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Acute, Recurrent, and Chronic Laryngopharyngeal Reflux: The IFOS Classification

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Objective: To investigate the clinical patterns and disease evolution of laryngopharyngeal reflux (LPR) patients.

Methods: Patients with LPR diagnosed by hypopharyngeal-esophageal impedance-pH monitoring were prospectively followed in three medical centers. Symptoms and findings were assessed with reflux symptom score (RSS) and reflux sign assessment (RSA). Patients were treated with 3-to 9-month diet and combination of proton pump inhibitors, alginate or magaldrate. Patients were followed for 3 years to determine the clinical evolution of symptoms over time. LPR that did not recur was defined as acute. Recurrent LPR consisted of reflux with one or several recurrences yearly despite successful treatment. Chronic LPR was reflux with a chronic course of symptoms. Predictive indicators of clinical evolution were investigated.

Results: One hundred forty patients and 82 healthy individuals completed the evaluations. Among patients, 41 (29.3%), 57 (40.7%), and 42 (30.0%) had acute, recurrent, or chronic LPR respectively. Baseline quality of life-RSS (QoL-RSS) and RSS total scores were significantly higher in chronic LPR patients. The post-treatment decrease of QoL-RSS and RSS of acute LPR patients were significantly faster as compared to recurrent and chronic patients. QoL-RSS >5 reported adequate sensitivity (94.2) and specificity (75.3). QoL-RSS thresholds defined acute (QoL-RSS = 6–25), recurrent (QoL-RSS = 26–38), and chronic (QoL-RSS > 38) LPR.

Conclusion: Baseline QoL-RSS may predict the clinical course of LPR patients: acute, recurrent, or chronic. A novel classification system that groups patients according to the longevity, severity, and therapeutic response of symptoms was proposed: the International Federation of Otorhinolaryngological Societies Classification of LPR.

Key Words: classification, gastroesophageal, head neck surgery, laryngeal, laryngology, laryngopharyngeal, larynx, otolaryngology, reflux, voice.

Level of Evidence: III

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INTRODUCTION

Laryngopharyngeal reflux (LPR) is an inflammatory condition of the upper aerodigestive tract tissues related to direct and indirect effect of gastroduodenal content reflux, which induces morphological changes in the upper aerodigestive tract.[1] The most common symptoms of LPR are hoarseness, throat pain, odynophagia, dysphagia, throat clearing, and cough.[1,2] Depending on the severity and the frequency of some symptoms, patients may report a significant impact of LPR on quality of life (QoL).[3] The most severe symptoms may affect sleep, daily life activity and may be associated with an increase of both anxiety and depressive outcomes.[4,5] To date, there is no clinical classification of reflux severity considering symptom scores, duration, and QoL features.

In the present study, we developed an international classification of LPR severity according to symptom evolution, related impact on quality-of-life, and short-to-long term therapeutic response to individualized treatment.

METHODS

Patients and Setting

A total of 171 patients with symptoms and signs of LPR were prospectively recruited from three European University medical centers (Cesar de Pape Hospital of Brussels,

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CHU Saint-Pierre of Brussels, and Foch Hospital of Paris) from September 2017 to January 2021. The LPR diagnosis was based on 24-h hypopharyngeal-esophageal multichannel intraluminal impedance-pH testing (HEMII-pH) off acid suppressive medication. Upper gastrointestinal (GI) endoscopy was offered to and completed in individuals with heartburn, gastroesophageal reflux disease (GERD) symptoms and age >55 years old. According to a recent review of the literature, a LPR diagnosis was confirmed if there was >1 acid or nonacid hypopharyngeal reflux event.[6]

To limit impact of confounders on initial symptom scores, exclusion criteria included active smoker, alcoholic (>3 alcohol glasses daily), history of upper respiratory tract infection within the last month, neurological or psychiatric illness, head and neck malignancy, head and neck radiotherapy, active allergies (at baseline or throughout the follow-up), asthma and intake of inhaled corticosteroids. Authors assessed the adherence of patients to treatment at each consultation. Only patients who reported adequate adherence to diet and medication were included. The study protocol was approved by the Brussels Institutional Review Board (CHUSP, no BE076201837630).

