ANNOTATION

to dissertation work **'' Method of early diagnosis of laryngopharyngeal reflux in an outpatient appointment of an otorhinolaryngologist"**, by Nukusbekova Gulnur Isbasarovna, submitted for the degree of Doctor of Philosophy (PhD) in the specialty 8D10103 - "Medicine"

Relevance

The problem of diagnosis and treatment of laryngopharyngeal reflux (LPR) attracts increased attention, which is associated with an increase in the incidence of this pathology in different countries of the world. According to a literature review conducted by researchers in Europe, the United States of America (USA), and South Korea, symptoms associated with LPR occur in approximately 4-10% of outpatient patients attending otolaryngology and head and neck surgery departments (Lechien, Mouawad, et al., 2019), and up to 50% of patients in the laryngology department (Koufman, 1991). Other sources also write that LPR affects 10% of patients undergoing treatment in otolaryngology, and more than 50% of patients suffering from voice disorders in the United States (Charles N Ford, 2005), (Lechien, Mouawad, et al., 2019) and the prevalence of LPR disease in Europe remains unknown. LPR also carries a high economic and social burden in the United States, where the assessment and treatment of LPR averaged $5,438 per patient in the first year (Francis et al., 2013). As a result, LPR in the United States costs $50 billion annually, which is five times the cost of gastroesophageal reflux disease (GERD) (Francis et al., 2013). There are a number of factors that contribute to the higher burden on healthcare associated with LPR, including delays in testing, ineffective treatment, and the widespread use of proton pump inhibitors (PPIs) (Francis et al., 2013).

Scientists conducted an online survey, in which a total of 824 otolaryngologists from 65 countries took part (Lechien et al., 2021). Regardless of geography, otolaryngologists pointed to ignorance of pH impedancometry, which they explain by a lack of knowledge in interpreting the results. Only 21.1% of respondents are aware of the existence of non-acidic LPR. In general, only 43.2% of otolaryngologists consider themselves sufficiently knowledgeable about LPR (Lechien et al., 2021). All this shows the low awareness of doctors about the LPR and its complications.

Identification of patients with LPR is a complex problem and represents one of the important tasks in otolaryngology and gastroenterology (Significance et al., 2019), (Barry & Vaezi, 2010),(Pearson et al., 2011). The absence of specific clinical manifestations makes it much more difficult to make a correct diagnosis in a timely manner. Back in 1991, Koufman (Koufman, 1991) was the first to clearly distinguish LPR from GERD and suggested the relationship of pathological reflux with chronic cough, hoarseness, contact ulcers and granulomas, a feeling of "lump" in the throat, dysphagia, subclavian stenosis, thyroid arthritis, and laryngeal cancer, which indicates a variety of complaints from patients with such pathology. Undiagnosed and untreated

LPR can damage the vocal cords, leave scars on the vocal folds, stimulate Barrett's esophagitis, and lead to long-term damage to the vocal cords (Maronian et al., 2001). Different types of reflux contents have different effects on the LPR, can cause various clinical manifestations, and inflammatory processes, and can contribute to the development of tumor-like diseases of the larynx (Li et al., 2021). The study showed that mucosal alkali damage during LPR can lead to increased sensitivity of the vocal folds to damage and subsequent formation of nodules, polyps, Reinke's edema (Boogers et al., 2022), leukoplakia and carcinoma of the vocal cord (Lechien, Saussez, et al., 2019), (Han et al.., 2022). According to one study, acid secretion by the gastric proton pump expressed in the laryngeal mucosa may induce mitochondrial damage and gene expression changes associated with inflammation and cancer in local cells (Zhang et al., 2022). There is a danger of not recognizing the LPR, while overdiagnosis of the LPR can lead to unnecessary costs and missed diagnoses. When the doctor cannot recognize the LPR, patients have long-term symptoms and delayed healing (C.N Ford, 1999). In this connection, an important task is not only the diagnosis of this pathological condition but also the conduct of targeted etiopathogenetic treatment. Currently, there is no "gold" standard providing the diagnosis of reflux, although the technology is developing - new studies measure both non-acidic and mixed reflux since each of them can cause reflux, and comparative studies show how pH metric alone can underestimate the diagnosis of reflux (Charles N Ford, 2005). One of the ways to solve this problem is the introduction into clinical practice of diagnostic methods of pathological reflux, which will contribute to the choice of optimal therapeutic tactics in each case, and will allow to obtain higher functional results and improve the quality of life of patients. It is necessary to develop an algorithm for diagnosing LPR in outpatient settings, taking into account the current circumstances in our country (lack of equipment: daily pH measurement, impedance measurement, video laryngoscopy or endoscopic laryngoscopy; there is also a shortage of specialists, poor awareness of specialists about the LPR, etc.).

