Predictors of response to short-term proton pump inhibitor treatment in laryngopharyngeal reflux patients

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Abstract
Objectives: To assess benefit from one and three months’ empirical proton pump inhibitor treatment in patients with suspected laryngopharyngeal reflux, and to define pre-therapy factors which may predict success with short-term proton pump inhibitor treatment.

Study design: Prospective, open clinical study.

Materials and methods: One hundred adult out-patients with suspected laryngopharyngeal reflux were enrolled in the study. Laryngopharyngeal reflux patients underwent endoscopy and received omeprazole for three months. Efficacy of treatment was assessed at one and three months. Patients were classified as responders if their total symptom score had improved at least 50 per cent, their videolaryngoscopic score had improved by at least two points, and they were satisfied with the results. Pre-therapy factors assessed for an effect on omeprazole outcomes included: patient demographics, reflux symptoms, videolaryngoscopic scores, endoscopic findings, overall vocal dysfunction degree, self-rated voice handicap index, hospital anxiety and depression scale scores, and general well-being score.

Results: Fifty-six per cent of patients were classified as responders at one month of treatment; this proportion rose to 92 per cent at three months. Those patients entering the study with a higher heartburn score showed a significant response after one month of omeprazole treatment. Non-responders were found to have significantly more anxiety than responders. Logistic regression analysis revealed these factors, plus the medication dose, as being relevant for faster response prediction. No significant association was found between pre-therapy factors and three-month response to proton pump inhibitor treatment.

Conclusion: Three months of proton pump inhibitor treatment twice daily is warranted for confirming suspicion of laryngopharyngeal reflux. Baseline anxiety levels and heartburn scores, and the medication dose, may be relevant factors when predicting faster response to proton pump inhibitor treatment in carefully selected patients.

Key words: Gastro-Oesophageal Reflux; Proton Pump Inhibitors

Introduction
The diagnosis of laryngopharyngeal reflux (LPR) can be made on the basis of symptoms and laryngeal findings. Ambulatory, 24-hour, double-probe (i.e. simultaneous oesophageal and pharyngeal) pH monitoring remains the ‘gold standard’ when a diagnosis of LPR is in question. As a screening tool, 24-hour, double probe pH monitoring has been criticised for its lack of sensitivity as well as its high cost and inconvenience to the patient. A small amount of pharyngeal reflux occurs in the normal population; therefore, the interpretation of results remains controversial.

An initial therapeutic trial of high-dose proton pump inhibitors (PPIs) has been advocated as the first step in diagnosis and treatment of patients with suspected LPR; however, no universally accepted recommendation exists for the length of the therapeutic trial. A minimum of four weeks is required before a diagnosis of ‘no response’ is made. Despite the limited benefit from PPI compared with placebo in placebo-controlled trials, patients diagnosed with LPR continue to be given empirical PPI treatment. Economic analysis has revealed empirical PPI treatment to be a cost-effective diagnostic tool. In uncontrolled trials, the response of LPR patients to...
diagnostic one-month PPI treatment is unpredictable, ranging from 27 to 83 per cent; for three months, the response is between 41 and 100 per cent.6,7,9 Placebo-controlled trials have also shown conflicting results.7

Few trials have analysed the predictors of response to PPI treatment. Park et al.10 found that pre-therapy interarytenoid mucosa and true vocal fold abnormalities were associated with a two-fold increase in symptom response to PPI treatment. Williams et al.6 concluded that pharyngeal pH-meter measurements may prove useful; while other investigated factors cannot predict the response to therapy with certainty.7,8

The aims of our study were to assess the benefit from one and three months of empirical PPI treatment in patients with suspected LPR, and to define pre-therapy factors which may predict success with short-term PPI treatment.

Materials and methods

One hundred and fifty-six consecutive adult patients consulting otorhinolaryngologists at the Kaunas Medical University Department of Otorhinolaryngology out-patient clinic were suspected of LPR, and considered for study enrolment, due to: chronic hoarseness (exceeding one month), throat-clearing, globus sensation, sore throat, or a cough with the typical laryngeal findings of reflux laryngitis (i.e. erythema, oedema, posterior glottis hypertrophy, vocal fold oedema and subglottic oedema).

