

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 2018;6:132-8)

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 June 9, 2017.

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2213-2198

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<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 al¹⁸ 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

TABLE I. Demographic characteristics

Characteristic	Non-LPR (n = 54 [64%])	LPR (n = 30 [36%])	Total (n = 84 [100%])	P value
RSI Score				<.01
Mean $\pm$ SD	18.3 $\pm$ 9.8	25.0 $\pm$ 8.3	20.7 $\pm$ 9.8	
Median	17	25	20	
Q1, Q3	11.0, 25.0	20.0, 32.0	13.5, 28.0	
Range	1.0-41.0	4.0-38.0	1.0-41.0	
Age (y)				.48
Mean $\pm$ SD	52.9 $\pm$ 17.9	56.0 $\pm$ 16.1	54.0 $\pm$ 17.3	
Median	56.5	60	57.5	
Q1, Q3	39.0, 68.0	42.0, 70.0	40.5, 68.5	
Range	19.0-85.0	27.0-80.0	19.0-85.0	
Sex, n (%)				.73
Female	34 (63)	20 (66.7)	54 (64.3)	
Male	20 (37)	10 (33.3)	30 (35.7)	
Asthma				.23
n (%)	36 (66.7)	16 (53.3)	52 (61.9)	
RSI score mean $\pm$ SD	19.6 $\pm$ 9.8	26.3 $\pm$ 6.8	21.6 $\pm$ 9.5	
Allergic rhinitis				.06
n (%)	35 (64.8)	13 (43.3)	48 (57.1)	
RSI score mean $\pm$ SD	17.3 $\pm$ 9.3	24.5 $\pm$ 9.3	19.3 $\pm$ 9.7	
Nonallergic rhinitis				.02
n (%)	16 (29.6)	17 (56.7)	33 (39.3)	
RSI score mean $\pm$ SD	17.8 $\pm$ 10.2	26.8 $\pm$ 7.6	22.4 $\pm$ 9.9	
Sinusitis				.86
n (%)	19 (35.2)	10 (33.3)	29 (34.5)	
RSI score mean $\pm$ SD	19.5 $\pm$ 10.6	25.3 $\pm$ 7.7	21.5 $\pm$ 10	

Bold values indicate statistical significance ($P < .05$).

and specificity of the questionnaire. Cronbach alpha was used to estimate internal consistency reliability of questionnaire.

RESULTS

Eighty-four patients were enrolled, of whom 30 (36%) were determined to have LPR by the allergist and 54 (64%) were determined to not have LPR. Patients with and without LPR were not significantly different regarding age or sex (Table I). Patients without LPR had a mean RSI score of 18.3 ± 9.8 and a median of 17 (interquartile range, 11.0-25.0), whereas patients with LPR had a mean RSI score of 25.0 ± 8.3 and a median of 25 (interquartile range, 20.0-32.0) ($P < .01$; Table I). Interestingly, RSI scores were not related to the use of PPIs/H2 blockers, age, or sex (see Tables E1-E3 in this article's Online Repository at www.jaci-inpractice.org). Five total allergists were included in the study, but the vast majority of the patients were seen by 2 of the allergists. Out of the 84 total patients, 62 were seen by Allergist A and 16 were seen by Allergist B. For Allergist A, 22 out of 62 patients were diagnosed with LPR (35%), whereas for Allergist B, 5 out of 16 patients were diagnosed with LPR (31%).

The RSI scores were also examined to see whether the distribution of responses to individual questions was related to physician-diagnosed LPR (Table II). This analysis revealed that 6 of the 9 questions were significantly different between the groups with and without LPR: hoarseness, throat clearing, throat mucus/postnasal drip, coughing after eating or lying down, sensations of something sticking in the throat/lump in the throat, and heartburn/chest pain/indigestion/stomach acid coming up. Questions addressing difficulty swallowing,

breathing difficulties/choking episodes, and troublesome cough were not significantly different between the groups.

