



# New Technology for the Diagnosis and Treatment of Clinical Manifestations of Laryngopharyngeal Reflux

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**Aim:** to present the algorithm for differential diagnosis in patients with laryngopharyngeal symptoms, as well as diagnostic opportunities of the 24-hour hypopharyngeal-esophageal multichannel intraluminal pH-impedance monitoring using a special multichannel probe catheter for diagnosis of laryngopharyngeal reflux.

**Key points.** Laryngopharyngeal symptoms are symptoms that can be caused by retrograde reflux of gastric contents to the proximal segment esophagus, pharynx and larynx, the so-called laryngopharyngeal reflux. These symptoms include cough, sore throat, clearing the throat, excessive mucus production, hoarseness/voice change. Patients should report these complaints at least twice a week for more than 8 weeks. Isolated laryngopharyngeal reflux may be the main factor in the pathogenesis of laryngopharyngeal reflux disease — a disease of the pharynx and upper respiratory tract caused by the pathological flow of contents from the stomach into the larynx, which is manifested by laryngopharyngeal symptoms. In addition, laryngopharyngeal symptoms may be based on hypersensitivity of the laryngopharyngeal mucosa. When laryngopharyngeal symptoms are combined with heartburn and regurgitation, the physician should rule out extraesophageal manifestations of gastroesophageal reflux disease. Due to the nonspecific nature of laryngopharyngeal symptoms, the patient's examination includes collecting complaints and medical history, filling out questionnaires, consulting specialists in related specialties, conducting laryngoscopy, esophago-gastroduodenoscopy, 24-hour hypopharyngeal-esophageal multichannel intraluminal pH-impedance monitoring using a multichannel probe catheter, which is the main method in diagnostics of laryngopharyngeal reflux with an assessment of the symptom index, as well as the chemical and physical properties of the refluxate. The staff of the Department and Clinic of Propaedeutics of Internal Diseases, Gastroenterology and Hepatology at Sechenov University has developed a new technology that includes a practical diagnostic algorithm and, for the first time in Russia, constructed the special probe catheter for hypopharyngeal-esophageal multichannel intraluminal 24-hour pH-impedance monitoring, which is registered as an invention in the Federal Service for Intellectual Property (Rospatent) as "The method for performing pH-impedance monitoring in the diagnosis of laryngopharyngeal reflux" (state registration number No. 2845916 dated August 27, 2025).

**Conclusion.** Differentiating between laryngopharyngeal reflux disease and extraesophageal manifestations of gastroesophageal reflux disease in patients with laryngopharyngeal symptoms based solely on clinical manifestations is challenging. To confirm the diagnosis, 24-hour pH-impedance monitoring with a specially designed laryngopharyngeal probe is necessary. This will determine further patient management, thereby improving the quality of medical care for patients with laryngopharyngeal reflux.

**Keywords:** laryngopharyngeal symptom, laryngopharyngeal reflux, laryngopharyngeal reflux disease, gastroesophageal reflux disease, hypopharyngeal-esophageal multichannel intraluminal 24-hour pH-impedance monitoring

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## Новая технология диагностики и лечения клинических проявлений ларингофарингеального рефлюкса

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**Цель:** представить алгоритм дифференциального диагноза у пациентов с ларингофарингеальными симптомами, а также диагностические возможности суточной рН-импедансометрии с применением ларингофарингеального зонда в верификации ларингофарингеального рефлюкса.

**Основные положения.** Ларингофарингеальные симптомы — это симптомы, которые могут быть вызваны ретроградным забросом содержимого желудка в проксимальный отдел пищевода, глотку и гортань, так называемым ларингофарингеальным рефлюксом. К данным симптомам относят кашель, боль/першение в горле, покашливание, избыточное образование слизи, осиплость/изменение голоса. Пациенты должны отмечать эти жалобы не реже двух раз в неделю на протяжении более 8 недель. Изолированный ларингофарингеальный рефлюкс может быть основным фактором патогенеза ларингофарингеальной рефлюксной болезни — заболевания глотки и верхних отделов дыхательных путей, обусловленного патологическим поступлением содержимого из желудка в гортаноглотку, которое проявляется ларингофарингеальными симптомами. Кроме того, в основе ларингофарингеальных симптомов может лежать гиперчувствительность слизистой гортаноглотки. При сочетании ларингофарингеальных симптомов с изжогой и регургитацией врачу следует исключать внепищеводные проявления гастроэзофагеальной рефлюксной болезни. Ввиду неспецифичности ларингофарингеальных симптомов обследование пациента включает в себя сбор жалоб и анамнеза, заполнение опросников, консультации специалистов смежных специальностей, проведение ларингоскопии, эзофагогастродуоденоскопии, суточной рН-импедансометрии с применением ларингофарингеального зонда, которая является основным методом верификации ларингофарингеального рефлюкса, с оценкой индекса симптома, а также химических и физических свойств рефлюктата. Сотрудниками кафедры пропедевтики внутренних болезней, гастроэнтерологии и гепатологии Института клинической медицины им. Н.В. Склифосовского и Клиники пропедевтики внутренних болезней, гастроэнтерологии и гепатологии им. В.Х. Василенко Сеченовского Университета была разработана новая технология, включающая практический диагностический алгоритм и впервые в России сконструированный ларингофарингеальный зонд, который в Федеральной службе по интеллектуальной собственности (Роспатент) зарегистрирован как изобретение «Способ проведения рН-импедансометрии при диагностике ларингофарингеального рефлюкса» (номер государственной регистрации № 2845916 от 27 августа 2025 г.).