Hypopharyngeal-Esophageal Multichannel Intraluminal Impedance-pH Testing

The HEMII-pH catheter model used was introduced transnasally at rest in the morning. The probe length was chosen according to the patient's esophageal length (patient height). HEMII-pH was composed of eight impedance electrode pairs and two pH sensors placed 2–5 cm above lower esophageal sphincter and 1–2 cm above upper esophageal sphincter (UES) (Versaflex Z®, Medtronic, Hauts-de-France, France). Six impedance segments were placed along the esophagus (Z1–Z6) below the UES. Two additional impedance segments were placed 1 and 2 cm above the UES in the hypopharyngeal cavity. An otolaryngologist employed flexible laryngoscopy to confirm the correct placement of the HEMII-pH probe by identifying the 2 upper most impedance sensors and the identifying a targeted, colored line above the UES.

A hypopharyngeal reflux event was defined as an episode reaching two pharyngeal impedance sensors. An acid reflux event consisted of an episode with pH ≤4.0. A nonacid reflux event consisted of an episode with pH >4.0. A patient was diagnosed as having acid LPR when the ratio of hypopharyngeal acid reflux episodes to nonacid reflux episodes was >2. Mixed or weakly acid reflux was diagnosed when the ratio ranged from 0.51 to 2.0. Nonacid LPR was diagnosed when the ratio of acid reflux episodes to nonacid reflux episodes was ≤0.5. A GERD diagnosis was given when the DeMeester score was >14.72 or the length of time the 24-h recording spent below pH 4.0 at the esophageal pH sensors was >6.0%, as described in the Lyon guidelines.[7]

Clinical outcomes and treatment

All LPR patients were prescribed a 3-month low-fat, low-quick-release sugar, high-protein, alkaline, and plant-based diet.[8,9] Medications were based on the patient's individual LPR characteristics as determined by HEMII-pH testing. These characteristics included the type of reflux (acid, nonacid, weakly acid); positions and times of the occurrence of reflux episode(s) (upright/daytime, supine/nighttime) and the presence of GERD.[10]

In sum, patients with any form of acid reflux (acidic GERD plus or minus LPR or those with acid or weakly acid LPR without GERD) were treated with proton pump inhibitors (PPIs; pantoprazole 20 mg, fasting, morning), and post-meal alginate (Gaviscon Advance®, Reckitt Benckiser, Slough, UK). Patients with nonacid LPR were treated with post-meal alginate (Gaviscon®) or magaldrate (Riopan®, Takeda, Zaventem, Belgium) for at least 3 months. Reflux symptom score (RSS) was used to assess symptoms and the impact of symptoms on QoL at baseline, 6 weeks (online assessment), 3- and 6 months after initiation of treatment. RSS is a validated 22-item patient-reported outcome questionnaire, which includes QoL scores. The scores of RSS and QoL-RSS range from 0 to 625 and 98, respectively (Appendix A).[11] Therapeutic response was defined as uncertain, mild, moderate, high, or complete by the following changes: RSS reduction of ≤20% or a worsening of RSS were defined as an uncertain therapeutic response; RSS reduction of 20%–39.9% was defined as a mild response; RSS reduction of 40%–59.9% was a moderate response; and RSS reduction of 60%–79.9% was defined as a high response. The response of patients with RSS reduction of ≥80% or a posttreatment RSS ≤13[11] were defined as a complete therapeutic response. The medication of responder patients was titrated with cessation or dose reduction of PPIs first; and then subsequently with progressive reduction of alginate/magaldrate intake when patients were PPI off. The medications were changed for non-responders (switch from alginate to magaldrate and PPI change). The treatment algorithm is available in Appendix B. Note that patients with supine GERD/reflux were instructed to use a wedge pillow or other elevation.

Baseline, 3- and 6-month findings were recorded (videolaryngostroboscopy and oral cavity photos) and assessed retrospectively with Reflux Sign Assessment (RSA).[12] The evaluations were performed in a blinded manner by two laryngologists who reported previous adequate interrater reliability.[13]

Classification Outcomes

Determination of reflux clinical pattern. All patients had to be followed in consultation or electronically over the 3-year posttreatment period to evaluate for potential recurrence of their LPR symptoms. In patients who did not have long-term symptoms (chronic course), the follow-up was performed every year to determine the pattern of LPR. The patterns seen in our population of LPR patients revealed three LPR profiles according to the evolution of symptoms: acute, recurrent, and chronic LPR. Acute LPR was defined as LPR that was successfully treated without posttreatment recurrence (3-year follow-up). Recurrent LPR consisted of LPR with one or several recurrent episodes yearly, all of them being successfully treated intermittently by medication or strict diet. Chronic LPR was reflux with a chronic course of symptoms despite treatment and/or in those patients who became readily symptomatic again when the medications were stopped and, therefore, needed to have long-term medications.

