April 20, 2017.
Available online ■■

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2213-2198

http://dx.doi.org/10.1016/j.jaip.2017.04.039

Abbreviations used
AUC- area under the curve
GERD- gastroesophageal reflux disease
LPR- laryngopharyngeal reflux
PPI- proton pump inhibitor
RFS- reflux finding score
ROC- receiver-operating curve
RSI- Reflux Symptoms Index
SERD- supraesophageal reflux

head-of-bed elevation to prevent the reflux of both acidic and nonacidic gastric components.[3] Furthermore, surgical intervention with fundoplication has been used to address LPR refractory to antisecretory agents.[12]

It is important to note that SERD and GERD are technically different entities in terms of pathogenesis. GERD is the result of a reduction in lower esophageal sphincter pressure ("incompetent lower esophageal sphincter"). Patients with pure SERD have a normal lower esophageal sphincter but an incompetent upper esophageal sphincter. Patients with 2 incompetent sphincters have both GERD and SERD symptoms. This is an important distinction because symptoms of SERD and GERD have been shown to be different, and in particular SERD has fewer heartburn and more regurgitation symptoms.[13] SERD symptoms are typically extraesophageal and thus in the respiratory tract. This is also important because testing for SERD versus GERD differs in some very important ways, not the least of which is the placement/location of pH probes to record low pH events (proximally for SERD and distally for GERD). Several studies raise the point that testing for SERD has been controversial because low pH events above the upper esophageal sphincter (for SERD) have not always correlated with events recorded more distally[14,15] in such a way that some patients can fulfill SERD criteria without fulfilling GERD criteria (and vice versa).[16] Some of this may be due to variability in cutoff levels for when a significant pH event is reached (pH < 4 at the upper esophageal sphincter is generally used as the standard), and studies are ongoing to determine what the best cutoff is to detect SERD more accurately.[17] In addition, another factor may be the use of pH probes that do not have the ability to test for impedance and thus will miss alkaline reflux events of gastric contents that could similarly irritate the oropharyngeal tissue and cause symptoms.[14] These tissues lack the buffering capacity of the esophagus as well as the peristaltic activity and thus are injured at lower levels of acid and nonacidic reflux than the esophagus.

In 2002, Belafsky et al[18] introduced the Reflux Symptom Index (RSI) as a clinical tool to document improvement in LPR symptoms after therapy. The RSI has subsequently been used in numerous studies to both monitor responses to therapy and confirm diagnosis of LPR in various patient populations.[8,19-25] An RSI score of more than 13 has commonly been considered to be positive for LPR in many of these published studies.[19-22] Correlation between the RSI score and pH monitoring has been previously demonstrated for the diagnosis of LPR.[26] In addition, the RSI has been validated against the RFS and been shown to correlate nicely with only about 5% of patients having a positive RSI (>13) but a negative RFS (<7), making it a very attractive in-office tool for use in diagnosing SERD/LPR.[21] Taken together, the RSI holds promise as a simple, quick, and noninvasive tool to confirm a physician's initial clinical suspicion of SERD/LPR based on clinical history. Because allergists see many patients who have suspected SERD/LPR, we believe this would be an especially useful diagnostic modality for use in an allergist's office.

However, to our knowledge, there has never been a study that has validated an RSI score of more than 13 as reflecting a diagnosis of LPR for use in an allergy patient population. Because of the overlapping symptomatology seen in atopic patients and those with LPR, it is our hypothesis that an RSI score of more than 13 would likely not be accurate for the diagnosis of LPR in this clinical environment. Thus, the purpose of this study was to examine the role of the RSI in an adult allergy patient population, attempting to establish a score that might better predict SERD/LPR in this unique setting.

METHODS

Study design

After approval was obtained from the Kaiser Permanente Southern California Institutional Review Board, adult patients 18 years and older being seen in the Kaiser San Diego Allergy Department were screened for signs of any respiratory disease (including chronic postnasal drip, sensation of mucus in the throat, throat clearing, cough, hoarseness, nasopharyngitis, and/or asthma). Patients with these symptoms were asked to participate in the study, and those who agreed completed the RSI, which is a questionnaire consisting of 9 questions originally designed by Belafsky et al.[18] The survey instructed the patients to rate how specific symptoms affected them within the past month on a scale of 0 to 5, with 0 being no problem and 5 being a severe problem. The scores could range from 0 to 45, with higher scores indicating more symptoms of greater severity. The symptoms listed were as follows: hoarseness; clearing your throat; excess throat mucus or postnasal drip; difficulty swallowing foods, liquids, or pills; coughing after you ate or after lying down; breathing difficulties or choking episodes; troublesome or annoying cough; sensations of something sticking in your throat or a lump in your throat; and heartburn, chest pain, indigestion, or stomach acid coming up.

During the patient's clinic visit, the patient's allergist (who was blinded to the patient's responses to the RSI) was instructed to complete a separate questionnaire that asked if he or she believed the patient had symptoms consistent with SERD/LPR. The questionnaire also inquired whether the patient was currently on a PPI or H2 blocker, whether the patient was tested for allergies, and whether medication was prescribed or behavior modification was recommended. Finally, the allergist was asked whether the patient had asthma, allergic rhinitis, nonallergic rhinitis, or sinusitis.

Continuous variables (age, RSI score) were compared using the Wilcoxon rank sum test, and categorical variables (sex and acid medication status) were compared using the chi-square test. The Wilcoxon test was also used to compare RSI scores between those treated with acid suppression medications versus those who were not, and to compare RSI scores in males versus females. The effect of age on the RSI score was examined using simple linear regression. The relationship between the RSI score and physician-diagnosed SERD/LPR was determined using the Wilcoxon test to compare score distributions for each question between LPR versus non-LPR. The Cochran Armitage trend test was used to determine whether there was a "dose relationship" between the severity of the symptoms found on the RSI questionnaire (0-5 scores) and its relationship to LPR versus non-LPR status. Receiver-operating curve (ROC) analysis was used to determine the optimal combination of sensitivity