The purpose of the research work: Creation of a unified diagnostic algorithm for timely detection of laryngopharyngeal reflux at an outpatient appointment of an otorhinolaryngologist.

In connection with this goal, the following tasks are solved:

1. To carry out language adaptation and validation of the reflux symptoms index questionnaire in Kazakh, with clarification of the translation into Russian from the original.
2. To conduct a comparative analysis of the results of the reflux symptoms index questionnaire, the reflux signs scale, and pH measurement of the medium from the larynx between the study groups and in the groups before and after the treatment.
3. To study the correlation of clinical manifestations in patients with laryngopharyngeal reflux and in a group of patients with gastroesophageal reflux, according to laryngeal endoscopy and significant indicators of the reflux symptoms index questionnaire.

4. To evaluate the results of acoustic analysis of the voice in patients of the voice profession with laryngopharyngeal reflux before and after treatment.

5. To develop an algorithm for diagnosis at an outpatient appointment of an otorhinolaryngologist to detect laryngopharyngeal reflux at an early stage.

Methodological base of the research:

1. Validation of research tools: questionnaire reflux symptoms index (RSI)
2. Assessment of complaints of patients with laryngopharyngeal reflux symptoms: standardized RSI questionnaire.
3. Clinical research method: anamnesis collection.
4. Sociological method: determination of lifestyle, nutrition, presence or absence of bad habits.
5. Laboratory and instrumental methods of investigation: assessment of the larynx condition according to the reflux finding score (RFS) using 90-degree endoscopic laryngoscopy and videolaryngostroboscopy (Heinemann, Xion, Germany) with a diameter of 5.0 mm and a working length of 158 mm.
6. Ph-metry: mucus sampling from the larynx to determine acid-base parameters.
7. Acoustic analysis of the voice in patients with voice disorders, the analysis was carried out using the LingWAVES program (Germany).
8. Development of practical recommendations for the diagnosis of laryngopharyngeal reflux at an outpatient appointment of an otorhinolaryngologist.
9. Statistical: Processing of research results using the IBM SPSS Statistics Subscription program for Windows (version 21.0, SPSS INC., Chicago, Illinois, USA).

9.1 To validate the RSI questionnaire in Kazakh, the following method of statistical processing was carried out: internal consistency was measured using Cronbach's Alpha and temporal stability using the intra-class correlation coefficient ($P < 0.05$). The distributions of groups according to the Kolmogorov-Smirnov criterion were analyzed. The average values of the group were analyzed using the t-test of independent samples to assess the reliability of the RSI-kz. Cronbach's alpha was used to determine the internal consistency of the RSI-kz. Retest reliability was evaluated using an intra-class correlation coefficient (CC). If the value was $P < 0.05$ this is considered a statistically significant result. An alpha coefficient value ≥ 0.7 was considered reliable; however, a value >0.8 was recommended. $CC > 0.75$ was considered reliable.

9.2 To represent clinical and epidemiological data on patients, mean values and standard deviation were calculated for continuous data, and frequency as a percentage for discrete data. To test the null hypothesis, we used a paired t-test to calculate the average value of the differences between paired observations. Statistical significance was determined at $p<0.05$, <0.005.

Object of study: patients with symptoms of laryngopharyngeal reflux, patients with gastroesophageal reflux, and patients without symptoms of laryngopharyngeal reflux.

Subject of study: indicators of the questionnaire of reflux symptoms, assessment of the laryngeal mucosa on the scale of reflux signs, pH of the laryngeal pharyngeal medium, and acoustic analysis of the voice.