Classification establishment. The classification was developed through the young otolaryngologist group of the International Federation of Otorhinolaryngological Societies (IFOS). IFOS is a non-political organization representing over 50,000 otolaryngologists belonging to about 120 member nations. The classification was developed to consider (1) the evolution of disease (acute, recurrent, and chronic), (2) the baseline RSS or QoL-RSS differences between acute, recurrent, and chronic patients, and (3) the potential predictive value of clinical scores on therapeutic response. The identification of potential predictive values of scores on clinical evolution was performed considering LPR patients and a control group of healthy individuals. The receiver operating characteristic (ROC) curve was used to determine RSS or RSS-QoL thresholds for disease diagnostic between patients and controls. Healthy individuals were carefully selected, applying exclusion criteria of study and did not have past or current history of reflux.

Statistical Methods

Statistical analyses were performed using the Statistical Package for the Social Sciences for Windows (SPSS version 27.0; IBM Corp, Armonk, NY, U.S.A.). According to the type of variables, the following tests were used to compare patients and healthy individuals: Mann–Whitney U test, Chi square, and t-test. The pre- to posttreatment outcome changes were evaluated with the Wilcoxon signed-rank test. Depending on variables, the group differences were assessed with Kruskal–Wallis test or ANOVA. Multivariate analysis was used to study the outcome associations. A level of significance of $p < 0.05$ was used.

RESULTS

A total of 140 patients completed the evaluations and were followed throughout the 3-year study period. Thirty-one patients were excluded because of lack of follow-up or differential diagnosis confusing the clinical evolution of reflux. Eighty-two healthy individuals completed the evaluations. Among patients, 41 (29.3%), 57 (40.7%), and 42 (30.0%) were classified as having acute, recurrent, or chronic LPR respectively. The mean age of patients was 50.9 ± 15.9 years old. There were 83 females (59.3%). The clinical features of patients are reported in Table I. The proportion of females was significantly higher in the chronic group compared with others ($p = 0.001$). Sixty-four patients had both LPR and GERD.

Baseline RSS, QoL-RSS, and RSA scores are reported in Table II. Otolaryngological, digestive, respiratory, and total RSSs were significantly different between groups. The mean QoL-RSS of asymptomatic individuals without any evidence of LPR was 3.6 (95% CI = 2.41, 4.87). The mean baseline QoL-RSS of patients with acute, recurrent, and chronic LPR were 20.3 (95% CI = 15.57, 25.03), 33.6 (95% CI = 28.4, 38.8), and 44.4 (95% CI = 38.04, 50.76) respectively. The receiver operating characteristic (ROC) curve reported adequate sensitivity (94.2) and specificity (75.3) for patients with a QoL-RSS >5 (Fig. 1). According to the QoL-RSS differences across groups, acute LPR disease may be defined regarding the following threshold of QoL-RSS: 6–25, while recurrent LPR disease may be defined as disease with QoL-RSS ranging from 26 to 38. Chronic LPR disease may consist of patients with QoL-RSS >38. Among the 42 chronic LPR patients, 11 (22.9%) had RSS-QoL <38. Sixteen (28.1%) and 4 (9.8%) recurrent and acute LPR patients, respectively, reported RSS-QoL > 38.

The evolutions of RSS and RSA throughout treatment are reported in Table III. RSS and QoL-RSS significantly decreased from baseline to 6-week posttreatment in acute LPR patients ($p = 0.001$). RSS ($p = 0.006$) and QoL-RSS ($p = 0.003$) continued to decrease from 6-week to 3-month posttreatment. RSA reported significant decrease only from baseline to 3-month posttreatment ($p = 0.001$) in the acute LPR group. In the recurrent LPR patient group, RSS and QoL-RSS significantly decreased from baseline to 6-week ($p = 0.001$) and from 3- to 6-month posttreatment (RSS: $p = 0.008$; QoL-RSS:

TABLE I.
Epidemiological and Clinical Features of Patients.

