Reflux Symptom Index and Reflux Finding Score in Otolaryngologic Practice

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Summary: Objectives. To evaluate whether patients with abnormal Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) benefit from proton pump inhibitor (PPI) therapy.

Study Design. Open, multicenter, prospective longitudinal cohort study.

Methods. Patients with suspected reflux-associated laryngologic symptoms were evaluated by 40 community practice otolaryngologists using RSI and RFS. Patients were treated with pantoprazole 40–80 mg/d for 8–12 weeks if RSI was greater than 9 and RFS greater than 7. Pre- and posttherapeutic RSI and RFS were compared using Wilcoxon signed rank test and additionally controlled with the symmetry test of Bowker.

Results. A total of 1044 patients were included over a period of 20 months. Median total score of RSI before therapy was 12 and decreased to 3 ($P \ll 0.001$). Median total score of RFS before therapy was 16 and decreased to 6 ($P \ll 0.001$). Assessment of the treatment effect by otolaryngologists and patients was judged as being excellent in at least 50%. In 2% of the patients, gastrointestinal side effects were documented.

Conclusion. RSI and RSF are easy to administer in the routine care of patients suspected of having laryngopharyngeal reflux. Patients identified by positive results of these tests have a high likelihood of excellent improvement after 8–12 weeks of PPI treatment. By implementation of RFS and RSI in daily use, most patients may not need time-consuming and cost-intensive examinations in the first-line assessment of LPR. These examinations can be reserved for nonresponders, and uncontrolled prescription of PPIs can be restricted.

Key Words: Laryngopharyngeal reflux–Laryngitis–Reflux Symptom Index–Reflux Finding Score.

INTRODUCTION

Reflux of gastric fluid to the pharynx and larynx (laryngopharyngeal reflux [LPR]) may result in symptoms because of laryngeal mucosal damage. A wide variety of otorhinolaryngologic symptoms have been attributed to LPR, although in individual patients, it may be difficult to establish the causal relationship.[1] Reflux may consist of liquid or gas, or both, and its pH may cover a wide range from highly acidic to neutral. In specialized centers, combined pH and impedance measurements have been introduced to identify the reflux of fluid and gaseous contents from the stomach into the pharynx. They have an acceptable sensitivity for detecting laryngopharyngeal acid and nonacid reflux. These tests are currently being evaluated for their use in establishing the causal link between reflux and laryngitis.[2] It is currently unclear whether they are helpful in choosing different treatment options, which may focus on the reduction of acid by proton pump inhibitors (PPIs) or reduction of the volume of reflux, for example, by operative procedures. Whether these tests will ever become widely used in routine clinical care remains doubtful, given the invasive nature of the time-consuming procedures, their limited availability, and the expertise required.

Therefore, markers for LPR and reflux-associated laryngitis are needed. It has been suggested that the Reflux Symptom Index (RSI) and Reflux Finding Score (RFS) may be useful parameters.[3,4] The RSI has been designed to raise the clinical suspicion of LPR in patients presenting with ears, nose, and throat (ENT) symptoms, whereas the RFS has been designed to characterize morphologic lesions presumably associated with LPR. It has remained unclear, however, as of today whether the results of RSI and RSF can be used to guide the treatment of suspected LPR.

In this study, we evaluated the symptoms and signs resolution after 8–12 weeks of acid-suppressive therapy with 40 or 80 mg pantoprazole in ENT patients who were selected for the treatment on the basis of abnormal results of RSI and RFS.

MATERIALS AND METHODS

Between January 2006 and October 2007, 1044 patients attending a community otolaryngology practice for evaluation of otorhinolaryngologic symptoms possibly related to LPR were evaluated. The likelihood of LPR was assessed using a diagnostic questionnaire. Forty community practice otolaryngologists contributed patients to this open, multicenter, prospective longitudinal cohort study. The number of patients contributed by individual otolaryngologists ranged between 4 and 43.