Sensitivity and specificity of various cutoff values for the RSI score to identify allergist-diagnosed LPR were determined using an ROC analysis (Table III). The greatest area under the curve (AUC) value matched with an RSI score of 19, which corresponded to an AUC of 0.694, a sensitivity of 0.8333, a specificity of 0.5556, and a positive predictive value of 0.5102. Thus, a score of 19 on the RSI appeared to be the most appropriate minimum score predictive of LPR in this allergy patient population. Of note, the 95% sensitivity rate corresponded to a score of 13 and the 95% specificity rate corresponded to a score of 38.

Because several questions in the RSI did not appear to discriminate between LPR and no LPR in our cohort, the data were reanalyzed to include only those 6 RSI questions that showed significant differences between patients with and without LPR. In this follow-up analysis (with a total possible score of 30 instead of 45), the mean RSI score of the group without LPR was 12.7, while the mean score for the LPR group was 18.4 ($P < .01$). The ROC analysis (see Table E4 in this article's Online Repository at www.jaci-inpractice.org) determined that a cutoff of 15 gave the highest AUC with the abbreviated questionnaire. With 15 or more as a predictor for LPR in the abbreviated questionnaire, we improved the specificity from 0.56 to 0.69 and the positive predictive value from 0.51 to 0.56. Sensitivity was reduced though from 0.83 to 0.73.

Finally, a Cronbach alpha was used to test the internal consistency reliability for both the original RSI data and the abbreviated RSI version, with values of 0.82 and 0.76, respectively.

TABLE II. RSI score by individual question

Question	Non-LPR (n = 54 [64%])	LPR (n = 30 [36%])	Total (n = 84 [100%])	P value
Q1: Hoarseness				.04
0	22 (40.7)	6 (20)	28 (33.3)	
1	6 (11.1)	1 (3.3)	7 (8.3)	
2	9 (16.7)	6 (20)	15 (17.9)	
3	7 (13)	11 (36.7)	18 (21.4)	
4	3 (5.6)	3 (10)	6 (7.1)	
5	7 (13)	3 (10)	10 (11.9)	
Q2: Throat clearing				.01
0	6 (11.1)	0 (0)	6 (7.1)	
1	9 (16.7)	2 (6.7)	11 (13.1)	
2	10 (18.5)	2 (6.7)	12 (14.3)	
3	7 (13)	10 (33.3)	17 (20.2)	
4	12 (22.2)	8 (26.7)	20 (23.8)	
5	10 (18.5)	8 (26.7)	18 (21.4)	
Q3: Throat mucus or postnasal drip				.01
0	7 (13)	1 (3.3)	8 (9.5)	
1	1 (1.9)	0 (0)	1 (1.2)	
2	7 (13)	1 (3.3)	8 (9.5)	
3	14 (25.9)	7 (23.3)	21 (25)	
4	10 (18.5)	7 (23.3)	17 (20.2)	
5	15 (27.8)	14 (46.7)	29 (34.5)	
Q4: Difficulty swallowing				.52
0	24 (44.4)	10 (33.3)	34 (40.5)	
1	9 (16.7)	8 (26.7)	17 (20.2)	
2	8 (14.8)	7 (23.3)	15 (17.9)	
3	8 (14.8)	4 (13.3)	12 (14.3)	
4	5 (9.3)	1 (3.3)	6 (7.1)	
5	0	0	0	
Q5: Coughing after eating or lying				.02
0	21 (38.9)	5 (16.7)	26 (31)	
1	7 (13)	6 (20)	13 (15.5)	
2	9 (16.7)	3 (10)	12 (14.3)	
3	4 (7.4)	4 (13.3)	8 (9.5)	
4	7 (13)	5 (16.7)	12 (14.3)	
5	6 (11.1)	7 (23.3)	13 (15.5)	
Q6: Breathing issues, choking				.21
0	20 (37)	7 (23.3)	27 (32.1)	
1	8 (14.8)	3 (10)	11 (13.1)	
2	5 (9.3)	6 (20)	11 (13.1)	
3	8 (14.8)	7 (23.3)	15 (17.9)	
4	7 (13)	5 (16.7)	12 (14.3)	
5	6 (11.1)	2 (6.7)	8 (9.5)	
Q7: Troublesome cough				.08
0	12 (22.2)	4 (13.3)	16 (19)	
1	8 (14.8)	2 (6.7)	10 (11.9)	
2	6 (11.1)	5 (16.7)	11 (13.1)	
3	10 (18.5)	3 (10)	13 (15.5)	
4	4 (7.4)	7 (23.3)	11 (13.1)	
5	14 (25.9)	9 (30)	23 (27.4)	
Q8: Sensation of throat stuck, lump				.01
0	17 (31.5)	4 (13.3)	21 (25)	
1	8 (14.8)	4 (13.3)	12 (14.3)	
2	9 (16.7)	4 (13.3)	13 (15.5)	
3	12 (22.2)	6 (20)	18 (21.4)	
4	4 (7.4)	6 (20)	10 (11.9)	
5	4 (7.4)	6 (20)	10 (11.9)	