Characteristics	Acute reflux ($N = 41$)	Recurrent Reflux Responders ($N = 57$)	Chronic Reflux ($N = 42$)	p-Value
Mean age (SD)	50.4 ± 16.2	52.1 ± 16.5	50.2 ± 15.0	NS
Body mass index	23.3 ± 6.2	26.0 ± 5.5	25.4 ± 4.1	NS
Gender (N, %)				
Male	18 (44)	28 (49)	11 (26)	0.028
Female	23 (56)	29 (51)	31 (74)	
Gastrointestinal endoscopy	$N = 25$	$N = 46$	$N = 33$	
Normal	5 (20)	6 (13)	4 (12)	NS
Esophagitis	10 (40)	30 (65)	15 (45)	NS
Hiatal hernia	4 (16)	14 (30)	11 (33)	NS
LES insufficiency	9 (36)	23 (50)	16 (48)	NS
Gastritis	11 (44)	23 (50)	13 (39)	NS
Helicobacter pylori infection	0 (0)	4 (9)	3 (9)	NS
HEMII-pH feature (M ± SD)				
Pharyngeal acid reflux episodes	19.6 ± 17.3	18.7 ± 17.0	19.0 ± 15.8	NS
Pharyngeal nonacid reflux episodes	13.1 ± 12.9	12.2 ± 11.0	9.5 ± 7.7	NS
Pharyngeal reflux episodes upright	27.3 ± 21.7	26.2 ± 16.2	22.8 ± 14.2	NS
Pharyngeal reflux episodes supine	6.7 ± 9.4	3.3 ± 4.4	5.2 ± 5.5	NS
Pharyngeal reflux episodes (total)	32.6 ± 27.0	30.2 ± 19.9	30.7 ± 25.1	NS
GERD				
Number of patients (%)	22 (54)	41 (72)	26 (62)	NS
Percentage of time with distal pH <4	3.2 ± 4.9	7.7 ± 13.5	7.1 ± 12.4	NS
DeMeester score	12.7 ± 19.3	27.8 ± 47.1	25.8 ± 39.3	NS

GERD = gastroesophageal reflux disease; HEMII-pH = hypopharyngeal-esophageal multichannel impedance pH monitoring; NS = non-significant.

TABLE II.
Reflux Symptom Score and Quality of Life Scores of Healthy and Patient Groups.

	Controls	Acute	Recurrent	Chronic	*p*-Value
Reflux Symptom Score					
Otolaryngological RSS	3.2 ± 6.3	29.2 ± 25.8	59.0 ± 38.4	73.2 ± 40.2	0.001
Digestive RSS	5.3 ± 14.6	23.3 ± 26.2	34.7 ± 31.5	54.6 ± 34.2	0.001
Respiratory RSS	1.8 ± 4.9	11.9 ± 15.4	16.9 ± 20.3	23.4 ± 23.0	0.001
RSS total score	10.3 ± 18.0	64.4 ± 55.9	110.5 ± 67.0	150.9 ± 64.6	0.001
QoL-RSS					
Otolaryngological	1.2 ± 2.1	9.9 ± 7.6	17.6 ± 12.5	22.4 ± 14.5	0.001
Digestive	1.9 ± 4.2	6.7 ± 6.9	10.9 ± 8.0	14.4 ± 8.8	0.001
Respiratory	0.6 ± 1.4	3.7 ± 4.1	5.2 ± 4.8	6.7 ± 5.0	0.001
QoL-RSS total score	3.6 ± 5.7	20.3 ± 15.5	33.6 ± 19.8	44.4 ± 20.8	0.001

QoL = quality of life; RSS = reflux symptom score.

