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The Impact of Nutrition on the Onset, Course of the Disease and Quality of Life of Patients with Laryngopharyngeal Reflux

Running head: Nutrition and Laryngopharyngeal Reflux

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SUMMARY

Research background. The role of dietary habits in patients with laryngopharyngeal reflux disease (LPR) is comparatively underexplored. The aim of the study is to examine dietary habits, onset and course of the disease as well as the quality of life of patients with LPR.

Experimental approach. The results of the modified food frequency questionnaire (FFQ-m) and Laryngopharyngeal Reflux Health-Related Quality of Life (LPR-HRQL) questionnaires were compared between subjects with and without LPR. There were a total of 100 subjects with LPR and 65 subjects in the control group. The group of subjects with LPR was further randomly divided into two subgroups; the first subgroup was treated with esomeprazole in a twice daily dose of 20 mg combined with dietary and general lifestyle changes instructions, and the other with pantoprazole in a twice-daily dose of 20 mg combined with dietary and general lifestyle changes instructions. Participants were instructed to fill out FFQ-m and LPR-HRQL questionnaires immediately after the initial examination and then after control examinations that were 30 and 60 days after the initial examination.

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Results and conclusions. Patients with LPR consume more food with high reflux potential, drink more carbonated drinks and juices, and have a worse quality of life compared to the control group ($p<0.001$). Proton pump inhibitors in a twice-daily dose of 20 mg with a change in dietary habits, such as avoiding acidic, spicy, fermented, sweet, and fried foods same as other foods with a high reflux potential as well as carbonated drinks and juices with the introduction of foods with a low reflux potential and water significantly reduces symptoms of LPR and increases the quality of life ($p<0.001$).

Novelty and scientific contribution. This is the first study showing the connection between dietary habits and quality of life in patients with LPR. The contribution of this research is an objective review of the follow-up of patients with LPR that could be used in their regular assessment.

Keywords: laryngopharyngeal reflux; food; quality of life; dietary habits

INTRODUCTION

Laryngopharyngeal reflux (LPR) is a clinical entity that represents the return of gastric contents into the space of the larynx and hypopharynx, where it makes close contact with the tissues of the upper aerodigestive tract (*1*). Two theories explain the pathogenesis of reflux laryngitis. The first is the theory of direct injury to the mucosa of the larynx and surrounding tissue by acid and pepsin. This results in damage to the mucociliary transport and accumulation of secretions in the throat, which causes additional irritation of the mucosa and contributes to the onset of symptoms of laryngopharyngeal reflux. Namely, the larynx does not have protective external cleaning mechanisms and saliva cover that neutralize acid, so the gastric refluxate remains undiluted for a longer period of time, resulting in tissue injury. The second theory that explains the pathogenesis of reflux laryngitis is the reflex theory. According to this theory, LPR occurs due to oesophageal reflux, which stimulates vagally mediated reflexes resulting in chronic throat clearing and coughing that leads to mucosal injury of the larynx (*2,3*). Nine of the most common symptoms of LPR were quantified by the American author Belafsky (*4*) in the so-called reflux symptom index (RSI), and based on years of experience, he concluded that if the RSI is greater than 13, suspicion of LPR can be raised. Depending on the severity of the symptoms, it is necessary to score the severity using a scale of 0–5 [0 (no symptoms) to 5 (strong presentation of symptoms)]. The most common symptoms of LPR are hoarseness, throat clearing, postnasal drip, swallowing difficulties, coughing after meals or upon lying down, feeling of choking, coughing attack, globus sensation, heartburn, and chest pain. Belafsky quantified the eight most common clinical signs of LPR in the reflux finding score (RFS). If the RFS is greater than 7, suspicion of LPR can be raised. The doctor calculates the RFS based on the presence or absence and severity of clinical signs of LPR. Some of the most common clinical signs of the disease are vocal

fold oedema, granulation tissue, laryngeal posterior commissure hypertrophy, erythema, subglottic oedema, diffuse laryngeal oedema, ventricular obliteration, and thick endolaryngeal secretion (*5*). Considering the severity of the symptoms and the impact on the quality of life of the patients, LPR can be mild, severe, and life-threatening. Mild LPR bothers patients but does not interfere with their daily activities. Severe LPR significantly impairs the quality of life and hinders patients in their daily tasks and personal activities. Life-threatening LPR is present in patients with airway obstruction (*6,7*).

There is no gold standard for the treatment of LPR. LPR is treated with changes in diet, lifestyle and drugs such as proton pump inhibitors (*8*). Dietary measures include: avoiding tea, coffee, greasy, fried, spicy foods, alcohol, fatty foods, chocolate, and soda. The intake of alkaline foods such as bananas and melons is recommended. As for drinks, only plain or alkaline water is recommended. Furthermore, food should be consumed in smaller portions, more frequently, and should not be taken within two hours of bedtime. It is necessary to elevate the top of the bed when lying down, and one should not lie down immediately after eating. If the person is a smoker, it is necessary to quit smoking (*3,9*). In addition to conservative treatment, surgical procedures such as transoral fundoplication and magnetic sphincter augmentation (*3,10*) can be performed in patients who are refractory to conservative therapy.