**Заключение.** Проведение дифференциального диагноза у пациентов с ларингофарингеальными симптомами между ларингофарингеальной рефлюксной болезнью и внепищеводными проявлениями гастроэзофагеальной рефлюксной болезни только на основании клинических проявлений представляет сложности. Для уточнения диагноза необходимо проведение суточной рН-импедансометрии со специально разработанным ларингофарингеальным зондом. Это определит дальнейшую тактику ведения пациента, тем самым улучшив качество оказания медицинской помощи пациентам с ларингофарингеальным рефлюксом.

**Ключевые слова:** ларингофарингеальный симптом, ларингофарингеальный рефлюкс, ларингофарингеальная рефлюксная болезнь, гастроэзофагеальная рефлюксная болезнь, суточная рН-импедансометрия, ларингофарингеальный зонд

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Recently, there has been an increase in the number of patients seeking medical help with complaints of hoarseness, throat pain, globus sensation, and cough. These symptoms significantly reduce the quality of life of patients and lead to frequent visits to doctors of various specialties. This group of patients often lacks the effect of long-term therapy [1]. Most often, they turn to either otorhinolaryngologists or gastroenterologists [2], accounting for 4 to 10 % of outpatient visits, respectively [3, 4].

Laryngopharyngeal symptoms (LPS) are symptoms that may be caused by retrograde reflux of gastric contents into the proximal esophagus, pharynx, and larynx, known as laryngopharyngeal reflux (LPR) [3].

The pathological effect of laryngopharyngeal refluxate not only leads to the formation of laryngopharyngeal symptoms, but also contributes to the development of inflammatory and dystrophic changes in the multi-row ciliated epithelium

of the laryngeal mucosa, and in some cases may cause complications such as the formation of laryngeal granulomas. In April 2025, an International Interdisciplinary Working Group of specialists in the field of otorhinolaryngology and gastroenterology published a consensus according to which cough, throat pain, throat crearing, excessive mucus production, hoarseness/voice change can be distinguished among the LPS. Patients should report these complaints at least twice a week for more than 8 weeks [3].

The most common LPS are semicough (98 %), persistent cough (97 %), globus sensation (95 %) and hoarseness of voice (95 %) [5]. It is believed that the direct role of laryngopharyngeal reflux in the development of complaints of a globus sensation is unlikely. In addition, experts also do not recommend considering burning of the tongue, burning sensation in the nose, postnasal congestion, and bad breath as part of laryngopharyngeal symptoms [3]. LPS are nonspecific in nature, and

this leads to frequent repeated referrals of patients with such symptoms to both otorhinolaryngologists and gastroenterologists.

Some patients have isolated laryngopharyngeal symptoms without proven presence of LPR, which in some cases can be regarded as a manifestation of hypersensitivity of the laryngopharyngeal mucosa. If, upon further examination, a connection is established between laryngopharyngeal symptoms and LPR, then the clinician is faced with the question of making a differential diagnosis between laryngopharyngeal reflux disease and extraesophageal manifestations of gastroesophageal reflux disease (GERD) [3].

Given the multifactorial etiology of the development of laryngopharyngeal symptoms, patients with their manifestation require a thorough examination in order to establish a diagnosis and subsequent selection of therapy.

Laryngopharyngeal reflux disease (LPRD) refers to a disease of the pharynx and upper respiratory tract caused by pathological reflux of contents from the stomach into the larynx and manifested by laryngopharyngeal symptoms [1, 6, 7]. It is worth noting that the presence of laryngopharyngeal reflux in the patient in the absence of objective evidence confirming the association of laryngopharyngeal symptoms with LPR does not allow us to talk about LPRD [3].