In order to be eligible for inclusion, patients were required to have: (1) at least two laryngeal symptoms rating no less than two points on a zero to three Likert severity scale, and (2) at least posterior laryngitis, after exclusion of other possible causes of laryngeal inflammation (i.e. allergy, infection, sinus pathology and asthma). Subjects were excluded if they met the following criteria: additional laryngeal findings such as nodule, polyp, cyst or neoplasm; prior anti-reflux surgery; upper respiratory tract infections in the last month; pregnancy during the study period; and diagnosed psychiatric illness.

Eligible subjects then completed questionnaires regarding: patient demographics; medical history; allergy history; tobacco use; voice training (practical voice training for not less than two hours/week for two years); symptoms and their severity; underwent videotaped laryngoscopy or upper gastrointestinal endoscopy; voice assessment with voice range profile; and quality of life assessment measures (i.e. voice handicap index, hospital anxiety and depression scale, and general well-being assessment).

Patient evaluation

Reflux symptom scores. These were self-assessed by patients, and included six laryngeal symptoms (i.e. hoarseness, throat-clearing, globus sensation, sore throat, chronic cough and choking episodes during the night) and three oesophageal symptoms (i.e. heartburn, regurgitation and odynophagia). The severity of each symptom was scored according to a four-point Likert scale, in which zero indicated no symptoms and three indicated severe symptoms (i.e. symptoms hard to tolerate and interfering with planned activities). A symptom was defined as being present if it was experienced for two or more days in a two-week period and scored more than zero points on the Likert scale. The sum of each individual symptom severity score, multiplied by the number of presenting laryngeal and oesophageal symptoms, made up the laryngeal (range, zero to 108 points) and oesophageal (range, zero to 27 points) scores; the sum of both these scores made up the total symptom score (range, zero to 135 points). This composite score was intended to enhance the power of the data, and has been used previously by the current authors and others.12,13)
Telescopic videolaryngoscopy. This investigation, using a Kay Elemetrics RLS (Kay Elemetrics Co., Lincoln Park, NJ, USA) equipment with 70° rigid endoscope, was performed according to a standard protocol, by the same examiner, using the same equipment, for each patient. Laryngeal abnormalities in the four laryngeal regions (i.e. posterior, vocal folds, vestibular folds and subglottic area) were evaluated by rating each region on colour, oedema and hypertrophy, using a four-point Likert scale (zero = no signs; three = severe signs), using a preprinted evaluation form. The sum of the separate region scores made up the videolaryngoscopic score (range, zero to 36 points). A score of more than 10 region scores made up the videolaryngoscopic score preprinted evaluation form. The sum of the separate scale (zero

Quantitative voice assessment. Voice was analysed by voice range profile. This was registered in an ordinary equipment, for each patient. Laryngeal abnormal-

Upper endoscopy findings. Endoscopy findings for the upper gastrointestinal tract were determined for each patient. The extent of oesophageal mucosal damage was assessed using the Los Angeles classification grading system. No less than A grade oesophagitis was required to confirm a diagnosis of gastroesophageal reflux disease.14

Quality of life parameters. Voice handicap index was self-rated by the patients using a 30-item questionnaire.17 Each statement was rated by frequency (zero = never; four = always). The voice handicap index generated a total score ranging from one to 120 and three subscale scores (functional, physical and emotional). The hospital anxiety and depression scale was self-assessed using a 14-item questionnaire with four response categories, measuring the levels of anxiety and depression in two separate subscales.18 Scale scores ranged from zero (no symptoms) to 21 (maximum distress). A score of 11 in either of the subscales indicated probable psychological distress. General well-being was self-rated using a 100 mm visual analogue scale (VAS), from zero (extremely bad) to 100 (excellent).

Statistical methods

Statistical analysis was performed using the Statistical Package for the Social Sciences version 10 for Windows software (SPSS Inc, Chicago, Illinois, USA). Univariate analysis between responders and non-responders was performed using the t-test for normally distributed quantitative parameters, and the Mann–Whitney U and chi-square or Fisher’s exact tests for non-parametric data. A level of significance of 0.05 was used. An analysis of variance model in repeated measures at three time points was used with Bonferroni correction for multiple comparisons, yielding significant p value if less than 0.001.