Inclusion criteria:

Informed consent of the patient

Age: from 18 to 74 years

Without severe somatic diseases.

Patients with complaints of sore throat, coughing, burning sensation in the throat, cough, frequent sore throat, difficulty swallowing, lump in the throat, feeling of a foreign body in the throat, voice change, heartburn, and belching.

Diagnosis: Chronic pharyngitis

Chronic laryngitis

Inclusion criteria:

Disagreement on participation in scientific research

Age: under 18

Severe somatic diseases, organic lesions of the gastrointestinal tract, and ENT organs

Patients with pulmonary pathology

Patients with allergic manifestations (Seasonal pollinosis, Bronchial asthma, etc.)

With diagnoses: Acute respiratory diseases

Patients with general neurological disorders.

Research stages: to fulfill the tasks of the dissertation work, the work was divided into several stages:

1. Validation of research tools: To validate the questionnaire, the IRS from the original American English was translated and adapted into Kazakh according to standard procedures after receiving written consent from the authors. To assess the reliability, the final version of Kz-RSI was evaluated twice (day 0 and day 14) for participants without symptoms of LPR and with symptoms of LPR (day 0 and day 14). Reliability, validity, and internal consistency of testing−retesting were calculated.

This study was approved by the Local Ethics Committee of the Kazakh Medical University of Continuing Education (identification number: 14-2020) and the Local Ethics Committee of the Kazakh National Medical University (KazNMU) named after S.D. Asfendiyarov (Study ID: 1399). Also, the protocol of the study is registered in ClinicalTrials.gov. Protocol registration and Results System (Study ID: NCT05296655).

To conduct the study, the RSI questionnaire was used in the original version, after receiving written consent from the authors (Belafsky et al., 2001) and translated into Kazakh by five native Kazakh specialists in the field of otorhinolaryngology, with a minimum of five years of work experience. The translated version of the questionnaire was combined by the authors of the study into a single version, which was later translated back into English by translators who did not know the original English version of the questionnaire. The translated version of the assignment was additionally evaluated for compliance, adequacy, accuracy, and ambiguity and consolidated into a single version by a professor who speaks Kazakh. They confirmed that the latest version of the questionnaire is sensitive to the social and cultural norms of the Kazakh language. The approved form of the Kazakh version of the RSI questionnaire was experimentally tested on 10 people with LPR and without symptoms of LPR. All participants reported that they understood the Kazakh version of the RSI and filled out a questionnaire. According to the procedures carried out, the final version of the IRS

in Kazakh was ready for use on the participants. It was decided from now on to name the final version of the RSI in the Kazakh language as RSI-kz. (Table 1)

Table 1 - Kazakh version of the Index of Reflux Symptoms (RSI-kz)

Соңғы айда сіз осы симптомдардың қайсысын өзіңізде байқадыңыз? Тиісті санды белгілеңіз?	**0 – симптомдар жоқ 5 - қатты**
1. Қарлығу немесе басқа да дауыстың бұзылуы	0 1 2 3 4 5
2. Тамақтың «жыбырлауы»	0 1 2 3 4 5
3. Артық шырышты немесе шырыштың жұтқыншаққа ағуын сезіну	0 1 2 3 4 5
4. Тамақты, сұйықтықтарды немесе дәрілерді жұту қиындықтары	0 1 2 3 4 5
5. Тамақ ішкеннен кейін немесе арқаға жатқаннан кейін жөтелдің пайда болуы	0 1 2 3 4 5
6. Ентігу немесе тыныс алудың қиындауы	0 1 2 3 4 5
7. Жөтел (күшейетін, тітіркендіргіш)	0 1 2 3 4 5
8. Алқымдағы кедергінің бар екенін сезіну, “қысылған алқым” сезімі	0 1 2 3 4 5
9. Қыжыл, кеудедегі ауырсыну, диспепсия, қышқыл дәм	0 1 2 3 4 5
Барлығы:	

Participants

From February 2021 to February 2022, 248 participants, including 124 asymptomatic control subjects and 124 patients with symptoms of LPR were recruited from an outpatient appointment of an otorhinolaryngologist at a specialized medical center.