The basis of LPRD is the presence of pathological laryngopharyngeal reflux in the patient. According to some modern data, the presence of even three occurrences of pathological LPR per week can lead to damage to the mucous membrane of the larynx. The presence of hydrochloric acid, as well as pepsin and bile acids in laryngopharyngeal reflux explains the lack of effect of proton pump inhibitors (PPIs) therapy in 40 % of cases [1, 8]. Pepsin and hydrochloric acid affect the expression of protective stress proteins (squamous epithelial proteins: Sep70 and Sep53) and carbonic anhydrase III in the epithelium of the laryngeal mucosa in patients with LPR, reducing their production [9]. Pepsin not only damages the laryngeal mucosa but can also cause chronic inflammation of the surrounding tissues, leading to the formation of polyps of the vocal cords, hypertrophy of the tonsils, the development of otitis media and the growth of malignant neoplasms of the larynx [1].

To date, there are two main pathogenetic theories of the effect of LPR on the laryngopharyngeal mucosa: “reflux” and “reflex”.

The “reflux” theory is based on the proximal spread of reflux from the stomach and its reaching the oropharynx, which leads to local pathological effects or to further aspiration of laryngopharyngeal reflux and damage to the upper and lower respiratory tract.

The protective anti-reflux mechanism that prevents reflux into the mucous membrane of the larynx includes the upper esophageal sphincter (UES), lower esophageal sphincter (LES) and crura of the diaphragm, effective peristalsis of the thoracic esophagus and esophageal clearance [1, 10]. Low pressure in UES or its reflex opening is a prerequisite for the occurrence of laryngopharyngeal reflux [11]. The upper esophageal sphincter is a high-pressure zone located between the pharynx and the cervical esophagus, is a musculocartilaginous structure. Its anterior wall is completely formed by the posterior surface of the cricoid cartilage, the upper part is represented by *m. constrictor pharyngis inferior* and *m. cricopharyngeus*, the posterior and lateral walls — by *m. cricopharyngeus*. The physiological function of the sphincter is to pass food and liquid from the pharynx into the esophagus, protect the respiratory tract from food ingress, and prevent air from entering the esophagus [12, 13]. The number of LPR that are pathological for the laryngeal mucosa remains the subject of lively discussion among specialists in this field [14].

Reflex theory considers esophageal-bronchial reflex as the basis of an indirect mechanism for the development of LPRD. Because the esophagus and bronchial tree share the same embryonic origin, the reflex theory proposes that the presence of abnormal reflux in the distal esophagus may stimulate chemical or mechanical receptors that trigger a vagus-mediated esophageal-bronchial reflex, resulting in bronchospasm, mucus accumulation and cough. This may explain why, when LPR occurs, patients often cough and need to “clear” their throat to relieve the feeling of discomfort. These actions further increase the swelling of the laryngopharyngeal mucosa, leading to its damage and sensory disorders, which in turn leads to the development of a vicious circle of chronic cough [1, 15, 16].

It is important to emphasize that the presence of LPRD in a patient can be discussed when laryngopharyngeal reflux is diagnosed and its connection with the development of symptoms is proven.

Patients with LPRD complain mainly during the daytime, unlike patients with GERD, who complain mainly at night when moving to a horizontal position, which may be due to impaired esophageal clearance, low pressure in the lower esophageal sphincter, and the presence of hernia of the esophageal in hiatus in patients with GERD. In addition, patients with LPRD complain of heartburn much less often than patients with GERD [17].

Due to the non-specific nature of the symptoms, it is difficult to make an accurate diagnosis based

on clinical manifestations alone, therefore, the patient needs to undergo an extended examination, which should include the implementation of instrumental research methods in order to identify signs of pathological effects of LPR on the mucous membrane of the larynx and the association of symptoms with reflux.

To identify a possible association of laryngopharyngeal symptoms with laryngopharyngeal reflux, patients should be provided to complete the questionnaire of the reflux symptom index (Reflux Symptom Index, RSI). The questionnaire contains 9 questions that require a quantitative assessment from 0 (no complains) to 5 points (severe complains). When filling it out the maximum total score can be 45. If a patient's total score exceeds 13 points, this allows a physician to suspect that patient has an LPR. The questionnaire includes the questions regarding the presence and severity of hoarseness or a problem with a patient's voice; the need to clear a throat; excess throat mucus or postnasal drip; difficulty swallowing food, liquids, or pills; coughing after food consumption or taking horizontal position; breathing difficulties or choking episodes; troublesome or annoying cough; sensations of a lump in your throat; heartburn, and chest pain. Thus, most of the questions are aimed at identifying laryngopharyngeal symptoms, but in addition, the presence of a symptom of heartburn is assessed, indicating the presence of GERD [18, 19].