Multivariate analysis for prediction of response to one and three months’ omeprazole treatment was performed using logistic regression analysis, initially by entering all independent variables at a single step. To stay in the model, variables were required to be significant, using a 5 per cent significance level. These variables were then separately analysed with binary logistic regression in order to obtain their predictive effect for positive treatment response. Odds ratios (OR) are expressed with their 95 per cent confidence intervals (CIs). The Spearman correlation coefficient was used for assessing intra-rater reliability (r > 0.30 were considered to represent significant association).

Results

Study population

Of the 156 consecutive patients considered for study, 56 were excluded as a result of the exclusion criteria and/or refusal of medical treatment, leaving 100 eligible patients. The study population comprised 75 female and 25 male subjects, with a mean age of 39.9 years ± a standard deviation of 13.8 years. Eleven patients were smokers and 23 had trained voices.

All patients had two or more laryngeal symptoms and posterior laryngitis. 85 patients had vocal fold oedema, and one had granuloma. The prevalence of laryngeal symptoms was as follows: throat-clearing, 92 per cent of cases; hoarseness, 85 per cent; globus sensation, 74 per cent; sore throat, 66 per cent; chronic cough, 62 per cent; and choking, 32 per cent.

Oesophageal symptoms were present in 76 of the cases with predominant heartburn symptom (i.e. 58 per cent of patients). Oesophagitis was confirmed in 21 of the selected patients: 17 (80.9 per cent) of
these patients had oesophagitis A and four (19.1 per cent) had oesophagitis B.

During the first month of treatment, 28 patients received omeprazole 20 mg once daily and 72 patients received omeprazole 20 mg twice daily. There was no significant difference in these patients' demographic characteristics, tobacco use, voice training, total symptom score or videolaryngoscopic score.

Response to therapy
After one month of treatment, analysis showed a significant improvement in the means of all tested efficacy parameters \((p < 0.001)\) (Table I). According to the selected criteria, 56 of 100 (56 per cent) LPR patients were classified as responders: 12 of the 28 (42.9 per cent) patients receiving omeprazole once daily, and 44 of the 72 (61.1 per cent) patients receiving omeprazole twice daily \((p > 0.05)\). Of the 56 responders, 10 (17.8 per cent) patients showed an improvement of equal to or greater than 80 per cent. An improvement of less than 50 per cent was noted in 30 (30 per cent) of the 100 LPR patients, while 14 (14 per cent) of these patients were classified as experiencing no change.

At three months of treatment, a further reduction of symptom and videolaryngoscopic scores and improvement in general well-being were achieved \((p < 0.001)\) (Table I). Thirty-six more patients were classified as responders, taking the total to 92 of 100 (92 per cent). Of these patients, recovery was noted in 67 (72.9 per cent). Increasing the omeprazole dose to twice daily for an additional two months resulted in an improvement in total symptom score and videolaryngoscopic score in 12 of 16 (75 per cent) non-responders who received 20 mg once daily during the first month. Three-month non-responders had signs of vocal abuse, psychological distress and active smoking, and one patient had erosive oesophagitis B with hiatal hernia.

Factors that may influence treatment outcomes
Prediction of response to omeprazole after one month’s treatment. After one month of treatment, 56 per cent of patients were considered to be responders because their total symptom score had improved at least 50 per cent, their videolaryngoscopic score had improved by at least two points and they were satisfied with the results. When comparing the general results of symptomatic responders vs non-responders for all treatment regimen patients combined, 12 independent pre-therapy factors were compared to determine potential predictors of therapy response (i.e. gender; age; active smoking; dose of medicine – 20 mg vs. 20 mg BID reflux symptom severity score; endoscopic findings; overall vocal dysfunction degree; voice handicap index; anxiety score by HAD scale; depression score by HAD scale; and general well-being assessment). Univariate analysis showed a significant difference between responders and non-responders regarding pre-therapy heartburn severity \((p = 0.019,\) Mann–Whitney U test) and mean anxiety score \((p = 0.036, t\)-test) (Table II). Patients who had entered the study with higher heartburn scores and lower anxiety scores responded significantly better to treatment. Logistic regression analysis revealed anxiety, heartburn and medication dose as relevant independent factors for the prediction of one-month treatment response. These variables are listed in Table III. An increase of one anxiety score point decreased the odds ratio for a positive response by 1.15 times \((p = 0.014)\), while a higher heartburn score on entry increased the odds by approximately two times (odds ratio 1.99, \(P = 0.004)\) and dose of omeprazole 20 mg twice daily – by three times (odds ratio 3.05, \(P = 0.027)\).