The participants of group 1 had no problems with their voice and it was not advisable to carry out laryngoscopy. Participants reported no complaints of hoarseness of voice, cough, heartburn, lump sensation, and other symptoms associated with LPR and did not have any chronic diseases associated with stomach reflux earlier.

In group II, LPR was confirmed using the RSI-kz questionnaire, laryngoscopic examination using 90-degree microscopy, video stroboscopy, and assessment of the larynx by RFS was also performed. The RFS was evaluated by two otolaryngologists who separately evaluated the RFS. We evaluated the RFS by consensus and basically agreed with each other. Monitoring of the daily pH was not carried out due to the absence of this remedy.

Questionnaire management and data collection. All participants were native speakers of the Kazakh language, who have auditory data within the normal range and understand the spoken language well. Before filling out the RSI-kz, the purpose of the study was explained to the participants and they were asked to fill out and sign an informed consent.

The participants were asked to answer the questionnaire on their own, in isolated cases, when it was difficult to answer questions and evaluate, the researchers conducted an explanation, the questionnaire took about 3-7 minutes. It should be noted that participants, especially those with symptoms of LPR, noted more complaints after filling in than when collecting complaints, thus identifying patients with LPR and adjusting treatment.

To assess the test-retest reliability, participants of both groups were asked to re-fill out the questionnaire within 14 days. This time interval was provided in order to prevent memory displacement, and also to ensure comparability between both tests. Both the participants and the interviewer did not have access to the results of the first RSI-kz questionnaire during the re-filling in order to prevent memorization and bias. Patients in the control group were asked to temporarily not undergo any treatment until the second test to ensure comparability between both measurements.

2. Conducting a cohort study to study the methods of diagnosis of LPR at the outpatient appointment of an otorhinolaryngologist:

Clinical characteristics of the examined patients, determination of the sample.

1. **Number of participants**. The smallest number of participants based on the calculation of the approximate sample size is 384, which is about 95% confidence level. (The calculation is given in Table 2).

Table 2- **Sample size for frequency in the population**

Population size (for the final correction factor of the population) (N): 1000000	
Estimated% of the frequency of the outcome factor in the population (p):	50% + / -
Confidence limits as % of 100 (absolute +/-%) (d):	5%
Design effect (for surveys- Deff cluster):	1
Sample size (n) for different confidence levels	
Confidence Level (%)	Sample Size
80%	165
90%	271
95%	384
97%	471
99%	664
99,9%	1082

99,99%	1512
Уравнение размера выборки n = [DEFF * Np (1-p)] / [(d2 / Z2 1- α / 2 * (N-1) + p * (1-p)]	
Results from OpenEpi, Version 3, Open source calculator - SSPropor	

The study involved 384 patients, and it was conducted between January 2021 and February 2022. The Local Ethics Committee of KazNMU named after S.D. Asfendiyarov approved this study (Study ID: 1399). Moreover, the study was registered in the Register of Clinical Trials ClinicalTrials.gov (study ID: NCT04771221).

Selection:

1) The main group includes:
   1) Individual registration cards of analyzed patients with complaints of sore throat, coughing, burning sensation in the throat, cough, frequent sore throat, difficulty swallowing, lump in the throat, feeling of a foreign body in the throat, voice change, heartburn, belching.
2) The control group includes:
   1) Individual registration cards of analyzed patients with a previously established diagnosis of GERD
   2) Individual registration cards of the analyzed patients who do not have the above complaints.

The RSI questionnaires were filled out jointly by patients and doctors (Table No. 1,3). The score of the RSI questionnaire can vary from 0 (no problems) to 5 (serious problems), with the maximum total score being 45.

In patients with LPR and GERD, the condition of the larynx was assessed by RFS (Table No. 4) using rigid endoscopic laryngoscopy and videolaryngstroboscopy with a diameter of 5.0 mm, a viewing angle of 90o and a working length of 158 mm of an ENT combine (Heinemann, Xion, Germany). It was confirmed that there were no additional features of the larynx, such as nodules, polyps and dysplasia, which could cause a change in voice. There was a range of estimates of RFS from 0 (normal larynx) to 26 (laryngeal pathology). Belafsky and co-authors initially developed the SRP and RSI questionnaires. Patients without LPR symptoms were not examined by laryngoscopy due to their lack of complaints. Patients with RSI score> 13 and RFS score> 7 were suspected of LPR.