It is known that lifestyle and dietary habits, such as smoking, alcohol consumption, and the consumption of acidic, sweet, and spicy foods, play a significant role in the development of LPR. The food frequency questionnaire is commonly used to assess dietary habits in clinical studies, which estimates the frequency of consumption of beverages and foods (*11,12*). Lifestyle habits, including eating habits, vary in different countries and are often culturally conditioned (*13,14*). Therefore, eating habits should be studied separately for each region. Furthermore, the role of eating habits in patients with laryngopharyngeal reflux disease is comparatively underexplored. In our study, we aim to examine eating habits and their impact on the onset, course of disease, and quality of life in patients with LPR in eastern Croatia.

MATERIALS AND METHODS

Study design

The study was designed as a controlled non-randomized clinical trial with the aim of investigating the impact of diet on the onset, course of disease, and quality of life in patients with LPR. Participants were divided into two main groups: patients with LPR and a control group without LPR. Each participant underwent a comprehensive otorhinolaryngological examination followed by laryngeal endoscopy.

The first group consisted of participants who suffered from LPR. The diagnosis of LPR was based on RSI (Reflux Symptom Index) and RFS (Reflux Finding Score) scores. Patients with RSI scores greater than 13 and RFS scores greater than 7 were included in the first group of LPR patients. Patients with RSI scores less than or equal to 13 and RFS scores less than or equal to 7 were included in the control, healthy group.

The first LPR group was randomly divided into two subgroups according to the type of proton pump inhibitor (esomeprazole or pantoprazole) using a remote computer-generated code to esomeprazole or pantoprazole. The first subgroup was treated with esomeprazole at a twice-daily dose of 20 mg and received written dietary and general lifestyle changes instructions. They adhered to the therapy and instructions for 60 days. The second subgroup was treated with pantoprazole at a twice-daily dose of 20 mg and received written dietary and general lifestyle instructions for 60 days as well.

The general lifestyle instructions included eating small meals, managing stress, sleeping with an elevated headrest, avoiding eating before bedtime, quitting smoking, and avoiding caffeine consumption before bedtime. All participants documented their daily food intake from the initial examination to the last follow-up examination. In addition, instructions were given on how to record daily food intake. According to the daily food intake diary, all patients' food consumption was evaluated using the Refluxogenic Diet Score, which was developed by Lechien *et al*. (*15*). The Refluxogenic Diet Score is based on the pH value of the food and its composition. Based on the final score, all foods are categorized into one of five categories depending on their refluxogenic potential. In line with the results of the Refluxogenic Diet Score, we classify foods into categories of low and high refluxogenic potential. Therefore, dietary instructions also included recommendations for consuming low-refluxogenic foods according to the Refluxogenic Diet Score, such as corn, rice, oatmeal, melons, watermelon, carrots, lettuce, and cereals, and avoiding high-refluxogenic foods such as yogurt, pears, apples, oranges, grapefruit, mandarins, nectarines, peaches, bacon, butter, and cookies. Additionally, each participant was required to complete a modified food frequency questionnaire (FFQ-m) and Laryngopharyngeal Reflux Health-Related Quality of Life (LPR-HRQL) questionnaires. Participants were instructed to fill out the FFQ-m and LPR-HRQL questionnaires immediately after the initial examination and after the follow-up examinations, which were conducted 30 and 60 days after the initial examination.

Participants

The study included adult patients with LPR who presented for the first time at the Clinic of Otorhinolaryngology and Head and Neck Surgery at the Clinical Hospital Center Osijek who

responded positively to the invitation to participate in the study. The control group consisted of healthy adult participants who did not have LPR and were scheduled for surgery for otapostasis, deviated septum, nasal polyps or were employees of the Clinical Hospital Center Osijek and agreed to participate in the study. Participants were informed about the study and their written consent was obtained. The study was approved by the Ethics Committee of the School of Medicine, University of Osijek (UR number: 2158-61-46-22-39).

Recruitment was conducted until a total of 200 participants was reached. Exclusion criteria were gastrointestinal ulcer disease, chronic atrophic gastritis, cancers, and treatment with proton pump inhibitors, antacids, or H2 blockers. Additionally, participants who did not correctly complete all the questionnaires were excluded from the analysis. Thirty-five participants did not meet the inclusion criteria. Therefore, 165 participants were included in the study, with 100 participants in the LPR group and 65 participants in the control group.

FFQ-m questionnaire

FFQ-m questionnaire is a tool used to estimate the frequency of consumption of foods and beverages in the last month (*16*). A modified questionnaire was used based on an existing one developed by Močić Pavić *et al.* (*17*) and validated in Croatia. The questionnaire was modified by regrouping certain food groups and only assessing the frequency of consumption of a particular food item, without evaluating the portion size. The modified FFQ contained 75 different food and beverage items divided into 12 different groups. The food categories were: fast food (i), milk and dairy products (ii), milk and dairy products with added sugar (iii), fats and oils (iv), cereals (v), salty snacks, sweets, and cakes (vi), breakfast cereals (vii), processed meat (viii), juices (ix), vegetables (x), fruit (xi), and meat, fish, and eggs (xii). The frequency of food consumption is scored in the range from 0 to 8, where 0 means never, 1 refers to one to three times a month, 2 to once every week, 3 to two to four times a week, 4 to five to six times a week, 5 once a day, 6 two to three times a day, 7 four to five times a day and 8 refers to six or more times a day (*17*).