Laryngoscopy should be performed to diagnose changes in the laryngopharynx in patients with laryngopharyngeal symptoms. First, laryngoscopy allows to exclude otolaryngological changes not associated with reflux, including malignant neoplasms [3]. Such laryngoscopic signs from the laryngopharynx organs as hyperemia and swelling of the mucous membrane when examined in white light are nonspecific and can be diagnosed even in healthy individuals [3]. In the study of D.M. Hicks et al., when examining 105 healthy individuals according to laryngoscopy, some of the signs of LPR were detected in 86 % of cases, and certain signs reached a prevalence of 70 % [20]. Another study also examined healthy volunteers and showed that signs characteristic of laryngopharyngeal reflux (swelling, redness of the mucous membrane) are present in many people without any complaints from the larynx [21]. When performing laryngoscopy in patients with suspected LPR, otorhinolaryngologists use the Reflux Finding Score (RFS). This scale is based on the physician's subjective assessment of such signs as subglottic edema, ventricular obliteration, erythema or hyperemia of the mucous membrane, swelling of the vocal cords, diffuse swelling of the larynx, hypertrophy of the

posterior commissure, granulomas or granulations, thickening of the endolaryngeal mucosa [22, 23].

Changes in the laryngeal mucosa detected by laryngoscopic examination have low specificity for LPR, and their validation is difficult due to the lack of a gold standard for diagnosis [22]. In this regard, laryngoscopy should not be used as the main method in the diagnosis of LPRD [3].

It is worth noting that patients with a complaint of hoarseness of voice in the absence of changes according to laryngoscopy in white light, it is advisable to recommend stroboscopy. This diagnostic method allows to assess the condition of the vocal cords by determining the symmetry, amplitude of movement of the vocal cords, and closure of the glottis. Stroboscopy is necessary to rule out other possible causes of dysphonia, a feeling of lump in the throat, and semicough [3].

Patients with laryngopharyngeal symptoms should undergo esophagogastroduodenoscopy (EGDS) in order to exclude changes characteristic of GERD [24]. EGDS is the main diagnostic method for gastroesophageal reflux disease, but its significance in the diagnosis of laryngopharyngeal reflux is less clear [22]. During the examination, the physician evaluates the integrity of the esophageal epithelium. In patients with LPRD, in contrast to patients with extraesophageal manifestations of GERD, erosive and ulcerative changes in the mucous membrane of the esophagus occur only in 25 % of cases [25].

EGDS also allows to visualize possible heterotopic gastric mucosa in the cervical esophagus, which may explain the patient's complaints such as a sour taste in the mouth and a lump in the throat, due to the ability of the heterotopic focus to produce hydrochloric acid, pepsin and mucus. However, today this postulate requires further study [3, 26].

Patients with laryngopharyngeal symptoms in the absence of complaints of heartburn and regurgitation, needed the 24-hour pH-impedance monitoring to diagnose LPR to confirm LPRD.

An important criterion proving the association of laryngopharyngeal symptoms with reflux is the calculated index of the symptom, which is positive at a value of more than 50 % [22]. It should be noted that the results obtained during the 24-hour pH-impedance monitoring should be analyzed together with the patient's complaints, medical history data and the results of other instrumental research methods.

Due to the increasing number of visits to otorhinolaryngologists and gastroenterologists of patients with laryngopharyngeal symptoms, it became necessary to modify the design of the probe for the 24-hour pH-impedance monitoring for



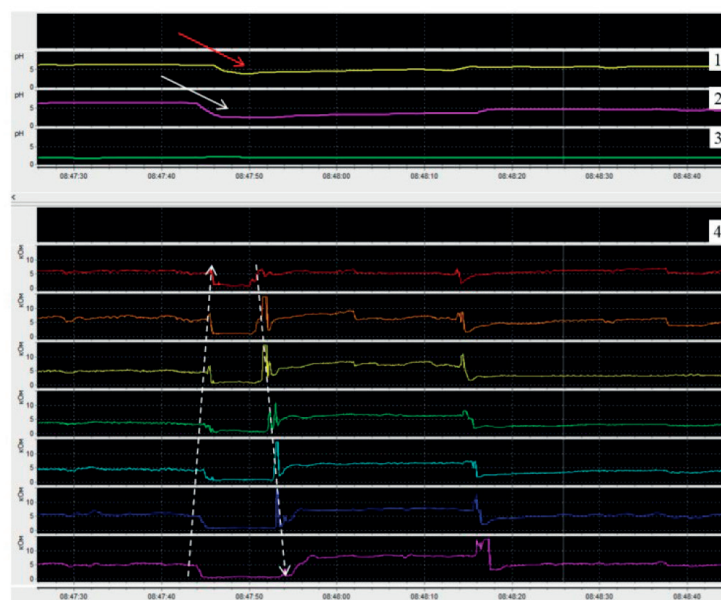
accurate verification of high refluxes reaching the level of the pharynx.