The diagnostic questionnaire and examination comprised the following parts:

1. General demographic data (exclusion criteria: noncompliance, malignant diseases, intolerance to PPIs, current medication with PPI, or a washout period of at least 6 weeks since a former PPI treatment).
2. RSI pre- and posttherapy.[4] As shown in Table 1, the symptom history and different symptom characteristics

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TABLE 1.
The Reflux Symptom Index[3]

Symptoms	Within the Past Month, How Did the Following Problems Affect? Ordinal Scale: 0–5 (0 = No Problem, 5 = Severe Problem)					
Hoarseness or other voice problems	0	1	2	3	4	5
Clearing throat	0	1	2	3	4	5
Excess throat mucus or postnasal drip	0	1	2	3	4	5
Difficulty swallowing food, liquid, or pills	0	1	2	3	4	5
Coughing after eating or after lying down	0	1	2	3	4	5
Breathing difficulties or choking episodes	0	1	2	3	4	5
Troublesome or annoying cough	0	1	2	3	4	5
Sensations of something sticking in throat or lump in throat	0	1	2	3	4	5
Heartburn, chest pain, indigestion, or stomach acid coming up	0	1	2	3	4	5

were evaluated by using the structured questionnaire of RSI in a German translation.

3. RFS pre- and posttherapy.[5] Otorhinolaryngologists were advised to use a rigid endoscope for the evaluation of the larynx (as in daily routine). Video documentation was not required. The criteria of examination are listed in Table 2.
4. Evaluation of the therapy based on its effectiveness and tolerance by physicians and patients (ordinal scale with five levels: IV = excellent, III = good, II = satisfactory, I = poor, and 0 = negative).
5. Evaluation of the change in quality of life (ordinal scale with four levels: III = significantly improved, II = improved, I = no change, and 0 = worse).
6. Reasons for unscheduled stop of therapy (descriptive: low efficacy, low tolerance, noncompliance, and other reasons).
7. Observed side effects.

If RSI was greater than 9 (of a possible maximum of 45) and RFS greater than 7 (of a possible maximum of 26), a treatment with pantoprazole 40 mg daily was started for a total treatment duration of 12 weeks (minimal treatment period was 8 weeks). If the treatment effect was considered to be inefficient after 6 weeks, the patient consulted the ENT specialist again, and together with the patient, the otolaryngologist decided whether to increase the dosage of pantoprazole to 40 mg twice a day or not.

On the last day of treatment, patients were reevaluated by their otolaryngologist and the RSI and RFS scores were determined again. The otolaryngologist was blinded to the result of his first evaluation and was able to access the results of his first reexamination only under emergency medical conditions, which was not required in a single case.

Single data entry with comprehensive range and consistency checks was used. All data from the questionnaires were collected and fed into the statistical analysis database. The very few illegible data entries were treated as missing in the database. All variables of the questionnaires were analyzed descriptively. Statistical analysis was based on the "intention-to-treat" principle. For analysis of efficacy, only data for which both time points existed in the patient data log where used (observed cases technique). All error probabilities presented are two-sided and refer to each individual test.

The change in efficacy parameters was determined using the Wilcoxon signed rank test and additionally controlled with the symmetry test of Bowker, as in some cases the required continuity assumption of the data was not fully warranted. Results with an error probability of $P < 0.05$ were considered significant and those with $P < 0.01$ as highly significant.