Monitoring of the daily pH was not carried out due to the lack of this equipment. Instead, the pH of hypopharyngeal mucus was measured in all participants using pH strips on an empty stomach or 2 hours after eating.

Table 3 - Questionnaire " Reflux symptom index " translated from the original version.

During the last month, how much have the following issues bothered you?	0 - no problem, 5 - severe problem
1. Hoarseness or a problem with your voice	0 1 2 3 4 5

2. Clearing your throat	0 1 2 3 4 5
3. Excess throat mucous or postnasal drip	0 1 2 3 4 5
4. Difficulty swallowing food, liquids, or pills	0 1 2 3 4 5
5. Coughing after you eat or after lying down	0 1 2 3 4 5
6. Breathing difficulties or choking episodes	0 1 2 3 4 5
7. Troublesome or annoying cough	0 1 2 3 4 5
8. Sensation of something sticking in your throat or a lump in your throat	0 1 2 3 4 5
9. Heartburn, chest pain, indigestion, or stomach acid coming up	0 1 2 3 4 5
Total (points)	

Table 4 - Reflux Finding Score.

Finding	Score
Subglottic edema	2 = present 0 = absent
Ventricular obliteration	2 = partial 4 = complete
Erythema/hyperemia	2 = arytenoids only 4 = diffuse
Vocal cord edema	1 = mild 2 = moderate 3 = severe 4 = polypoid
Diffuse laryngeal edema	1 = mild 2 = moderate 3 = severe 4 = obstructing
Posterior commissure hypertrophy	1 = mild 2 = moderate 3 = severe 4 = obstructing
Granuloma/granulation	2 = present 0 = absent
Thick endolaryngeal mucus/other	2 = present 0 = absent
Total (points)	

Patients with LPR with voice professions and voice disorders were analyzed using the LingWAVES program for acoustic voice analysis. A sound level meter is a device that measures the sound level of speakers and contains software running on Windows computers that evaluates voice and speech turns, standardized recording equipment, a USB connector, and pre-calibrated sound level measurements. To ensure the success of the procedure, the room should be quiet and without additional noise. Software applications receive data about the microphone and sound level from the equipment in real-time. As for the vocal range of the profile recording, LingWAVES follows the recommendations of the Union of European Phoniatrists (the sound microphone is located at a distance of 30 cm from the participant's mouth). In the Union of European Phoniatrists, LingWAVES is an approved medical product and a standard method for diagnosing voice disorders of various levels (Vertigan et al., 2017).