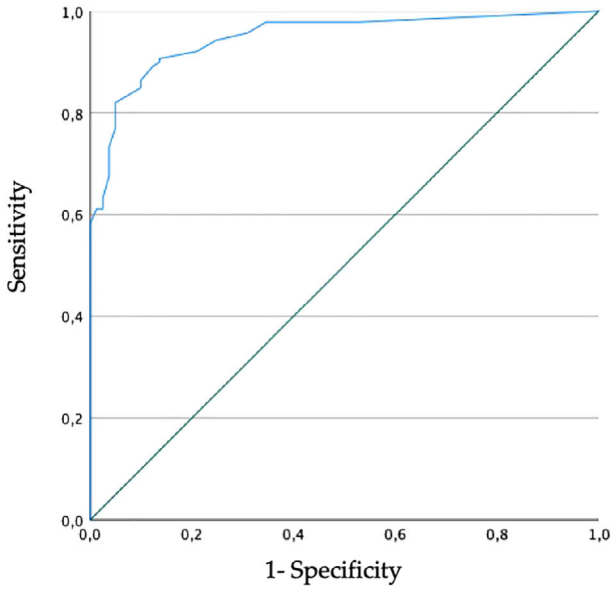
$p = 0.005$). The RSS difference between 6-week to 3-month posttreatment was not significant. RSA significantly reduced in the recurrent LPR group from pre- to 3-month posttreatment ($p = 0.001$) and from 3-month to 6-month posttreatment ($p = 0.015$). In patients with a chronic course of LPR, QoL-RSS was the only score that significantly reduced from baseline to 6-week posttreatment ($p = 0.014$). RSA significantly decreased after 3 months of treatment ($p = 0.007$) in the chronic LPR group. RSS and QoL-RSS were significantly different across all groups at baseline and throughout the 3-point posttreatment, whereas RSA did not vary between groups.

The therapeutic success rates after 6-month posttreatment of acute, recurrent, and chronic LPR patients were described in Table IV. The high and complete responder rates were significantly higher in acute and recurrent patient groups compared with chronic LPR group ($p < 0.001$).

The International Federation of Otorhinolaryngological Societies (IFOS) Classification of LPR Types is summarized in Table V. The multivariate analysis did not reveal any significant positive association between RSS and RSA scores in any groups, and there was no predictive value of GI endoscopy or HEMII-pH outcomes on the therapeutic response. There were no statistical differences between responder groups regarding distal esophageal reflux exposure (GERD).

DISCUSSION

Therapeutic success in LPR remains difficult to predict.[14,15] Many factors have been identified as indicators of therapeutic failure, such as hiatal hernia[16,17] or longest acid episodes on HEMII-pH.[18] However, to date, a clinical indicator of reflux evolution based on symptoms or the impact of symptoms on QoL does not exist.



RSS-QoL	Sensitivity	1-Specificity
-1.0000000	1.000	1.000
0.500000000	0.978	0.531
1.50000000	0.978	0.420
2.50000000	0.978	0.370
3.50000000	0.978	0.346
4.50000000	0.957	0.309
5.50000000	0.942	0.247
6.50000000	0.921	0.210
7.50000000	0.914	0.173
8.50000000	0.906	0.136
9.50000000	0.899	0.136
10.5000000	0.892	0.123
11.5000000	0.863	0.099
12.5000000	0.849	0.099
13.5000000	0.827	0.062
14.5000000	0.820	0.049

Fig. 1. Receiver operating characteristic curve. The receiver operating characteristic (ROC) curve reported that a QoL-RSS >5 is suggestive of mild laryngopharyngeal reflux with adequate sensitivity (94.2) and specificity (75.3). QoL = quality of life; RSS = reflux symptom score. [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

TABLE III.
Evolution of Symptom and Finding Score Throughout Treatment.

Scores	Patient group	Baseline	*p*-Value	6 weeks	*p*-Value	3 months	*p*-Value	6 months	*p*-Value
RSS	Acute reflux	64.4 ± 55.9		29.6 ± 35.6**		25.1 ± 35.5**		25.8 ± 27.5	
	Recurrent reflux	110.5 ± 67.0	0.001	61.7 ± 44.7**	0.001	74.8 ± 54.8**	0.001	65.0 ± 74.8**	0.001
	Chronic course	150.9 ± 64.6		117.0 ± 93.5		100.0 ± 84.3		118.5 ± 91.2	
QoL-RSS	Acute reflux	20.3 ± 15.5		11.2 ± 10.5**		9.4 ± 11.1**		11.7 ± 12.5	
	Recurrent reflux	33.6 ± 19.8	0.001	21.4 ± 13.5**	0.001	23.7 ± 12.7**	0.001	19.4 ± 18.7**	0.001
	Chronic course	44.4 ± 20.8		33.7 ± 21.0*		28.6 ± 19.4		32.2 ± 20.9	
RSA	Acute reflux	26.0 ± 9.6		-		17.6 ± 8.6**		16.6 ± 6.3	
	Recurrent reflux	27.8 ± 9.3	NS	-		20.8 ± 7.8**	NS	17.6 ± 8.0*	NS
	Chronic course	27.1 ± 9.1		-		21.6 ± 8.1**		18.8 ± 7.7	

The pre- to posttreatment analyses were performed from baseline to 6-weeks, 3-month, and 6-month posttreatment.
*$p < 0.05$.
**$p < 0.01$.
NS = non-significant; QoL = quality of life; RSS = reflux symptom score; TSA = reflux sign assessment.