Prediction of response to omeprazole after three months’ treatment. Comparison of 12 independent pre-therapy factors for responders \((n = 92)\) and non-responders \((n = 8)\), after three months’ omeprazole treatment, showed no statistically significant difference. With logistic regression, similarly, no statistically significant association with response was found for any of these pre-therapy factors. Of 44 non-responders after one month of omeprazole treatment, 38 (86.3 per cent) were considered to be responders at three months. A higher baseline videolaryngoscopic score had a significant influence on these patients’ positive responses \((p = 0.007)\) (Table IV), although logistic regression analysis showed no significant association for any of the pre-therapy factors analysed.

Discussion
The association of gastroesophageal reflux with extraoesophageal disorders is often made by symptoms and findings alone; however, ambulatory, 24 hour, two- or three-site pharyngoesophageal pH monitoring and trials of acid suppression solidify the diagnosis of Laryngopharyngeal reflux (LPR).1,4,5 Treatment with Proton Pump Inhibitors (PPI) has been shown to be sensitive in up to 85.7 per cent of cases and establishes a causal relationship.2,19 The length of diagnostic PPI trials has varied from two to 12 weeks.2,10,19 Treatment frequently requires six months or more for optimal relief and disappearances of physical findings.1,5 Previous trials have suggested

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**TABLE I**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>1 mth</th>
<th>3 mth</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total symptom score</td>
<td>50.3 (34.1)</td>
<td>21.9 (25.1)†</td>
<td>4.0 (2.7)†</td>
</tr>
<tr>
<td>Videolaryngoscopic score</td>
<td>8.4 (5.7)</td>
<td>4.1 (2.5)†</td>
<td>2.9 (1.9)†</td>
</tr>
<tr>
<td>General well-being score</td>
<td>47.2 (21.0)</td>
<td>65.1 (20.6)†</td>
<td>69.9 (17.7)†</td>
</tr>
</tbody>
</table>

Data are expressed as mean and standard deviation. The reduction in total symptom score and laryngeal scores and increase in general well-being score shows improvement. \(n = 100\). Statistically significant difference between baseline and each follow-up measurement: \(p < 0.001\). Bonferroni correction. LPR = laryngopharyngeal reflux; mth = months.
that PPI therapy should be extended for at least one month before a diagnosis of ‘non-responder’ can be made.\(^5\) Identification of the characteristics of patients who would respond to PPI treatment has been indicated by recent, reliable studies.\(^20\) An earlier positive response to treatment has benefits for both the patient and physician. Patients who responded during the one-month period could be reassured regarding the accuracy of diagnosis and the effectiveness of administered treatment.

The aims of our study were to assess the benefit from one and three months of empirical PPI treatment in patients with highly suspected LPR, and to define pre-therapy factors which may predict success with short-term PPI treatment. Our analysis demonstrated that after one month of empirical omeprazole treatment, 56 per cent of selected patients were classified as responders, and that 92 per cent of patients responded to three months of treatment. These data are in concordance with the findings of other studies, that is: for four weeks’ empirical high-dose PPI treatment, response rates of 27 to 83 per cent; and for three months’ treatment, response rates of 41 to 100 per cent in uncontrolled studies and of 40 to 90 per cent in controlled studies.\(^4–7\)

Differences between studies are mainly related to patient selection and varying outcome criteria.

Our study showed that response to one-month omeprazole treatment was significantly associated with three factors: low pre-therapy anxiety score, high heartburn score and receiving omeprazole 20 mg twice daily (Table III). The last two factors significantly increased the odds (by approximately two and three times for positive response), while a high anxiety level decreased the odds. No significant differences were found for all other evaluated factors (Table II). The significance of anxiety may be explained by more anxious patients who are more distrustful of their LPR diagnosis.\(^12\) The significance of initial heartburn score as a relevant predictor for one-month empirical omeprazole treatment is not surprising, as heartburn is a classical symptom of gastroesophageal reflux disease which has a long history of good response to PPI treatment, as described elsewhere. A previous report advocating twice daily PPI treatment gave findings similar to this study. Twice daily PPI treatment is more effective than once daily treatment.\(^2,4,6,10,19\)