(continued)

TABLE II. (Continued)

Question	Non-LPR (n = 54 [64%])	LPR (n = 30 [36%])	Total (n = 84 [100%])	P value
Q9: Heartburn, chest pain, indigestion				<.01
0	21 (38.9)	3 (10)	24 (28.6)	
1	10 (18.5)	4 (13.3)	14 (16.7)	
2	8 (14.8)	7 (23.3)	15 (17.9)	
3	7 (13)	2 (6.7)	9 (10.7)	
4	7 (13)	6 (20)	13 (15.5)	
5	1 (1.9)	8 (26.7)	9 (10.7)	

Values are n (%). Bold values indicate statistical significance ($P < .05$).

TABLE III. ROC analysis

RSI Score cutoff	AUC	Sensitivity	Specificity	PPV
3	0.509	1	0.0185	0.3614
4	0.519	1	0.037	0.3659
6	0.502	0.9667	0.037	0.358
7	0.539	0.9667	0.1111	0.3766
8	0.548	0.9667	0.1296	0.3816
9	0.557	0.9667	0.1481	0.3867
10	0.594	0.9667	0.2222	0.4085
11	0.604	0.9667	0.2407	0.4143
12	0.622	0.9667	0.2778	0.4265
13	0.631	0.9667	0.2963	0.4328
14	0.617	0.9	0.3333	0.4286
15	0.639	0.8333	0.4444	0.4545
16	0.648	0.8333	0.463	0.463
17	0.657	0.8333	0.4815	0.4717
18	0.676	0.8333	0.5185	0.4902
19	0.694	0.8333	0.5556	0.5102
20	0.689	0.7667	0.6111	0.5227
21	0.639	0.6667	0.6111	0.4878
22	0.641	0.6333	0.6481	0.5
23	0.643	0.6	0.6852	0.5143
24	0.652	0.6	0.7037	0.5294
25	0.635	0.5667	0.7037	0.5152
26	0.613	0.4667	0.7593	0.5185
27	0.631	0.4667	0.7963	0.56
28	0.659	0.4667	0.8519	0.6364
29	0.652	0.4333	0.8704	0.65
30	0.635	0.4	0.8704	0.6316
31	0.619	0.3667	0.8704	0.6111
32	0.594	0.3	0.8889	0.6
33	0.544	0.2	0.8889	0.5
34	0.506	0.1	0.8889	0.3333
35	0.504	0.1	0.9074	0.375
36	0.513	0.0667	0.9074	0.2857
37	0.52	0.0333	0.9259	0.2
38	0.502	0.0333	0.963	0.3333
41	0.509	0	0.9815	0

PPV, Positive predictive value.