This work presents the IFOS Classification of LPR Types (IFOSCLT), an original classification schema to better describe LPR disease, its treatment patterns and the impact that LPR symptoms have on QoL. Significant baseline QoL-RSS differences were observed between patients with different clinical patterns and therapeutic success rates. From these data thresholds, definitions of acute, recurrent or chronic LPR disease were designated. To date, few authors have reported different clinical patterns of LPR patients. In 1991, Koufman reported that a quarter of patients had a chronic course of the disease despite high dose PPI-therapy.[2] Similarly, Verhasselt et al. observed via survey that one third of patients had a chronic course.[19] The baseline higher RSS and QoL-RSS in patients with chronic course of the disease may be explained by a longer history of gastroduodenal content refluxate and, therefore, mucosal irritation.[20] Theoretically, recurrent chemical injuries of the laryngopharyngeal mucosa may lead to sensitivity modifications, thus supporting the higher symptom scores. Moreover, it was observed that patients with recurrent LPR needed more time to cure in the first therapeutic trial as compared to those with acute LPR.

A clinical classification that could help predict the evolution of disease over years and thus help choose an adequate treatment for patients is desirable. Several therapeutic options have been investigated in LPR including diet only,[9,21,22] PPI- or PPI-alginate combination,[14,18] and surgery.[23] This is likely why prior studies demonstrated that patients with mild/acute LPR were better responders to diet only,[9] while patients with chronic LPR usually benefited from the addition of acid suppressive medications and barrier agents,[1] or, in some centers, surgery.[23] Thus, the IFOSCLT may lead to future studies that consider 'precision medicine' where different cost-effective therapeutic strategies could be implemented after taking into account the severity classification of one particular patient. This study suggests that patients with a low QoL-RSS, and thus a higher probability to have acute LPR, could benefit from diet and stress management recommendations as opposed to those with suspected chronic LPR, based on a severe QoL-RSS score, to whom medications would be immediately prescribed. The use of personalized treatments,

TABLE IV.
Therapeutic Response of Patient Groups.

Types of Reflux Patients	Therapeutic Response	*N*	%
Acute LPR	No response	3	7.3
	Mild response	1	2.5
	Moderate response	3	7.3
	High response	6	14.6
	Complete response	28	68.3
Recurrent LPR	No response	6	10.5
	Mild response	4	7.0
	Moderate response	18	31.6
	High response	10	17.6
	Complete response	19	33.3
Chronic LPR	No response	14	33.3
	Mild response	1	2.4
	Moderate response	12	28.6
	High response	12	28.6
	Complete response	3	7.1

The therapeutic response was defined considering the following changes: RSS reduction of ≤20% or a worsening of RSS were defined as an uncertain therapeutic response; RSS reduction of 20%–39.9% was defined as mild response; RSS reduction of 40%–59.9% consisted of a moderate response; and RSS reduction of 60%–79.9% was defined as high response. The response of patients with RSS reduction of ≥80% or a posttreatment RSS ≤13[11] were defined as complete therapeutic response.
LPR = laryngopharyngeal reflux; RSS = reflux symptom score.

TABLE V.
The IFOS Classification Laryngopharyngeal Reflux Types.

Stages of LPR	Thresholds
No symptomatic reflux	RSS 0–13
	QoL-RSS: 0–5
Acute reflux disease	QoL-RSS: 6–25
Recurrent reflux disease	QoL-RSS: 26–38
Chronic reflux disease	QoL-RSS >38

QoL = quality of life; RSS = reflux symptom score.

which consider patterns of clinical predictors of disease, could profoundly impact and decrease the cost burden associated with treating LPR[24,25] (previously estimated to be 5.6 times the cost of treating GERD, with a total expenditure estimated as >$50 billion per year in the United States).