To diagnose laryngopharyngeal reflux, the staff of the Department and Clinic of Propaedeutics of Internal Medicine, Gastroenterology, and Hepatology named after V.Kh. Vasilenko (Sechenov University), under the supervision of Professor A.S. Trukhmanov (Head of the Department and Director of the Clinic – Academician of the Russian Academy of Sciences, Professor V.T. Ivashkin), and Research and Production Enterprise ZAO Istok-Sistema developed a new technology, including a practical diagnostic algorithm and the first-ever laryngopharyngeal probe. The installation of this probe is controlled by high-resolution esophageal manometry based on the length of the esophagus of a particular patient, depending on which one of the three types of probe designs is selected

(20–22 cm, 23–25 cm and 26–28 cm). The use of special probes makes it possible to position the proximal pH sensor and the probe's impedance channel directly 1 cm above the upper esophageal sphincter, providing fundamentally new opportunities for qualitative and quantitative assessment of high laryngopharyngeal reflux (Fig. 1).

During the course of the research, the new technology was thoroughly studied, validated, and put into practical use. The patent for the invention “The method for performing pH-impedance measurement in the diagnosis of laryngopharyngeal reflux” was granted by the Federal Service for Intellectual Property (Rospatent) (State Registration Number No. 2845916, dated August 27, 2025).

It is worth noting that in 60 % of patients with an established diagnosis of LPRD only on the basis of laryngoscopy data, no laryngopharyngeal reflux



**Figure 1.** Data from 24-hour hypopharyngeal-esophageal multichannel intraluminal pH-impedance monitoring using a special multichannel probe catheter in a patient with laryngopharyngeal reflux (own data of the V.Kh. Vasilenko Clinic of Propaedeutics of Internal Diseases, Gastroenterology and Hepatology): 1 – pH graph in the pharynx, 2 – pH graph in the esophagus, 3 – pH graph in the stomach, 4 – impedance graphs in the esophagus; liquid reflux is indicated on the impedance graphs by dotted white lines: retrograde and then antegrade movement of the bolus; the upper impedance sensor is located 1 cm above the upper esophageal sphincter; acidic pH values of 2 units are recorded in the esophagus (solid white arrow), and acidic pH values of 3.9 are also recorded in the pharynx (solid red arrow)

**Рисунок 1.** Данные суточной рН-импедансометрии с ларингофарингеальным зондом у пациента с ларингофарингеальным рефлюксом (собственные данные Клиники пропедевтики внутренних болезней, гастроэнтерологии и гепатологии им. В.Х. Василенко): 1 – график рН в глотке, 2 – график рН в пищеводе, 3 – график рН в желудке, 4 – графики импеданса в пищеводе; жидкий рефлюкс обозначен на графиках импеданса пунктирными белыми линиями: ретроградное, а затем антероградное движение болюса; верхний импедансный датчик расположен на 1 см выше верхнего пищеводного сфинктера; в пищеводе регистрируются кислые значения рН – 2 единицы (сплошная белая стрелка), в глотке регистрируются также кислые значения рН – 3,9 (сплошная красная стрелка)

is detected during 24-hour pH-impedance monitoring. Such overdiagnosis of laryngopharyngeal reflux is due to the untimely implementation of 24-hour pH-impedance monitoring for the objective diagnosis of reflux from the stomach to the larynx [3].

To date, a significant number of studies have been conducted to determine the normal values for 24-hour pH-impedance monitoring of reflux and pH of the pharynx. In one study, it was demonstrated that LPR in the average amount of 8 episodes is not accompanied by laryngopharyngeal complaints in GERD patients [45]. In another study, the authors admit the presence of up to 5 asymptomatic LPR per day on average in healthy volunteers, which is confirmed by a large systematic review, including the results pH-impedance monitoring of 720 healthy volunteers [27]. However, a number of researchers believe that chronic damage to the laryngeal mucosa can develop as early as three laryngopharyngeal refluxes occur within a week [28]. According to a recent consensus, reflux reaching the pharynx, regardless of its nature, can lead to laryngopharyngeal symptoms [29]. Depending on the pH values, according to pH impedance, acid (pH < 4), weakly acid (pH 4–7), non-acid (pH > 7) laryngopharyngeal reflux can be distinguished in the pharynx. In laryngopharyngeal reflux disease, reflux is usually mixed, has a weakly acid and non-acid character [30].