Analysis of selected pre-therapy factors which may influence three-month empirical PPI treatment outcome showed no statistically significant associations. However, regarding duration of treatment, our study results decisively showed that three months of potent PPI treatment was successful for most carefully selected patients. After one month of ineffective treatment with PPIs, attention should be paid to the baseline videolaryngoscopic score. A higher score could indicate a further, positive response following three months of treatment (the maximum videolaryngoscopic score for further non-responders was low-seven points, of a possible 36

### Table II

<table>
<thead>
<tr>
<th>Factor</th>
<th>Responders(^1)</th>
<th>Non-responders(^1)</th>
<th>(p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female/male (n (%))</td>
<td>42 (75.0) / 14 (25.0)</td>
<td>33 (75.0) / 11 (25.0)</td>
<td>1.0</td>
</tr>
<tr>
<td>Age (yr; mean (SD))</td>
<td>39.6 (12.6)</td>
<td>40.0 (15.5)</td>
<td>0.927</td>
</tr>
<tr>
<td>Active smoking (n (%))</td>
<td>8 (14.5)</td>
<td>3 (6.8)</td>
<td>0.337</td>
</tr>
<tr>
<td>Omeprazole dose 20/40 mg/day (n (%))</td>
<td>12 (21.4) / 44 (78.6)</td>
<td>16 (36.4) / 28 (63.6)</td>
<td>0.099</td>
</tr>
<tr>
<td>Symptom severity score (median (IQR))</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>– Hoarseness</td>
<td>2.0 (1.0, 3.0)</td>
<td>2.0 (1.0, 2.0)</td>
<td>0.398</td>
</tr>
<tr>
<td>– Throat-clearing</td>
<td>2.0 (1.0, 2.0)</td>
<td>2.0 (1.0, 2.0)</td>
<td>0.458</td>
</tr>
<tr>
<td>– Globus</td>
<td>1.0 (0.0, 2.0)</td>
<td>2.0 (1.0, 2.0)</td>
<td>0.555</td>
</tr>
<tr>
<td>– Sore throat</td>
<td>1.0 (0.0, 2.0)</td>
<td>1.0 (0.0, 2.0)</td>
<td>0.190</td>
</tr>
<tr>
<td>– Chronic cough</td>
<td>1.5 (0.0, 2.0)</td>
<td>1.0 (0.0, 2.0)</td>
<td>0.071</td>
</tr>
<tr>
<td>– Choking at night</td>
<td>0.2 (0.0, 1.0)</td>
<td>0.5 (0.0, 1.0)</td>
<td>0.883</td>
</tr>
<tr>
<td>– Heartburn</td>
<td>1.0 (0.0, 2.0)</td>
<td>0.5 (0.0, 1.0)</td>
<td>0.019(^2)</td>
</tr>
<tr>
<td>– Regurgitation</td>
<td>0.2 (0.0, 1.0)</td>
<td>0.2 (0.0, 1.0)</td>
<td>0.763</td>
</tr>
<tr>
<td>– Odynophagia</td>
<td>0.0 (0.0, 1.0)</td>
<td>0.0 (0.0, 1.0)</td>
<td>0.721</td>
</tr>
<tr>
<td>Erosive oesophagitis (n (%))</td>
<td>14 (25)</td>
<td>7 (15.9)</td>
<td>0.268</td>
</tr>
<tr>
<td>Videolaryngoscopic score (mean (SD))</td>
<td>8.9 (3.4)</td>
<td>7.6 (4.0)</td>
<td>0.083</td>
</tr>
<tr>
<td>Vocal dysfunction degree (mean (SD))</td>
<td>0.9 (0.9)</td>
<td>0.9 (0.9)</td>
<td>0.654</td>
</tr>
<tr>
<td>Total VHI score (mean (SD))</td>
<td>27.3 (21.9)</td>
<td>26.3 (21.6)</td>
<td>0.834</td>
</tr>
<tr>
<td>HAD, anxiety score (mean (SD))</td>
<td>4.7 (6.2)</td>
<td>8.6 (4.9)</td>
<td>0.036(^3)</td>
</tr>
<tr>
<td>HAD, depression score (mean (SD))</td>
<td>4.5 (3.7)</td>
<td>4.6 (3.6)</td>
<td>0.880</td>
</tr>
<tr>
<td>General well-being score (mean (SD))</td>
<td>48.5 (20.6)</td>
<td>45.7 (21.5)</td>
<td>0.531</td>
</tr>
</tbody>
</table>