LPR-HRQL questionnaire

The LPR-HRQL questionnaire is comprised of 43 queries that assess how often or to what degree the respondent experiences certain feelings. The first 12 queries pertain to speech, singing, and voice, and, when combined with the 13th query on the impact of voice on quality of life, constitute the Voice/Hoarse domain. The Cough domain is comprised of queries 14-19, which evaluate coughing, along with the 20th query on the impact of coughing on quality of life. The Clear Throat domain consists of queries 21-26, which evaluate clearing the throat, and the 27th query on the impact

of clearing the throat on quality of life. Queries 28-32 pertain to swallowing and general throat-related symptoms, with the 33rd query assessing the impact of swallowing on quality of life, thus comprising the Swallow domain. Finally, queries 34-43 evaluate the impact of acid reflux symptoms on quality of life and constitute the Overall Impact of the Acid Reflux domain. A standard Likert scale ranging from 0 to 6 is used, with a higher score indicating more frequent LPR symptoms, i.e. 0 refers to never, 1 to once a month, 2 to two to three days a month, 3 to one day a week, 4 on two to three days a week, 5 on four to 5 days a week and 6 refers to six to 7 days a week. The score for the last question in each domain, as well as all 10 questions in the Overall Impact of Acid Reflux domain, range from 1 (no effect on Health-Related Quality of Life) to 10 (enormous effect on Health-Related Quality of Life) (*18,19*).

Statistical analysis

Categorical data are represented by absolute and relative frequencies. The normality of the distribution of numerical variables was tested with the Shapiro-Wilk test. Numerical data are described by the median and the limits of the interquartile range. Differences between two independent groups were tested with the Mann-Whitney U test (95 % CI difference), and between measurements with the Friedman test (post hoc Conover). All P values were two-sided. The significance level was set at Alpha = 0.05. The statistical analysis was performed using MedCalc® Statistical Software and SPSS (*20,21*).

RESULTS AND DISCUSSION

The study was conducted on 165 participants, among whom 65 (39.4 %) were in control group and 100 (60.6 %) were participants with symptoms of laryngopharyngeal reflux (LPR). There was a total of 69 (41.8 %) men and 96 (58.2 %) women. The median age of all participants was 49 years (interquartile range 18 to 82 years). In the group of participants with LPR, 36 (51 %) were on Pantoprazole therapy and 34 (49 %) were on Esomeprazole therapy. In our study, the LPR-HRQL questionnaire was used to assess the quality of life of patients with LPR and the control group as the treatment outcome. In addition to pantoprazole and esomeprazole therapy, other proton pump inhibitors such as omeprazole, lansoprazole, and rabeprazole have often been used in other studies. The success rate in treating LPR symptoms with these proton pump inhibitors ranges from 18 % to 87 % without significant differences in treatment outcomes based on the therapy used (*4,22,23*). Comparable to the results of these studies and considering the treatment outcome through subjective assessment of quality of life using the LPR-HRQL questionnaire, there was no significant difference in any of the domains of the LPR-HRQL questionnaire between patients who used esomeprazole and

pantoprazole after 30 and 60 days of therapy. Additionally, the median value of the overall impact of acid reflux is lower after 30 and 60 days in both mentioned groups compared to the value at the initial examination (Table 1).

In the group of patients with LPR, at the initial examination, there were significantly higher values (more frequent occurrence of symptoms, $p<0.001$) in all domains of the LPR-HRQL questionnaire, compared to the control group. It should also be noted that the most common symptom in the group of patients with LPR was voice hoarseness (Table 2). Patients with LPR had similar median values in all of the domains of the LPR-HRQL questionnaire compared to values reported by other authors (*18,19*). However, small differences were found between our study and a Swedish study (*18*), in which the results show lower values of all LPR-HRQL domains compared to our study, which could be explained by different cultural settings and differences in dietary habits.

In the group of patients with LPR, the values of all LPR-HRQL domains were significantly lower ($p<0.001$) after 60 days from the initial examination (Table 3). Therefore, we can say that the recommended therapy with proton pump inhibitors along with instructions on diet and lifestyle changes was definitely a success. Carrau *et al.* (*19*) in their study measured the LPR-HRQL at baseline, after 4 and 6 months, and the therapy used was omeprazole twice a day at a dose of 20 mg. Our study shows a similar improvement in scores between pre-treatment and post-treatment status compared to Carrau's study, although the measurements were taken after 4 and 8 weeks. Furthermore, in our study, dietary and general lifestyle instructions were given to the patients in addition to proton pump inhibitors as part of the treatment. Several studies using the LPR-HRQL and surgical interventions such as fundoplication for LPR treatment have also shown significant improvement in scores pre- and post-operatively (*24,25*).