Because the IFOSCLT considers only QoL-RSS scores and not physical exam findings, symptoms or pH/pH -impedance study features to determine reflux severity, it is simpler to use for patient stratification.[26,27] There are practical reasons this may prove helpful. While reflux testing, including pH and pH-impedance studies (i.e. dual pH probes, oropharyngeal pH monitoring, and HEMII-pH), is helpful for diagnosis, it is not available in all centers and currently remains underutilized in clinical practice.[28] From a theoretical standpoint, the development of a severity classification of a disease would involve the use of an objective tool to determine the severity classifications through objective findings. However, in the case of LPR disease, there are no correlations between HEMII-pH features, symptoms, and signs[1]; thus, HEMII-pH features are poorly reliable as a determinant of severity outcomes.[29,30]

The main limitation of the present study is the lack of a patient-reported outcome questionnaire to assess the general QoL of patients, that is, a control assessment. However, because RSS and the QoL-RSS were both validated in two previous studies, both validity and reliability features being determined adequate in the French and Korean versions, it was felt to be satisfactory to present with this omission.[11,31] Admittedly, there may also be risk of unintended group heterogeneity after the first 3 months of treatment as the ongoing 3–6 month therapies were based on the initial HEMII-pH diagnosis and subsequent treatment response. Additionally, the thresholds defining acute, recurrent, and chronic LPR did not apply to all patients; for example, some chronic LPR patients have a RSS-QoL <38. Future studies are needed to improve the determination factor between acute, recurrent, and chronic patients. In the present study, we designated a diagnosis of LPR in patients with >1 hypopharyngeal reflux event as suggested in a recent review.[6] However, there are no international guidelines supporting this threshold.

CONCLUSION

The IFOSCLT is a novel clinical classification of LPR symptom presentation that stratifies patients based on the impact that their LPR symptoms have on their quality of life. It affords insight into how LPR disease may improve and/or evolve over time with an appropriate, severity-based treatment course. Implementing IFOSCLT will hopefully prove more cost effective, less invasive and more clinically available than what is currently practiced. Future studies are needed to study these factors as well as the reliability of IFOSCLT among ethnically, culturally, and geographically different populations.

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APPENDIX A

REFLUX SYMPTOM SCORE

Within the last month, I suffered from one/several followed symptoms

Severity: 0 = problem is not severe, 5 = problem very troublesome when it occurs

Frequency: 0 = I don't have this complaint over the past month, 1;2;3;4 = I had 1-2;2-3;3-4;4-5 weekly over the past month; 5 = complaint occurs daily