3. Algorithm of diagnosis of laryngopharyngeal reflux at an outpatient appointment of an otorhinolaryngologist.

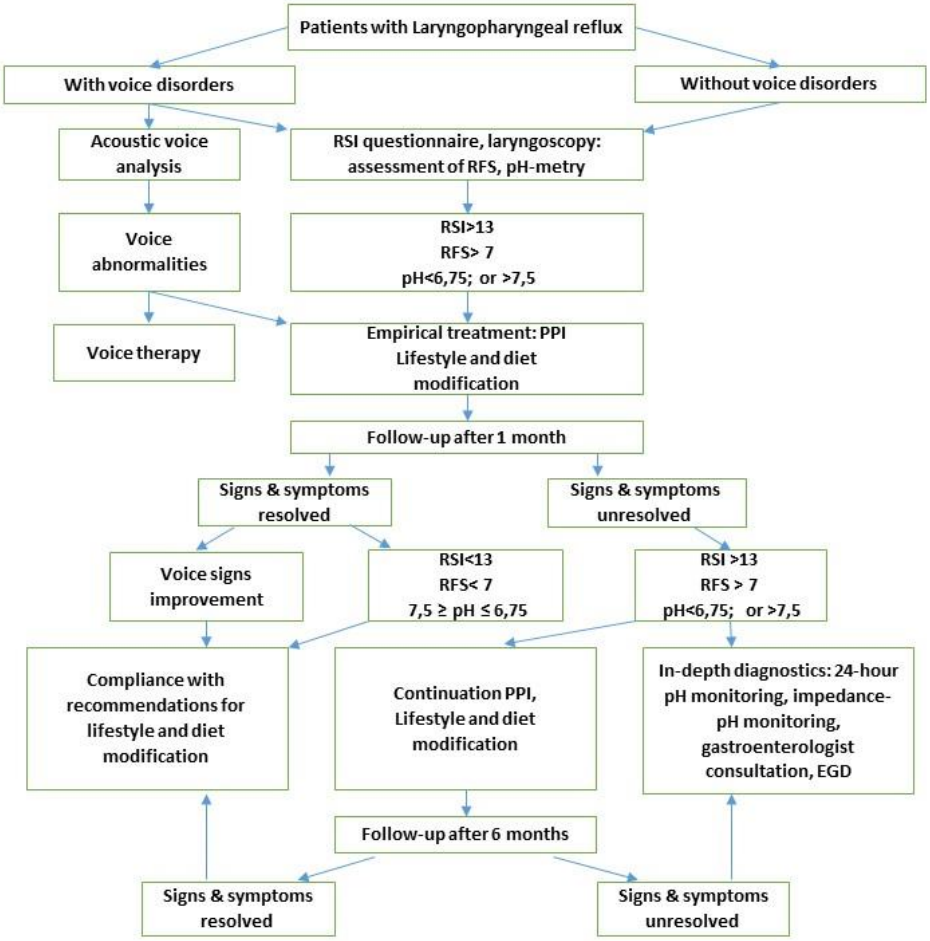

Figure 1 - The proposed algorithm for the diagnosis of LPR.

Abbreviations: RSI = reflux symptom index; RFS = reflux finding score; PPIs = proton pump inhibitors; EGD = esogastroduodenoscopy.

Patients with LPR or GERD were prescribed PPIs at a dose of 20 mg twice a day, given recommendations on lifestyle and nutrition for a month, and also recommended voice therapy to patients with voice disorders. The above indicators were re-evaluated after a month, and if there was no clinical improvement, the therapeutic recommendations were extended to 6 months, as shown in the figure (Figure 1). If no effect has been achieved, additional studies and consultations with specialists are considered.

- The effectiveness of diagnostic methods will be determined by the following criteria:
- Absence of the above complaints or reduction of symptoms
- Positive effects after treatment
- Improvement of the condition of the laryngeal mucosa
- Control pH-metry after treatment and compliance with recommendations
- Improvement of the acoustic analysis of the voice after the treatment and compliance with the recommendations.

Provisions for defense

1. Patients with laryngopharyngeal reflux have high values of the reflux symptom index and the reflux finding score in the early period after diagnosis.
2. Timely diagnosis and treatment contribute to improving the condition of patients, reducing the values of the reflux symptom index and the reflux finding score, as well as improving the indicators of acoustic analysis of the voice and pH of the pharyngeal environment.
3. To improve the provision of primary medical care in the healthcare system, it is necessary to carry out a transformation, including the participation of a general practitioner, a therapist, and otorhinolaryngologists in the timely diagnosis of extraesophageal manifestations of GERD.
4. The use of the reflux symptoms reflux symptom index and the reflux finding score increases the detectability of laryngopharyngeal reflux symptoms and the assessment of changes during laryngoscopy.
5. The developed algorithm for the diagnosis of laryngopharyngeal reflux allows for early diagnosis of this condition and the results obtained using the reflux symptoms index questionnaire, reflux finding score, acoustic voice analysis, and pH measurement of the laryngopharyngeal environment are important for determining further patient management tactics.