We examined the dietary habits of participants with LPR and the control group using a modified food frequency questionnaire (FFQ). Compared to patients with LPR at the beginning of the research, the control group significantly more frequently consume pudding, semolina, polenta, rice, corn (cooked/baked), cornflakes, oatmeal, muesli, sugar-free soft drinks, bananas, melons, watermelon, carrots, spinach, chard, and lettuce. The group of patients with LPR symptoms significantly more frequently consume sour cream (12 % fat “blue”), yogurt, acidophilus milk, kefir (2.8 % to 3.2 % fat), fruit yogurt, white bread (pastries and puff pastry), carbonated soft drinks, fruit syrups (fruit concentrate), apples or pears, oranges, grapefruits, mandarins, peaches, nectarines, grapes, onions, garlic, breaded pork, bacon, cookies, margarine, oils, and hamburgers (Table 4). According to the results, patients with LPR significantly more frequently consume more fatty, fermented, sweet, and acidic foods and acidic drinks, which can increase the number of proximal reflux episodes and are important risk factors for developing LPR (*8,26*). Lechien *et al.* (*15*) developed the Refluxogenic Diet

Score as an objective score for assessing the refluxogenic potential of the food. In our study, participants without signs of LPR consume more food classified as low refluxogenic food according to the Refluxogenic Diet Score, such as corn, rice, oatmeal, bananas, melons, watermelon, carrots, lettuce, and cereals. According to our results, participants with LPR symptoms significantly more frequently consume food classified as high refluxogenic food according to the Refluxogenic Diet Score, such as yogurt, pears, apples, oranges, grapefruits, mandarins, nectarines, peaches, bacon, pork, butter, and cookies (Table 4).

In addition to proton pump inhibitors, patients with LPR received written instructions on diet and lifestyle changes. They documented their daily food intake, and according to the instructions, it was explained to them which foods were low and which were high refluxogenic (*15*). Patients with LPR significantly reduced the frequency of consumption of a large number of foods that are considered high refluxogenic according to the Refluxogenic Diet Score (Table 5 and Table 6). Such a change in diet could have an effect on the reduction of LPR symptoms, i.e. on a significant reduction in the value of all LPR-HRQL domains and an improvement in the quality of life, which can be seen in Table 3. It is very important to give clear instructions to patients to change their lifestyle and diet, to encourage them to write down the foods they consume daily and of course to monitor and advise them regularly. Runggaldier in their analysis of LPR therapy, particularly emphasize the significance of diet, which they consider one of the key factors for the success of LPR treatment (*27*). Also, the meta-analysis by Min and associates demonstrated that avoiding fatty foods, chocolate, and coffee while adopting a Mediterranean diet and consuming alkaline water significantly reduces the symptoms and clinical signs of LPR (*28*). However, although there is a great emphasis on lifestyle and diet changes, the patients in our study used proton pump inhibitors daily, which could have contributed to better LPR-HRQL results. It is also interesting to mention the study by Yang and colleagues, in which they compared the treatment of LPR using dietary change and lifestyle with medication-based treatment. As much as 95% of the participants in the group treated with diet change reported subjective improvement of LPR symptoms after the treatment. On the other hand, in the group of participants treated solely with anti-reflux medications, improvement was reported by only 48% of the participants (*29*).

One of the limitation of this study is that the dietary habits in this study are specific to the population of eastern Croatia and may differ greatly from other regions, but despite this, it shows a difference in the consumption of certain food groups between participants with and without LPR. Also, FFQ-m questionnaire is so far only validated for the adolescent population and not for adults. Furthermore, one of the limitations of this study is that the treatment outcome was assessed using the subjective LPR-HRQL questionnaire, which is still a subjective measure, and the comparison of

the quality of life was conducted only between the use of esomeprazole and pantoprazole. Additionally, this study could be further adapted and expanded by including an additional dietary questionnaire and comparing the quality of life after the use of various different proton pump inhibitors available on the market.

CONCLUSIONS

Treatment with proton pump inhibitors in a twice-daily dose of 20 mg with dietary and general lifestyle changes for a duration of two months reduces symptoms across all domains of LPR and improves the quality of life. Patients with LPR consume more high-reflux potential foods and drink more carbonated beverages and juices compared to the healthy population, which consumes more low-reflux potential foods and non-alcoholic beverages. Changing dietary habits to include low-reflux potential foods and water while avoiding acidic, spicy, fermented, sweet, fried foods, high-reflux potential foods, carbonated beverages, and juices significantly reduces symptoms in all domains of LPR and improves quality of life. The use of LPR HRQL as an instrument can facilitate future research aimed at evaluating and comparing different LPR therapies.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

AUTHORS' CONTRIBUTION

The authors confirm their contribution to the paper as follows: T. Prpić and A. Včeva designed the study. T. Prpić, T. Mendeš and M. Peček Prpić collected the data. T. Prpić and A. Šestak analyzed and interpreted the results. T. Prpić prepared the draft of the manuscript. All authors reviewed the results and approved the final version of the manuscript.

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REFERENCES

1. Silva ÁS, Duprat AC, Machado SR, Melo DN, Nascimento Ribeiro DK. Evaluation of the Reflux Symptom Index and the Endolaryngeal Findings Scale after Treatment in Individuals with Laryngopharyngeal Reflux. Int Arch Otorhinolaryngol. 2021;25(1):e115–e122. https://doi.org/10.1055/s-0040-1702967

2. Kowalik K, Krzeski A. The role of pepsin in the laryngopharyngeal reflux. Otolaryngol Pol. 2017;71(6):7-13. https://doi.org/10.5604/01.3001.0010.7194

3. Včeva A, Mihalj H, Zubčić Ž, Kotromanović Ž, Birtić D, Mihalj M, *et al*. Laryngopharyngeal reflux is not gastroesophageal reflux. Med Vjesn. 2011;43(1-4): 73-84 (in Croatian).