DISCUSSION

The results of this study suggest that an RSI score of 19 likely represents the appropriate minimum predictive score for LPR in an allergy patient population. This is important, because a score

of more than 13 is commonly used in the medical literature to be indicative of LPR in various clinical settings and would result in much less specificity (Table E4).¹⁹⁻²² To our knowledge, no study has previously been performed to validate the scoring threshold of the RSI in regard to predicting the presence of LPR in an allergy patient population.

There are some possible explanations for the discrepancy between this study's scoring threshold and the commonly used cutoff. The most likely reason is that many of the questions on the RSI address symptoms that are commonly found in allergy clinic patients, regardless of whether or not they carry the diagnosis of LPR. Thus, it should not be surprising that an allergy patient population would score higher on the RSI at baseline when compared with a nonallergy patient population. It is also possible that the commonly used cutoff score requires further validation, which we went on to perform using a different statistical approach.

The RSI score of 19 was chosen because it corresponded to the best balance of sensitivity and specificity based on the ROC analysis. Using a cutoff of 19 on the RSI score yielded a sensitivity of 0.8333 and a specificity of 0.5556 with a positive predictive value of 0.5102. We believe that this represents a significant step forward toward improving accuracy when diagnosing LPR in an allergy patient population. Because symptoms of LPR can be easily confused (or overlap with) symptoms from other conditions such as asthma and allergic rhinitis, having a screening test that allows allergy physicians to more accurately diagnose LPR would be a very useful tool. This is especially true given current concerns regarding the adverse effects of PPIs.^{5,27} These efforts will hopefully help improve diagnostic accuracy, increase the ease of the diagnostic process, expedite the initiation of therapy, and avoid unnecessary interventions.

We did not observe a relationship between RSI score and age, sex, or any of the respiratory diagnoses made (other than nonallergic rhinitis). This may suggest that the RSI should be equally useful in patients of varying ages, sexes, and with varying respiratory diagnoses (asthma, allergic rhinitis, sinusitis), but additional (larger) studies may be needed to clarify this observation. Concurrent diagnoses of asthma and sinusitis also did not appear to affect RSI scoring (Table I). In addition, it is interesting to note that the baseline use of PPIs/H2 blockers did not have a significant effect on RSI scoring in this study. This is somewhat unexpected considering that previous studies have shown improvement in RSI scores with PPI therapy.^{18,28} One explanation is that the patients being seen for these symptoms in our specialty clinic may have already failed to respond to these therapies, especially to H2 blocker

treatment. Another explanation may be that nonacidic reflux plays a larger role in SERD/LPR symptoms than previously thought, which might cause a physician to implement head-of-bed elevation as the next modality of therapy in patients with a high RSI score.

This study revealed that 6 of the 9 RSI questions achieve statistical significance when attempting to predict the presence of LPR. These 6 questions that did achieve statistical significance (addressing hoarseness, throat clearing, throat mucus/postnasal drip, coughing after eating or lying down, sensations of something sticking in the throat/lump in the throat, and heartburn/chest pain/indigestion/stomach acid coming up) were then incorporated into an abbreviated questionnaire that did not include the 3 nonsignificant questions. The abbreviated questionnaire would increase the ease of administration (given that there are fewer questions to answer) and provide increased specificity (0.6852 vs 0.5556 when compared with the full RSI). However, the AUC for the proposed cutoff score was only marginally improved (0.7093 vs 0.694 for the full RSI) and the sensitivity was somewhat reduced (0.7333 vs 0.8333 with the full RSI). Of note, the Cronbach alpha computed for both versions demonstrated good internal consistency reliability.