It is necessary to separate the concept of true non-acid (weakly acid, non-acid) reflux, when the pH values in the distal part of the esophagus and larynx are the same, and “false” non-acid reflux, when acid gastroesophageal reflux in the distal part of the esophagus, reaching the larynx, becomes non-acid due to the ability of the carbonic anhydrase III enzyme to lead to the hydration of carbon dioxide to bicarbonate, which helps neutralize hydrochloric acid [31–33]. The definition of true and “false” LPR can further influence the selection of therapy and patient management tactics [31].

Thus, there is still a need to conduct further research in order to determine the reference values for LPR, which can cause manifestations of LPRD. In clinical practice, 24-hour pH-impedance monitoring is currently recognized as the only method that can reliably diagnose LPR in patients with laryngopharyngeal symptoms.

In patients with laryngopharyngeal symptoms combined with complaints of heartburn and regurgitation, the presence of extraesophageal manifestations of gastroesophageal reflux disease should be excluded. According to the Montreal Classification, extraesophageal manifestations of GERD include those whose association with reflux esophagitis is based on convincing evidence (chronic cough, chronic laryngitis, bronchial

asthma, dental erosion), and those whose association with GERD is only suspected (pharyngitis, sinusitis, pulmonary fibrosis, chronic otitis media) [34].

The results of a 5-year prospective multicenter open cohort study of ProGERD, which included 6215 patients, demonstrated a significant prevalence of extraesophageal manifestations in GERD patients. Extraesophageal manifestations of GERD were diagnosed in 32.8 % of cases, and the prevalence was significantly higher in the group of patients with erosive form of the disease (34.9 % vs. 30.5 %;  $p = 0.0002$ , OR = 1.22, 95% CI: 1.09–1.35). Laryngeal symptoms were detected in 10.4 % of patients and were also more common in the group with erosive form ( $p = 0.0234$ , OR = 1.21, 95% CI: 1.03–1.42) [35].

A feature of the course of extraesophageal manifestations of GERD is the presence of such complaints characteristic of this pathology, as heartburn and regurgitation, and not only the laryngopharyngeal symptoms described above. In addition, as noted earlier, complaints in patients with GERD are more often noted at night and are associated with the transition to a horizontal position, as well as in the postprandial period. According to the literature, cough complaints can bother from 21 to 41 % of patients with GERD [22], hoarseness of voice occurs in 14.8 % of cases [17].

Although laryngopharyngeal symptoms are widely considered in the literature as extraesophageal manifestations of GERD, there is no consensus among the authors on the diagnostic criteria of the disease.

If extraesophageal manifestations of GERD are suspected, it is advisable to use questionnaires, for example, the Reflux Symptom Score (RSS), which allows one to assess symptoms from both the upper gastrointestinal tract and symptoms related to complaints from the ear, throat, nose, respiratory tract and chest pain unrelated to diseases of the esophagus. It is also possible to re-interview the patient against the background of ongoing therapy in order to assess its effectiveness [36]. Once again, it should be emphasized that when analyzing the results of the survey, one should not forget that clinical symptoms alone are not enough to establish a diagnosis due to their nonspecificity [3, 37].

The detection of erosive and ulcerative changes or intestinal metaplasia of the esophageal epithelium during EGDS in patients with laryngopharyngeal complaints makes it more likely to be considered as a component of the extraesophageal manifestations of GERD in the case of a diagnosis of LPR [2]. In patients with extraesophageal symptoms of GERD, the incidence of

erosive esophagitis, according to available data, ranges from 18 to 52 % [3]. The presence of Los Angeles Grade C/D esophagitis or Barrett's esophagus justifies the trial therapy of PPIs in patients with laryngopharyngeal reflux as part of the extraesophageal manifestations of GERD [36].

Patients with LPR and complaints of heartburn and regurgitation also need 24-hour pH-impedance monitoring [24, 38]. This technique is recognized as the gold standard for the diagnosis of GERD and allows for a differential diagnosis with functional heartburn and hypersensitive esophagus. According to the Lyon Consensus 2.0, additional evidence of the presence of GERD was identified according to 24-hour pH-impedance monitoring, such as percent of time with a pH of less than 4 units in the esophagus during the day > 6 % and the number of gastroesophageal reflux > 80, the value of the mean basal night impedance < 1500 ohms. In turn, the percentage of the time with a pH < 4 units in the esophagus during the day < 4 %, the number of refluxes up to 40 per day, mean basal night impedance > 2500 ohms indicate the absence of the disease. Intermediate values were accepted as doubtful in establishing the diagnosis of GERD [39]. However, in a patient with laryngopharyngeal symptoms, heartburn and regurgitation, it is necessary to confirm, in addition to pathological gastroesophageal reflux, high laryngopharyngeal reflux, which together will allow the patient to establish the diagnosis of extraesophageal manifestations of GERD.