4. Belafsky PC, Postma GN, Koufman JA. The validity and reliability of the reflux finding score (RFS). Laryngoscope. 2001;111(8):1313-7. https://doi.org/10.1097/00005537-200108000-00001

5. Pizzorni N, Ambrogi F, Eplite A, Rama S, Robotti C, Lechien J, *et al.* Magnesium alginate versus proton pump inhibitors for the treatment of laryngopharyngeal reflux: a non-inferiority randomized controlled trial. Eur Arch Otorhinolaryngol. 2022;279(5):2533–42. https://doi.org/10.1007/s00405-021-07219-0

6. Lechien JR, Saussez S, Muls V, Barillari MR, Chiesa-Estomba C, Hans S, *et al.* Laryngopharyngeal Reflux: A State-of-the-Art Algorithm Management for Primary Care Physicians. J Clin Med. 2020;9(11):3618. https://doi.org/10.3390/jcm9113618

7. Han H, Lyu Q, Zhao J. Laryngopharyngeal Reflux in Hypertrophic Laryngeal Diseases. Ear Nose Throat J. 2022;101(4):NP158-NP163. https://doi.org/10.1177/0145561320953232

8. Kuo CFJ, Kao CH, Dlamini S, Liu SC. Laryngopharyngeal reflux image quantization and analysis of its severity. Sci Rep. 2020;10:10975. https://doi.org/10.1038/s41598-020-67587-1

9. Zalvan CH, Hu S, Greenberg B, Geliebter J. A Comparison of Alkaline Water and Mediterranean Diet vs Proton Pump Inhibition for Treatment of Laryngopharyngeal Reflux. JAMA Otolaryngol Head Neck Surg. 2017;143(10):1023–9. https://doi.org/10.1001/jamaoto.2017.1454

10. Krause AJ, Walsh EH, Weissbrod PA, Taft TH, Yadlapati R. An update on current treatment strategies for laryngopharyngeal reflux symptoms. Ann N Y Acad Sci. 2022;1510(1):5-17.

https://doi.org/10.1111/nyas.14728

11. Willett W, editor. Nutritional epidemiology. Oxford, UK: Oxford University Press; 2012.

12. Fernández-Cao JC, Aparicio E. Design, development and validation of Food Frequency Questionnaires for the diabetic population: protocol for a systematic review and meta-analysis. BMJ Open. 2022;12(9):e058831.
https://doi.org/10.1136/bmjopen-2021-058831

13. Wang M, Mo T, Tan J, Dai Y, Li X. Risk Factor-Related Lifestyle Habits of Patients With Laryngopharyngeal Reflux. Ear Nose Throat J. 2022;1455613221078182.
https://doi.org/10.1177/01455613221078182

14. Li F, Lin Q, Jang Q, Xi Y, Liu H, Luo J, *et al*. The Association between Free Sugars Consumption and Laryngopharyngeal Reflux: A Cross-Sectional Study among Chinese Adolescents. Nutrients. 2021;13(9):3012.
https://doi.org/10.3390/nu13093012

15. Lechien JR, Bobin F, Mouawad F, Zelenik K, Calvo-Henriquez C, Chiesa-Estomba CM, et al. Development of scores assessing the refluxogenic potential of diet of patients with laryngopharyngeal reflux. Eur Arch Otorhinolaryngol. 2019;276(12):3389-404.
https://doi.org/10.1007/s00405-019-05631-1

16. Vered SA, Levi CS, Rozen GA, Solt I, Rozen GS. Development and validation of a computerized web-based quantitative food frequency questionnaire. Clin Nutr ESPEN. 2022;52:169-77.
https://doi.org/10.1016/j.clnesp.2022.10.012

17. Močić Pavić A, Sila S, Niseteo T, Hojsak I, Kolaček S. Development and Validation of a Food Frequency Questionnaire for Population of Adolescents in Croatia. Food Technol Biotechnol. 2021;59(1):74-81.
https://doi.org/10.17113/ftb.59.01.21.6630

18. Andersson O, Ryden A, Ruth M, Ylitalo Moller R, Finizia C. Validation of the Swedish translation of LPR-HRQL. Med Sci Monit. 2010;16(10):CR480-7.

19. Carrau RL, Khidr A, Gold KF, Crawley JA, Hillson EM, Koufman JA, *et al*. Validation of a quality-of-life instrument for laryngopharyngeal reflux. Arch Otolaryngol Head Neck Surg. 2005;131(4):315-20.
https://doi.org/10.1001/archotol.131.4.315

20. MedCalc® Statistical Software version 20.218 (MedCalc Software Ltd, Ostend, Belgium; https://www.medcalc.org; 2023).

21. SPSS ver. 23 (IBM Corp. Released 2015., Version 23.0. Armonk, NY: IBM Corp.).

22. Lechien JR, Mouawad F, Barillari MR, Nacci A, Khoddamo SM, Enver N, *et al.* Treatment of laryngopharyngeal reflux disease: A systematic review. World J Clin Cases. 2019;7(19):2995-3011. https://doi.org/10.12998/wjcc.v7.i19.2995