The statistical software was developed by the company Neumann+Team (Vienna, Austria) and is written in IBM APL2 version 2 service level 6 (IBM, Armonk, NY). This software was

TABLE 2.
The Reflux Finding Score[4]

Laryngoscopic Findings	Ordinal Scale
Infraglottic edema (pseudosulcus)	0 = absent, 2 = present
Ventricular obliteration	0 = none, 2 = partial, 4 = complete
Erythema/hyperemia	0 = none, 2 = arytenoids only, 4 = diffuse
Vocal fold edema	0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = polypoid
Diffuse laryngeal edema	0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = obstructing
Posterior commissure hypertrophy	0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = obstructing
Granuloma/granulation	0 = absent, 2 = present
Thick endolaryngeal mucus	0 = absent, 2 = present

TABLE 3.
Demographic Data (N = 1044)

Demographic Data	n (%)
Age (years)	
Mean	53
Minimum	15
Maximum	96
Gender	
Men	407 (39)
Women	595 (57)
Missing	42 (4)

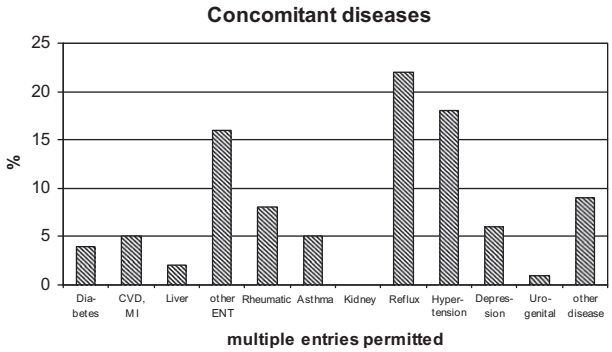

FIGURE 1. Concomitant diseases of the patients. CVD, cardiovascular disease; MI, myocardial infarction; ENT, ears, nose, and throat.

written and tested in accordance with the Guidelines of the European Organization for Quality, Section for Quality in the Pharmaceutical Industry, *Principles of Computer Use in a Regulated Pharmaceutical Industry*, 1989.

RESULTS

One thousand forty-four patients were included in the study (407 = 39% men, 595 = 57% women, 42 = 4% of entries missing). The final visit was after a median of 72 days (mean, 78 days) (Table 3). In 78% of the patients (n = 814), the treatment ended after 12 weeks. In 17% of the patients (n = 177), the treatment ended unexpectedly but with documented reason, and in 5% (n = 52), there was no reason for interruption documented. The reasons for unexpectedly ending were the following: 11% (n = 115), poor compliance of the patient; 2% (n = 21), no or little effect of therapy; 1% (n = 10), no or little tolerance; and 3% (n = 31), other reasons.

Twenty-three percent of the patients were smokers and 22% had a previous diagnosis of reflux disease (but no current running therapy). The concomitant diseases are listed in Figure 1. The predominant concomitant diseases were reflux (gastroesophageal reflux disease, 22%), hypertension, other otorhinolaryngologic diseases, depression, rheumatic diseases, asthma, and cardiovascular diseases.

Eighty-nine percent of the patients were treated with pantoprazole 40 mg daily and 11% with pantoprazole 40 mg twice a day. No correlation was found between any concomitant disease and the necessity of twice a day dosage of pantoprazole. There was also no significant correlation between smoking and dosage of PPI.

The median total score of the RSI before therapy was 12 (range, 10–41) and decreased at the end of therapy to 3 (range, 0–44). This decrease was highly significant ($P \ll 0.001$).

The median total score of the RFS before therapy was 16 (range, 8–20) and decreased at the end of therapy to 6 (range, 0–16). This decrease also was highly significant ($P \ll 0.001$).

A breakdown of the individual categories in the RSI and RSF scoring is shown in Tables 4 and 5, respectively.

Assessment of the treatment effect by the otolaryngologists was judged excellent in 52% of patients, good in 30%, satisfactory in 12%, poor in 5%, and negative in 1%. Assessment of the treatment effects by the patients resulted in similar results: excellent in 50%, good in 29%, satisfactory in 11%, poor in 8%, and negative in 2% (Table 6).