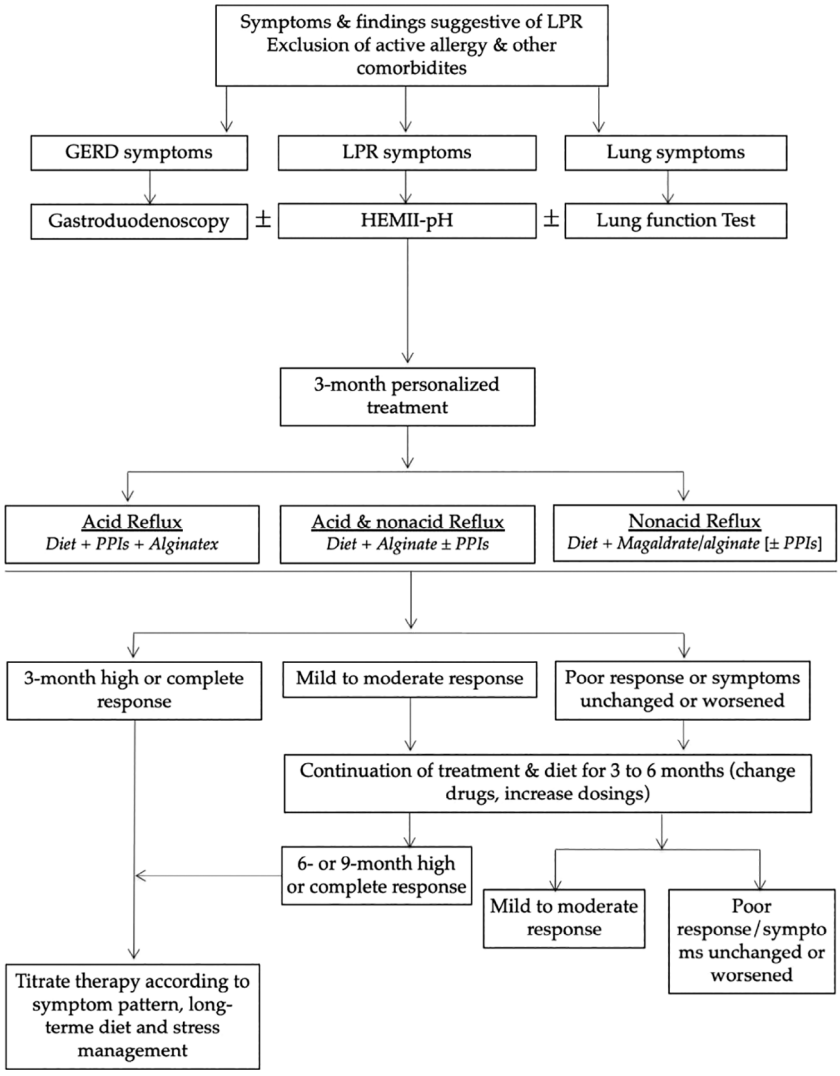
	Disorder Frequency	**Disorder Severity**		**Quality of Life impact**	
Ear Nose and Throat Disorders			Total score		Total score
1. Hoarseness or a voice problem	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
2. Throat pain	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
3. Pain during swallowing time	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
4. Difficulty swallowing (pills, liquids or solid foods)	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
5. Clearing your throat	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
6. Sensation of something sticking in the throat	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
7. Excess mucous in the throat or post nasal drip sensation	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
8. Ear pressure/pain (daytime or nigh-time)	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
9. Tongue burning	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
10. Other:	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
Abdominal Disorders					
1. Heartburn, stomach acid coming up	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
2. Regurgitations of liquids, solid foods or burps	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
3. Abdominal pain	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
4. Diarrheas	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
5. Constipation	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
6. Indigestion	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
7. Abdominal distension and/or flatus	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
8. Halitosis	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
9. Nausea	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
10. Other:	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
Chest/respiratory Disorders					
1. Cough after eating or lying down	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
2. Cough (daytime)	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
3. Breathing difficulties,breathlessness, or wheezing	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
4. Chest pain	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....
5. Other:	0 - 1 - 2 - 3 - 4 - 5	0 - 1 - 2 - 3 - 4 - 5	.....	0 - 1 - 2 - 3 - 4 - 5	.....

Do you think that this questionnaire well assesses your current complaints ? YES - NO **RSS total score:**..... **Quality of Life score:**.....

The questionnaire is subdivided into three parts according to the complaints: ear, nose, and throat (part 1, 9 items); digestive (part 2, 9 items); and respiratory (part 3, 4 items) symptoms. The frequency and severity of each symptom are rated with a 5-point scale. Regarding the frequency, 0 = patient did not have the complaint over the past month; 1, 2, 3, 4 = patient had the complaint 1–2, 2–3, 3–4, 4–5 times weekly over the past month; 5 = patient had the complaint daily over the past month. Regarding the severity, 0 = the complaint is absent, 5 = the complaint is very troublesome when it occurs. For each item, the severity score is multiplied by the frequency score to obtain a symptom score ranging from 0 to 25. The sum of these symptom scores is calculated to obtain the RSS final score (ranging from 0 to 550; with the possibility for the physician and the patient to add three symptoms not identified in the RSS, leading to a maximal possible score of 625). The RSS also assesses the symptom impact on quality of life. The total quality of life score is calculated by the sum of each item score.

APPENDIX B

MANAGEMENT ALGORITHM OF PATIENTS



According to the type of LPR (acid, nonacid, mixed), patients received a treatment considering the combination of alginate, magaldrate, and PPI. Only patients with acid and mixed (association of acid and nonacid events) LPR received PPI once (if the reflux events occurred daytime and upright) or twice (if the reflux events occurred daytime and nighttime) daily and alginate after the meals. Patients with nonacid LPR were treated with magaldrate or alginate thrice daily with additional dose before sleep in case of nighttime/supine reflux events. GERD = gastroesophageal reflux; HEMII-pH = hypopharyngeal-esophageal multichannel intraluminal impedance-pH monitoring; LES = lower esophageal sphincter; LPR = laryngopharyngeal reflux; PPI = proton pump inhibitor; RSS = reflux symptom score.