Scientific novelty:

1. For the first time in Kazakhstan, the international reflux symptoms index questionnaire, the reflux finding score, and acoustic voice analysis were used to diagnose laryngopharyngeal reflux to prevent complications, including oncological ones. (copyright of the Republic of Kazakhstan No. 32043 dated 26.01.2023).
2. The results of the cohort study show that in patients with LPR and GERD before treatment, the indices of the reflux symptoms index questionnaire were higher than 13 and the reflux finding score was higher than 7, the average difference in pH after treatment compared to pH before treatment was 1.14±0.50 (95% CI (1.06-1.22)) p0.001, and in the GERD group, the average difference in pH after treatment compared to the pH before treatment was 1.13±0.63 (95% CI (1.01-1.27)) p0.001.
3. The results obtained made it possible to determine significant indicators of laryngeal endoscopy with an assessment of the reflux finding score from 8 to 4 and the symptoms of the reflux symptoms index questionnaire from 9 to 4.
4. The results of the cohort study show that in patients with LPR with a voice profession, indicators of acoustic voice analysis statistically significant differences (*p <0.05) were determined by the following indicators of acoustic voice analysis: optimal shimmer (95 CI (11.04; 13.02)), strong shimmer (95 CI (11.86; 14.95)), loud shimmer (95 CI(-18.86; -7.25)), optimal jitter (95 CI (-1.53;-1.08)), loud jitter(95 CI (-5.45;-3.26)), dysphonia severity index (95 CI (-1.96;-1.23)) and norm profile coverage (95 CI (-14.45;-11.45)) (p <0.05).

Theoretical significance of the study results

The results obtained in the course of the dissertation research are important for the development of theoretical and methodological foundations for the study of LPR symptoms, changes in laryngoscopy and pH parameters of the laryngopharyngeal medium in normal and pathological conditions. In the course of the study, new

knowledge was obtained about the parameters of acoustic voice analysis in LPR patients with voice professions. The results of the dissertation research can become the basis for the formulation of new research tasks: the development of new methods for the diagnosis of laryngopharyngeal reflux in outpatient and inpatient conditions.

The practical value of the research results:

1. The introduction of new methods of diagnosis of LPR at the outpatient appointment of an otorhinolaryngologist makes it possible to determine the causes of many chronic ENT diseases. It will allow to identify complications at an early stage, not only ENT pathology, but also gastroenterological and oncological diseases.
2. The use of LPR diagnostic methods allows you to identify at the initial visit to an otorhinolaryngologist, which reduces the volume and time of examination by specialists of other profiles (gastroenterologist, FGDS, endocrinologist, therapist, etc.)
3. Materials from the dissertation work can be used in educational programs and training of specialists in otorhinolaryngology, gastroenterology, phoniatry, and medical science, contributing to the expansion of their knowledge and practical skills in the field of laryngopharyngeal reflux.
4. The introduction of a new diagnostic method and timely treatment will reduce the time of disability, prevent infection, including oncological (laryngeal cancer)

The author's personal contribution

The presented work is the author's work of Gulnur Isbasarovna Nukusbekova, where she independently planned all stages of research, and design, and conducted a thorough literary analysis. The author carried out the preparation for the study, data collection, data analysis, and design. As a result of the work, the author carried out the validation of the RSI questionnaire in the Kazakh language and developed a method for diagnosing laryngopharyngeal reflux at an outpatient appointment, which is confirmed by a security document (Certificate of entry of information in the state register of copyrighted objects No. 32043 dated 26.01.2023 "Method for diagnosing laryngopharyngeal reflux to prevent complications"). The proposed method of diagnosis of laryngopharyngeal reflux and the algorithm of work has been introduced into the clinical activities of the specialized clinic of the GCP at the City Hospital No. 5 in Almaty (The Act of introduction of the "Method of diagnosis of laryngopharyngeal reflux to prevent complications" dated 13.02.23).

Conclusions

1. The developed questionnaire of the Kazakh version of the RSI has strong internal consistency, high reliability of repeated testing, and optimal clinical reliability, the analysis of internal consistency showed a result of Cronbach's alpha 0.94, which shows a remarkable measurement of internal consistency. RSI-kz can be used to diagnose and evaluate the effectiveness of treatment, both by otorhinolaryngologists and primary health care specialists.
2. The developed algorithm for the diagnosis of laryngopharyngeal reflux makes it possible to carry out diagnostics in a timely manner, and reduce unnecessary examinations and consultations of specialists.

3. Timely initiation of treatment and explanation of the importance of lifestyle modification to patients prevent complications of oncological and other diseases of the head and neck organs, prevents surgical interventions.