TABLE 4.
RSI Before and at the End of Therapy

RSI	Pretherapeutic Median (Mean)	Posttherapeutic Median (Mean)	*P* Value, Wilcoxon Test, Symmetry Test of Bowker
Hoarseness or other voice problems	1.5 (1.7)	0.0 (0.7)	≪0.001
Clearing throat	2.0 (2.4)	1.0 (1.0)	≪0.001
Excess throat mucus or postnasal drip	2.0 (2.1)	1.0 (0.8)	≪0.001
Difficulty swallowing food, liquid, or pills	0.0 (0.7)	0.0 (0.2)	≪0.001
Coughing after eating or after lying down	0.0 (1.0)	0.0 (0.3)	≪0.001
Breathing difficulties or choking episodes	0.0 (0.9)	0.0 (0.3)	≪0.001
Troublesome or annoying cough	0.0 (1.1)	0.0 (0.3)	≪0.001
Sensations of something sticking in throat or lump in throat	3.0 (1.7)	0.0 (0.5)	≪0.001
Heartburn, chest pain, indigestion, or stomach acid coming up	1.0 (1.7)	0.0 (0.5)	≪0.001
Total RSI	12.0 (13.8)	3.0 (4.9)	≪0.001

"≪" means small (by powers of 10) compared to.

TABLE 5.
RFS Before and at the End of Therapy

RFS	Pretherapeutic Median (Mean)	Posttherapeutic Median (Mean)	*P* Value, Wilcoxon Test, Symmetry Test of Bowker
Infraglottic edema (pseudosulcus)	0.0 (0.4)	0.0 (0.1)	$\ll 0.001$
Ventricular obliteration	0.0 (0.7)	0.0 (0.3)	$\ll 0.001$
Erythema/hyperemia	2.0 (2.5)	2.0 (1.3)	$\ll 0.001$
Vocal fold edema	1.0 (1.1)	0.0 (0.4)	$\ll 0.001$
Diffuse laryngeal edema	1.0 (0.8)	0.0 (0.3)	$\ll 0.001$
Posterior commissure hypertrophy	2.0 (1.7)	1.0 (0.8)	$\ll 0.001$
Granuloma/granulation	0.0 (0.1)	0.0 (0.0)	$\ll 0.001$
Thick endolaryngeal mucus	2.0 (1.0)	0.0 (0.4)	$\ll 0.001$
Total RFS	16.0 (15.8)	6.0 (7.0)	$\ll 0.001$

"$\ll$" means small (by powers of ten) compared to.

Tolerance of the therapy was judged excellent or good by 96% of the otolaryngologists and 94% of the patients (observed cases, Table 6).

In 85% of the patients, quality-of-life ratings could be obtained. Quality of life after therapy significantly improved (=level 4 of 4) in 31% of patients, improved (=level 3 of 4) in 41%, and unchanged or worsened in 13% (Table 7). Even if all the missing results were counted as being worsened, the variable Dixon and Mood sign test would still suggest a significant result in the direction of improvement with $P \ll 0.001$.[6]

Worsening of quality of life was observed in 0.4% of available ratings at the end of therapy (95% confidence interval [CI], 0.1–1.0).

In 2% of the patients, a gastrointestinal side effect (diarrhea) was documented.

DISCUSSION

This study was designed to assess the usefulness of RSI and RFS for the selection of patients for PPI treatment in daily otorhinolaryngologic practice.

Our results show that the patient group that was selected for treatment based on the results of RSI and RFS responded very positively to PPIs. This suggests that RSI and RSF can be used to select responders efficiently.

The RSI > 9 was chosen in accordance with the findings of Belafsky et al,[3] which judged patients with RSI < 10 as asymptomatic (95% CI = 9.7–13.6) for LPR.

The RFS > 7 predicts a 95% certainty in patients with LPR.[4]

The study demonstrates that in routine care of patients with otorhinolaryngologic symptoms, RSI and RFS are very useful for identifying those patients who have a high likelihood to improve considerably during treatment with PPIs.