We acknowledge that a major limitation of this study is the use of the allergist's clinical diagnosis to compare to the individual subject's RSI score. It is possible that using a different diagnostic standard such as pH probe testing or laryngoscopy, rather than the clinical diagnosis alone, could affect some of these metrics. However, we do suggest that the similar rates of LPR diagnosis between this study's 2 main allergists (35% and 31%, respectively) and the overall study LPR diagnosis rate of 36% strengthen the validity of these data. The reality is that there is no true "criterion standard" method of diagnosing SERD/LPR.²⁹ A recent study found that upper esophageal pH probe monitoring could not predict improvement in RSI scores following PPI therapy,³⁰ while yet another study used pharyngeal impedance monitoring and found that RFS scores do not correlate well with proximal acid exposures (interestingly the RSI score correlated better).³¹ Taken together, there is no ideal "confirmatory" evaluation that could definitively corroborate the individual RSI scores obtained from our subjects. In the setting of a typical allergist's office, the diagnosis of SERD/LPR is made clinically on the basis of patient's symptoms. The value of the RSI in this clinical setting, therefore, is to provide objective support to the clinician's subjective suspicions. In defining a cutoff of more than 19 on the RSI, it is our hope that allergists will now be able to implement this diagnostic tool in their day-to-day clinical practice in a way that is both simple and noninvasive.

Another potential limitation is the sample size. Although statistical significance was obtained in several categories and the AUCs obtained were encouraging, it is possible that a larger number of patients could have led to even stronger results. In addition, generalizability to other patient populations, both of allergists and of nonallergists, cannot be assumed. Further studies are needed to define predictive RSI scores in other patient populations. Pending more information, allergists may want to use the RSI or the abbreviated version and the cutoffs identified in this study to supplement other diagnostic modalities for patients suspected of having LPR.

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TABLE E1. RSI score of patients treated with PPI vs not treated with PPI

RSI Score	Without PPI (n = 50 [60%])	With PPI (n = 34 [40%])	Total (n = 84 [100%])	P value
Mean ± SD	20.5 ± 9.6	21.0 ± 10.2	20.7 ± 9.8	.81
Median	19	20.5	20	
Q1, Q3	14.0, 27.0	13.0, 30.0	13.5, 28.0	
Range	3.0-41.0	1.0-38.0	1.0-41.0	

TABLE E2. Effect of sex on RSI score

RSI Score	Male (n = 30 [36%])	Female (n = 54 [64%])	Total (n = 84 [100%])	P value
Mean ± SD	21.5 ± 9.82	20.3 ± 9.83	20.7 ± 9.78	.58
Median	21	20	20	
Q1, Q3	14.0, 28.0	13.0, 28.0	13.5, 28.0	
Range	1.0-41.0	3.0-37.0	1.0-41.0	

TABLE E3. Effect of age on RSI score

	Estimate	SE	95% CI lower	95% CI upper	t statistic	P value
Age	0.04	0.06	−0.09	0.16	0.61	.55

TABLE E4. ROC analysis using abbreviated questionnaire

RSI Score cutoff	AUC	Sensitivity	Specificity	PPV
3	0.5093	1.0000	0.0185	0.3614
4	0.5278	1.0000	0.0556	0.3704
5	0.5296	0.9667	0.0926	0.3718
6	0.5481	0.9667	0.1296	0.3816
7	0.5852	0.9667	0.2037	0.4028
8	0.6037	0.9667	0.2407	0.4143
9	0.6130	0.9667	0.2593	0.4203
10	0.6148	0.9333	0.2963	0.4242
11	0.6611	0.9333	0.3889	0.4590
12	0.7074	0.9333	0.4815	0.5000
13	0.7037	0.8333	0.5741	0.5208
14	0.6981	0.7667	0.6296	0.5349
15	0.7093	0.7333	0.6852	0.5641
16	0.6759	0.6667	0.6852	0.5405
17	0.6963	0.6333	0.7593	0.5938
18	0.6648	0.5333	0.7963	0.5926
19	0.6407	0.4667	0.8148	0.5833
21	0.6500	0.4667	0.8333	0.6087
22	0.5926	0.3333	0.8519	0.5556
24	0.5778	0.2667	0.8889	0.5714
25	0.5648	0.1667	0.9630	0.7143
26	0.5315	0.1000	0.9630	0.6000
27	0.5241	0.0667	0.9815	0.6667
28	0.5074	0.0333	0.9815	0.5000

PPV, Positive predictive value.