Quantitative parameters are expressed as mean and standard deviation (SD); non-parametric data are expressed as median and interquartile range (IQR; 25th and 75th percentiles). *\(n = 56; \quad n = 44; \quad \text{Statistically significant difference}; \quad p < 0.05. \quad \text{Yr} = \text{years}; \quad \text{VHI} = \text{voice handicap index}; \quad \text{HAD} = \text{hospital anxiety and depression scale}*

### Table III

**Factors significantly predictive of response to one-month omeprazole treatment: logistic regression analysis**

<table>
<thead>
<tr>
<th>Factor</th>
<th>B</th>
<th>(p)</th>
<th>OR</th>
<th>95.0% CI for OR</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lower</td>
<td>Upper</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medication dose</td>
<td>-1.11</td>
<td>0.027</td>
<td>3.05</td>
<td>1.13 8.33</td>
</tr>
<tr>
<td>Heartburn score</td>
<td>0.68</td>
<td>0.004</td>
<td>1.99</td>
<td>1.24 3.20</td>
</tr>
<tr>
<td>Anxiety score</td>
<td>-0.13</td>
<td>0.014</td>
<td>1.15</td>
<td>1.03 1.28</td>
</tr>
</tbody>
</table>

Significance level, \(p < 0.05. \text{B} = \text{logistic regression coefficient}; \text{OR} = \text{odds ratio}; \text{CI} = \text{confidence interval}**
points). However, these data should be interpreted with caution, because of the small number of further non-responders (n = 6).

- **Diagnostic criteria for patients with laryngopharyngeal reflux (LPR) are symptoms, videolaryngoscopic findings and positive response to empirical proton pump inhibitor (PPI) treatment**
- **This study investigated whether patients with suspected LPR benefited from one and three months of empirical PPI treatment, and whether any pre-therapy factors predicted the success of treatment**
- **Results suggest that three months’ PPI treatment is warranted to confirm suspicion of LPR. Patients without psychological distress, with hoarseness, and receiving omeprazole 20 mg twice daily were most likely to benefit from one month’s empirical PPI treatment**

In a few trials analysing predictors of response to PPI treatment, Williams et al.\(^5\) evaluated 20 LPR patients and found that neither baseline symptoms, endoscopic findings, laryngitis severity, oesophageal acid exposure (on pH testing) nor speaking voice measures predicted the outcome throughout three months of treatment. Park et al.\(^10\) found that pre-therapy interarytenoid mucosa and true vocal fold abnormalities were associated with a two-fold increase in symptom response after four months of PPI treatment. Garrigues et al.\(^11\) in a study of 91 patients with posterior laryngitis, found that response to omeprazole 20 mg twice daily was associated with a lower age (after three months) and a lower duration of laryngeal symptoms (after six months), but concluded that a consistent prediction of response could not be made. Our analysis showed no predictive value for age.

Our study could have been limited by including LPR diagnosis without pH monitoring, although we followed currently accepted recommendations.\(^1,4\) Because of the very small number of non-responders at three months of treatment, data on pre-therapy predictors of response should be interpreted with caution. Further investigation on this point is needed.

However, our study findings are in agreement with others, that is, at least three months of empirical PPI treatment, of adequate dose, are required to confirm LPR diagnosis. Careful selection of patients is critical for positive treatment response. Our results suggest that patients without psychological distress and with hoarseness, treated with twice daily PPI, are more likely to benefit from empirical PPI treatment more quickly, i.e. in one month.

### Conclusion

Three months of twice daily PPI treatment is warranted in order to confirm the suspicion of LPR. Three pre-therapy factors were revealed as significant predictors for one-month omeprazole treatment response: anxiety, heartburn score and medication dose. A high pre-therapy anxiety score decreased the odds ratio of a positive response 1.15-fold.
while a high heartburn score and omeprazole 20 mg twice daily increased the odds by two- and threefold.

We found that patients’ demographic parameters, laryngeal symptoms, videolaryngoscopic scores, endoscopic findings, vocal dysfunction degree, voice handicap index and general well-being assessment scores did not predict the one-month omeprazole treatment outcome.

No statistically significant association was found between any of the evaluated pre-therapy factors and the response to three-month omeprazole treatment.

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Dr N Siupsinskiene takes responsibility for the integrity of the content of the paper.

Competing interests: None declared