23. Eherer AJ, Habermann W, Hammer HF, Kiesler K, Friedrich G, Krejs GJ. Effect of pantoprazole on the course of reflux-associated laryngitis: a placebo-controlled double-blind crossover study. Scand J Gastroenterol. 2003;38(5):462-7. https://doi.org/10.1080/00365520310001860

24. Aiolfi A, Cavalli M, Saino G, Khor D, Sozzi A, Rausa E, *et al*. Laparoscopic Toupet Fundoplication for the Treatment of Laryngopharyngeal Reflux: Results at Medium-Term follow-Up. World J Surg. 2020;44(11):3821-8. https://doi.org/10.1007/s00268-020-05653-5

25. Addo A, George P, Zahiri HR, Park A. Patients with ineffective esophageal motility benefit from laparoscopic antireflux surgery. Surg Endosc. 2021;35(8):4459-68. https://doi.org/10.1007/s00464-020-07951-4

26. Kesari SP, Chakraborty S, Sharma B. Evaluation of Risk Factors for Laryngopharyngeal Reflux among Sikkimese Population. Kathmandu Univ Med J (KUMJ). 2017;15(57):29-34.

27. Runggaldier D, van Schie B, Marti S, Bohlender JE. Aktuelle Möglichkeiten und Herausforderungen bei der Therapie des laryngopharyngealen Refluxes [Current possibilities and challenges in the treatment of laryngopharyngeal reflux]. HNO. 2023 May;71(5):294-303. (in German). https://doi.org/10.1007/s00106-023-01280-3

28. Min C, Park B, Sim S, Choi HG. Dietary modification for laryngopharyngeal reflux: systematic review. J Laryngol Otol. 2019 Feb;133(2):80-86 https://doi.org/10.1017/S0022215118002256

29. Yang J, Dehom S, Sanders S, Murry T, Krishna P, Crawley BK. Treating laryngopharyngeal reflux: Evaluation of an anti-reflux program with comparison to medications. Am J Otolaryngol. 2018 Jan-Feb;39(1):50-55. https://doi.org/10.1016/j.amjoto.2017.10.014

Table 1. Differences in the LPR-HRQL scale based on applied therapy at three measurement points

Group with LPR symptoms	Median (interquartile range)		Difference (95 % confidence interval)	p*
	Pantoprazol	*Esomeprazol*		
First examination				
Voice/hoarseness	22 (14–28)	16 (9–22)	-5 (-9–0)	0.03
Cough	11 (9–14)	9 (6-11)	-3 (-5–0)	0.06
Clearing the throat	11 (7–14)	8 (5–16)	-2 (-4–2)	0.33
Swallowing	7 (4–11)	8 (6–12)	1 (-2–3)	0.48
The overall impact of acid reflux	36 (29–47)	34 (28–40)	-3 (-10–3)	0.34
After 30 days				
Voice/hoarseness	14 (9–22)	11 (7–19)	-2 (-7–2)	0.25
Cough	6 (2–10)	3 (0–9)	-2 (-5–0)	0.09
Clearing the throat	6 (2–10)	4 (1–6)	-1 (-3–1)	0.38
Swallowing	4 (2–9)	6 (3–10)	1 (-1–3)	0.44
The overall impact of acid reflux	31 (15–40)	28 (22–39)	-1 (-8–7)	0.78
After 60 days				
Voice/hoarseness	11 (9–14)	9 (6–11)	-3 (-5–0)	0.05
Cough	2 (1–7)	3 (0–4)	0 (-2–1)	0.61
Clearing the throat	2 (1–5)	3 (1–5)	0 (-1–2)	0.83
Swallowing	3 (2–6)	3 (2–6)	0 (-2–2)	0.88
The overall impact of acid reflux	20 (13–25)	20 (14–29)	0 (-6–6)	0.90

*= Mann Whitney U test

Table 2. The difference in individual domains of the LPR-HRQL scale compared to the groups at the initial examination

	Median (interquartile range)		Difference (95 % confidence interval)	p*
	Control group	Group with LPR		
Initial examination				
Voice/hoarseness	5 (4–7)	19 (11–26)	10 (8–14)	<0.001
Cough	0 (0–3)	8 (3–12)	6 (4–7)	<0.001
Throat clearing	0 (0–2)	9 (5–14)	8 (6–9)	<0.001
Swallowing	0 (0–3)	7 (4–11)	6 (4–7)	<0.001
The overall impact of acid reflux	10 (9–20)	32 (24–43)	19 (15-22)	<0.001

*= Mann Whitney's U test

Table 3. Ratings of LPR-HRQL questionnaire in a group of patients with LPR at three measured points

Group with symptoms of LPR	Median (interquartile range)			p*
	Initial examination	After 30 days	After 60 days	
Voice/hoarseness	19 (11–26)	13 (8–21)	10 (7–13)	<0.001†
Cough	8 (3–12)	4 (1–9)	2 (0–6)	<0.001†
Throat clearing	9 (5–14)	5 (2–10)	2 (1–5)	<0.001†
Swallowing	7 (4–11)	7 (3–10)	3 (2–6)	<0.001†
The overall impact of acid reflux	32 (24–43)	31 (18–40)	20 (14–26)	<0.001†