For the use in our patients, RSI was translated into German language. Although a translation of RSI has not been validated scientifically before, our results suggest that it can be used in identifying patients for treatment with PPIs. There is no indication that the patient population in Austria varies considerably from the population in which RSI was validated originally by Belafsky et al, but the missing German validation is a potential bias.[7,8]

Our study was performed in a large number of busy private practices of otolaryngologists. Both RFS and RSI could be implemented into daily routine patient care without being overly time consuming. Any kind of recording of the laryngoscopies would have improved the reliability of the subjective RFS, but in routine patient care, it was not possible to demand additional recording from the participating community practice otorhinolaryngologists.

TABLE 6.
Effectiveness and Tolerance of Treatment Judged by Physicians and Patients

Subjective Evaluation	Five-Point Ordinal Scale	Patients (%)	Physicians (%)
Effectiveness of treatment	Excellent	50	52
	Good	29	30
	Satisfactory	11	12
	Poor	8	5
	Negative	2	1
Tolerance of treatment	Excellent	94	96
	Good	2	2
	Satisfactory	1	1
	Poor	2	1
	Negative	1	0

TABLE 7.
Change of Quality of Life (Subjective Description by the Patient)

Change of Quality of Life (Four-Point Ordinal Scale)	%	Variable Dixon and Mood Sign Test
Significantly improved	31	Overall improvement with $P \ll 0.001$
Improved	41	
No change or worse	13	
Missing	15	

"$\ll$" means small (by powers of ten) compared to.

Patients who were identified by the results of RFS and RSI to have a high likelihood of LPR were treated with 40–80 mg pantoprazole per day over 3 months. Dose and duration of pantoprazole treatment are within the range reported in previous studies.[9–11] Most patients improved on 40 mg of pantoprazole, and only 11% of the patients required an increase of the dosage to pantoprazole 40 mg twice a day. The improvement was highly significant for both the subjective parameters covered by RSI and the objective parameters of inflammation covered by RFS.

It has to be acknowledged, however, that the treatment success also includes a placebo effect, which has been demonstrated to play a very significant role in LPR disease.[12,13] However, previous studies have suggested that in a subset of patients, PPIs are helpful.[11] It remains, however, unclear how this subset should be identified.

More than 75% of the patients and of the otolaryngologists judged the efficacy of the therapy as being good or excellent.

Our study does not allow conclusions on the natural course of these patients without any treatment and on the magnitude of the placebo effect. Even in the unlikely case, that all patients were placebo responders, the identification of patients with positive results of the RSI and RFS would be useful as a prognostic factor indicating a high likelihood of spontaneous resolution of symptoms and inflammatory changes.

The age spectrum of patients identified as having LPR in our study was similar to the age spectrum of those with gastroesophageal reflux disease.[14] Twenty-two percent of the patients reported a history of a gastroesophageal reflux disease diagnosed by a gastroenterologist. As mentioned earlier in the exclusion criteria, patients had no current running PPI therapy or a washout period of 6 weeks since the last PPI treatment. However, our patients were more likely to be female, which is in contrast to gastroesophageal reflux disease, which shows nearly equal proportions of affected men and women in general but a male predominance in esophagitis and Barrett esophagus.[13] It is unclear whether this female predominance represents gender-specific reactions of laryngopharyngeal mucosa to reflux or whether it is the result of increased health care–seeking behavior among women.

The application of reliable and documented indications can help to avoid uncontrolled prescription of PPIs. RFS and RSI may help to prevent unjustified and unselected prescription with an impact on health insurance systems.

CONCLUSION

RSI and RSF can be easily included in the daily clinical care of patients suspected of having LPR and are helpful in identifying patients who have a high likelihood of a favorable response during PPI treatment. However, double-blind placebo-controlled studies are needed to address the proper treatment.

By implementation of RFS and RSI in daily use, most patients do not need time-consuming and cost-intensive examinations in the first-line assessment, and these examinations can be reserved for nonresponders. Additionally, the uncontrolled prescription of PPIs can be restricted.

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