4. Statistically significant differences (*p<0.05; **p<0.005) were determined between the groups with LPR and GERD according to the following RSI indicators: cough after eating or lying down, difference -0.53 (95 confidence interval (CI) (-0.90; -0.16)); shortness of breath or difficulty breathing, difference -1.15 (95 CI (-1.31; -1.08)); cough, difference. -0.45 (95 CI (-0.81; -0.10)); and heartburn, chest pain different 1.52 (95 CI 1.06; 1.99)).

5. Statistically significant differences (*p<0.05; **p<0.005) between the groups with LPR and GERD were determined by the following indicators of RFS: difference in ventricular obliteration 1.10 (95 CI (1.07; 1.25)); difference in diffuse laryngeal edema -0.27 (95 CI (-0.44; -0.09)); difference in hypertrophy of the posterior commissura 0.27 (95 CI (0.13; 0.40)); and the difference in granulation -0.19 (95 CI (-0.35; -0.03)).

6. Statistically significant differences (*p<0.05) were determined after the treatment according to the following indicators of acoustic voice analysis: optimal shimmer (95 CI (11.04; 13.02)), strong shimmer (95 CI (11.86; 14.95)), loud shimmer (95 CI (-18.86; -7.25)), optimal jitter (95 CI(-1.53;-1.08)), loud jitter(95 CI (-5.45;-3.26)), etc (95 CI (-1.96;-1.23)) and coverage of the norm profile (95 CI (-14.45;-11.45)).

Approbation of the dissertation

The main results of the dissertation were presented and discussed at scientific and practical seminars and meetings of the Department of Otorhinolaryngology at KazNMU and KazMUCE universities.

The results of the study were presented in the form of oral reports at scientific conferences and symposiums devoted to the relevant field of research:

International scientific and practical conference of young scientists "Apsatar readings: "New vectors in science of the 21st century: questions, hypotheses, answers", JSC "Kazakh Medical University of Continuing Education", (May 15, 2020. Almaty, Kazakhstan)

International Conference - Voice in All Aspects "VOICEISTANBUL 2022" (14-17 April 2022, Istanbul, Turkey)

1st International Congress of the Azerbaijan Society of Otorhinolaryngologists (AOS) and the Association of ORL HNS of Central and Western Asia (CASOS) (02-03 September 2022. Baku. Azerbaijan)

International Forum of Otorhinolaryngologists. NAO "Astana Medical University" (September 28-30, 2022, Aktau, Kazakhstan)

30th International Congress of the European Union of Phoniatrists (April 27-30, 2023 Antalya. Turkey)

Republican Forum "Topical issues of otorhinolaryngology" together with the 2nd International Congress CASOS. (June 16-18, 2023, Almaty, Kazakhstan)

Scientific and practical conference “Medicine of Tomorrow: the scientific heritage of academician M.A. Aliyev" (June 19-20, 2023, Almaty, Kazakhstan).

Publications

The results of the dissertation research were published in 12 scientific publications, including:

- Scientific publication in the Journal of Voice, indexed by the Scopus database. CitesScore 2,9, percentile-65%, Q2 "Reflux Symptom Index: Translation to the Kazakh Language and Validation";
- In journals recommended by the Committee for Quality Assurance in Education and Science of the Ministry of Education and Science of the Republic of Kazakhstan (COXON of the Ministry of Education and Science of the Republic of Kazakhstan), (3 articles);
- In the programs of 7 republican and international scientific and practical conferences;
- Protected copyright, certificate of entry of information into the state register of rights to objects, No. 32043 dated January 26, 2023. Object name: Method of diagnosis of laryngopharyngeal reflux to prevent complications;
- The act of introducing the "Method of diagnosis of laryngopharyngeal reflux to prevent complications" 2023. to the clinical work of the GKP on the PCV "City Hospital No. 5"

Scope and structure of the dissertation

The dissertation work was carried out in accordance with the established rules and includes the following sections: normative references, definitions, a list of abbreviations and designations, introduction, literature review, description of materials and methods, research results, conclusion with conclusions, practical recommendations and a list of references consisting of 173 sources. The dissertation consists of 108 pages of computer text and is designed in accordance with the requirements of the standards. The paper contains 13 tables and 19 images that clearly represent the results of the study.