*= Frideman's test (post hoc Conover), †= at the level of $P < 0.05$, the ratings significantly differ in all three measurement points

Table 4. Differences in the frequency of consumption of individual food items (divided in food categories according to modified FFQ) at initial examination with respect to the groups

	Median (interquartile range)		p*
	Control group	Group with LPR	
Milk and dairy products			
Cream (12 % milk fat content, "blue")	2 (1-2)	3 (1-4)	<0.001
Yogurt, acidophilus, kefir (2.8-3.2 % milk fat content)	2 (1-3)	3 (1-4)	<0.001
Fruit yogurt	1 (1-2)	2 (1-3)	0.02
Pudding	2 (1-3)	2 (0-2)	0.02
Cereals			
White bread (rolls and croissants)	3 (1-4)	5 (3-5)	<0.001
Semolina	2 (1-3)	1 (0-2)	<0.001
Polenta	2 (1-3)	1 (0-2)	<0.001
Rice	3 (2-4)	2.5 (1-3)	0.03
Corn (cooked/roasted)	2 (2-3)	1 (0-2)	<0.001
Breakfast cereals			
Cornflakes	2 (1-3)	1 (0-2)	<0.001
Oatmeal and muesli	2 (1-2)	1 (0-2)	<0.001
Juices			
Orange juice	2 (2-3)	3 (2-4)	0.01
Carbonated soft drinks	2 (1-3)	3 (2-4)	<0.001
Non-alcoholic drinks (sugar-free)	6 (5-7)	4.5 (3-5)	<0.001
Fruit syrup (syrup concentrates)	2 (0-2)	2 (1-3)	<0.001
Fruit			
Apple or pear	2 (1-3)	3 (2-4)	0.01
Orange, grapefruit, mandarin	2 (1-3)	3 (1.25-4)	<0.001
Banana	3 (2–3.5)	2 (1-3)	<0.001
Peach, nectarine	1 (0-2)	2 (0-3)	0.02
Melon, watermelon	2 (1-3)	1 (0-1)	<0.001
Grapes	1 (0-2)	2 (1-3)	<0.001
Vegetables			
Onion, garlic	2 (1-3)	3 (2-4)	<0.001

Carrot	2 (1.5-3)	2 (1-3)	<0.001
Spinach, chard	2 (2-3)	2 (1-2)	<0.001
Lettuce	3 (2-4)	3 (2-4)	<0.001
Meat, fish and eggs			
Breaded pork	2 (1-3)	2.5 (1-3)	<0.001
Processed meat			
Bacon	2 (2-3)	3 (2-3)	<0.001
Salty snacks, sweets and cakes			
Biscuits	2 (1-2)	2.5 (1-3)	<0.001
Fats and oils			
Margarine	2 (2–3.5)	3 (1–3.75)	0.02
Oils	3 (2-5)	4 (2-5)	0.03
Fast food			
Hamburger	1 (0-2)	2 (1-3)	<0.001

*= Mann Whitney's U test

Table 5. Differences in the frequency of consumption of certain food items (divided in first six food categories according to modified FFQ) by patients with LPR at three measurement points

Patients with LPR	Median (interquartile range)			p*
	First examination	After 30 days	After 60 days	
Milk and dairy products				
Milk	3 (2-5)	2 (1-4)	2 (0-3)	0.01†
Fresh cottage cheese	2 (1-3)	2 (0-3)	1 (0-2)	0.005‡
Cream (12% milk fat content, „blue“)	3 (1-4)	2 (0-3)	1 (0-3)	0.009§
Semi-hard and hard cheese	2 (1-3)	1 (1-2)	1 (0-2)	0.006§
Cheese spread (30% milk fat content)	2 (1-3)	2 (1-3)	1 (0-2)	0.003‡
Yogurt, acidophilus, kefir (2.8-3.2% milk fat content)	3 (1-4)	2 (1-3)	1 (0-2)	0.001‡
Milk and dairy products with added sugar				
Cocoa/chocolate milk	2 (0-2)	1 (0-2)	1 (0-1)	0.02‡

Fruit yogurt	2 (1-3)	2 (0-2)	1 (0-2)	0.02‡
Cereals				
White bread (rolls and croissants)	5 (3-5)	3 (2-5)	3 (0.5-4)	<0.001‡
Rye/wholemeal bread (rolls and croissants)	2 (0-3)	3 (1.75-4)	4 (3-5)	<0.001‡
Polenta	1 (0-1)	1 (0-2)	2 (1-3)	<0.001‖
Breakfast cereals				
Chocolate wheat flakes	1 (0-2)	2 (0-3)	1 (0-2)	0.006**
Cornflakes	0 (0-2)	1 (0-3)	1,5 (0-2)	0.02††
Juices				
Juice (orange)	3 (2-4)	2 (0-3)	1 (0-2)	<0.001‡‡
Other juices	3 (2-4)	1 (0-3)	1 (0-2)	<0.001‡‡
Fruit juice	2 (1-3.75)	1 (0-2.25)	1 (0-2)	0.007†
Sweet vitamin drink	2 (1-3.75)	1.5 (0-3)	0 (0-2)	0.005‡
Ice tea	2 (1-3)	1 (0-2)	0 (0-2)	<0.001†
Carbonated soft drinks	3 (2-4)	2 (0-4)	1 (0–2.5)	<0.001‡‡
Non-alcoholic drinks (sugar-free)	4.5 (3-5)	5 (4-6)	6 (5-7)	<0.001‡‡
Fruit syrup (syrup contetrates)	2 (1-3)	2 (0-3)	1 (0-2)	0.002‡
Fruit				
Apple or pear	3 (2-4)	2 (0-3)	2 (0-2)	<0.001‡‡
Orange, grapefruit, mandarin	3 (1.25-4)	1 (0-2)	0 (0-1)	<0.001‡‡
Banana	2 (1-3)	3 (1-4)	3 (2-4)	<0.001‡‡
Melon, watermelon	1 (0-1)	2 (0-3)	2 (1–3)	<0.001‡‡
Grapes	2 (1-3)	1 (0-3)	0 (0-1.5)	<0.001‡‡
Pineapple	0 (0-1)	1 (0-2)	1 (0–1.25)	0.009‖