According to the pH-impedance monitoring, patients with proven GERD are more likely to have an acid reflux than patients with LPRD [40].

There is a large group of patients with laryngopharyngeal symptoms, complaints of heartburn, regurgitation, in whom, according to the results of EGDS and pH-impedance monitoring, there is no data for the presence of GERD, but LPR is confirmed. In this case, the physician can diagnose this patient with LPRD. It should be noted that the absence of pathological acid gastroesophageal refluxes casts great doubt on the expediency of prescribing antisecretory therapy to patients with LPRD in the absence of proven GERD.

Currently, in patients with extraesophageal manifestations of GERD, as well as in patients with LPRD, the reference values of the number of laryngopharyngeal reflux, diagnosed by hypopharyngeal-esophageal multichannel intraluminal 24-hour pH-impedance monitoring, are only being established. In addition, laryngopharyngeal reflux should not always be regarded as pathological, in some cases they can be detected in people without laryngopharyngeal symptoms. This statement is confirmed in the work performed at the V.Kh. Vasilenko Clinic of Propaedeutics

of Internal Diseases, Gastroenterology and Hepatology (Sechenov University).

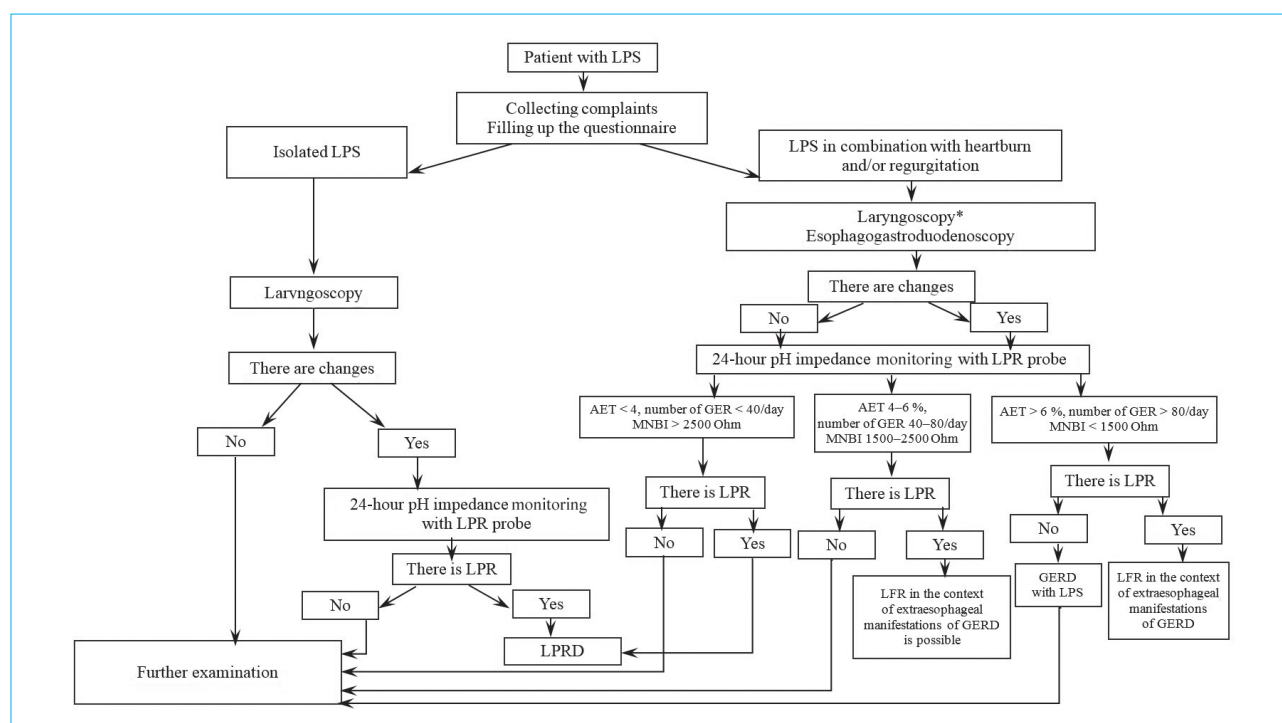
The study included 30 patients with GERD without extraesophageal manifestations. Under high-resolution manometry control, the pH sensors were located at a level of 5 cm above the lower esophageal sphincter and 1 cm above the upper esophageal sphincter and 7 impedance channels (the proximal one is 1 cm above the upper esophageal sphincter). The authors demonstrated that in GERD patients without extraesophageal manifestations, LPR in the amount of 8 [1; 16] episodes with a minimum pH value of 4.6 [2.1; 6.5] units and a pH in the range of 5 to 6 units during 2.2 [0; 64.8] % of the study time did not cause laryngopharyngeal complaints in patients. Mixed LPR significantly prevailed over liquid ones ( $t = 2.782$ ;  $p = 0.027$ ) and reached the oropharynx due to the gas component in the reflux [41].