*=Friedeman's test (post hoc Conover), †= at the P < 0.05 level, significantly more is consumed at the first examination compared to the other two controls, ‡= at the P < 0.05 level, significantly the least consumed after 60 days compared to the first examination and control after 30 days, §= at the

P < 0.05 level, it is consumed significantly less at the control after 60 days compared to the first examination, ‖= at the P < 0.05 level, it is significantly consumed the least at the first examination compared to both controls, **= at the P < 0.05 level, significantly more is consumed in the control after 30 days compared to the control after 60 days, ††= at the P < 0.05 level, significantly less is consumed at the first examination compared to the control after 30 days, ‡‡= at the P < 0.05 level, the frequency of consumption is significantly different between all measurements

Table 6. Differences in the frequency of consumption of certain food items (divided in other six food categories according to modified FFQ; continuation of Table 5.) by patients with LPR at three measurement points (2/2)

Patients with LPR	Median (interquartile range)			p*
	First examination	After 30 days	After 60 days	
Vegetables				
Onion, garlic	3 (2-4)	2 (1-4)	2 (1–2.75)	<0.001‡‡
Peppers (fresh, sauces)	3 (2-4)	2 (1-3)	1 (0-2)	0.002§
Tomato (fresh, sauces, salsas)	3 (2-4)	2 (1-2)	1 (0–1.5)	<0.001‡‡
Cabbage, kale	2 (1-3)	1 (1–2.25)	1 (0-2)	0.002§
Lettuce	3 (2-4)	2 (1-2)	1 (0-2)	<0.001‡‡
Mixed vegetables	3 (1-3)	2 (1-2)	2 (1-3)	0.03†
Meat, fish and eggs				
Minced meat schnitzel	2 (1-3)	1 (1-2)	1 (0-2)	<0.001‡‡
Breaded chicken	2 (2-3)	2 (1-2)	1 (0-3)	0.004‡
Fish (white, blue)	1 (0-2)	2 (1-3)	2 (1-3)	<0.001‖
Processed meat				
Hotdog	2 (1-3)	1.5 (0-2)	1 (0-2)	<0.001‡‡
Sausages	2 (1-3)	2 (1–2.5)	1 (0-1)	<0.001‡‡
Salami	3 (2-4)	2 (1-3)	1 (0-2)	<0.001‡‡
Pate	3 (1-3)	2 (1-3)	1 (1-2)	0.007‡
Bacon	3 (2-3)	1.5 (1-2.25)	1 (0-2)	<0.001‡‡

Pariser	2 (0-4)	1 (0-2)	1 (0-2)	<0.001‡
Salty snacks, sweets and cakes				
Crisps (any kind)	2 (1-3)	1 (0-3)	1 (0-1)	<0.001**
Biscuits	2 (1-3)	1 (0.5-2)	1 (0-1)	0.001**
Cakes (dry,creamy)	2 (1-3)	1 (0-2)	1 (0–1.5)	<0.001‡‡
Chocolate	3 (2-3)	2 (1-3)	1 (1-2)	<0.001‡‡
Chewing gum (with sugar, sugar-free)	3 (2-4)	2 (1-3)	2 (0.5-3)	0.001‡
Fats and oils				
Butter	3 (1-4)	2 (1-3)	2 (1-3)	0.02‡
Oils	4 (2-5)	3 (2-4)	3 (1-4)	0.001§
Fast food				
Hamburger	2 (1-3)	1 (0-2)	0 (0-1)	<0.001‡‡
Pizza	2 (1-3)	1 (0-2)	0 (0-1)	<0.001‡‡

*= Friedeman's test (post hoc Conover), †= at the P < 0.05 level, significantly more is consumed at the first examination compared to the control after 30 days, ‡= at the P < 0.05 level, significantly more is consumed at the first examination compared to both controls, §= at the P < 0.05 level, significantly less is consumed at the control after 60 days compared to the first examination, ‖= at the P < 0.05 level, significantly less is consumed at the first examination compared to both controls, **= at the P < 0.05 level, significantly less is consumed at the control after 60 days compared to the first examination and the control after 30 days, ‡‡= at the P < 0.05 level, the frequency of consumption is significantly different between all measurements