Therefore, there is still a need for further research to determine the reference values for laryngopharyngeal reflux, which can cause laryngopharyngeal symptoms.

Figure 2 shows an algorithm for examining a patient with laryngopharyngeal symptoms. As a result of the examination in a patient with isolated LPS after collecting complaints, laryngoscopy, hypopharyngeal-esophageal multichannel intraluminal 24-hour pH-impedance monitoring using a special probe catheter, and with objective confirmation of the presence of laryngopharyngeal reflux, one can think of the presence of LPRD. In the absence of pathological reflux, the patient should be referred for further follow-up to rule out other possible causes of laryngopharyngeal symptoms.

A patient with LPS in combination with heartburn and regurgitation should complete a questionnaire to assess the symptom index, perform laryngoscopy, esophagogastroduodenoscopy, and hypopharyngeal-esophageal multichannel intraluminal 24-hour pH-impedance monitoring for differential diagnosis. In the absence of data in favor of GERD and confirmation of LPR, the physician establishes the diagnosis of LPRD, and in the absence of laryngopharyngeal reflux, the patient should be recommended for further follow-up to exclude other possible causes of complaints. In a patient complaining of heartburn and regurgitation in combination with laryngopharyngeal symptoms, laryngopharyngeal symptoms will be considered within the framework of extraesophageal manifestations of GERD. The absence of LPR and reflux esophagitis according to the results of the examination requires further follow-up to clarify the diagnosis.

The difficulty of treating patients with laryngopharyngeal symptoms is due to the lack of uniform clinical recommendations to date.



**Figure 2.** The algorithm for examining a patient with laryngopharyngeal symptoms: ЛФС — laryngopharyngeal symptoms, ЛФР — laryngopharyngeal reflux, ГЭРБ — gastroesophageal reflux disease, ЛФРБ — laryngopharyngeal reflux disease, ГЭР — gastroesophageal reflux, АЕТ — acid exposure time (percentage of the time with pH < 4 units in the esophagus), СНБИ — average nocturnal basal impedance; \* — laryngoscopy is provided in order to exclude other possible causes of laryngopharyngeal symptoms, including malignant neoplasms

**Рисунок 2.** Алгоритм обследования пациента с ларингофарингеальными симптомами: ЛФС — ларингофарингеальные симптомы, ЛФР — ларингофарингеальный рефлюкс, ГЭРБ — гастроэзофагеальная рефлюксная болезнь, ЛФРБ — ларингофарингеальная рефлюксная болезнь, ГЭР — гастроэзофагеальный рефлюкс, АЕТ — acid exposure time (процент времени с pH < 4 единиц в пищеводе), СНБИ — средний ночной базальный импеданс; \* — проведение ларингоскопии предусмотрено с целью исключения других возможных причин ларингофарингеальных симптомов, в том числе злокачественных новообразований

One of the groups of medications prescribed to patients with extraesophageal manifestations of GERD are PPIs. The American College of Gastroenterology suggested that the clinical response to PPIs therapy should be considered as a method for diagnosing and treating extraesophageal manifestations of GERD before conducting an in-depth examination. In this case, the course of PPIs therapy is up to 12 weeks [22]. However, the appointment of PPIs is often ineffective, and prolonged use of antisecretory drugs can only delay the establishment of a correct diagnosis and the appointment of appropriate treatment [22]. PPIs therapy in the treatment of LPR is often criticized, as it is based on a low level of evidence, and in a significant number of randomized clinical trials, the authors fail to convincingly demonstrate the significant advantage of PPIs over placebo [13]. In recent years, the issue of the expediency of prescribing drugs containing magaldrate and alginate to patients with verified physical therapy has been increasingly discussed [1, 13, 42–44]. A number of authors

believe that alginates can be effective even as monotherapy for physical therapy and their administration in a dosage regimen of 4 times a day (3 times a day after meals and at night) helps to reduce laryngopharyngeal complaints [42, 43].

## Conclusion

In recent years, clinicians have begun to encounter more patients in their practice complaining of hoarseness, throat pain, dryness in the throat, globus sensation and cough. In this regard, the issues of diagnosis and treatment of laryngopharyngeal reflux, a possible cause of laryngopharyngeal symptoms, are increasingly discussed among doctors of various specialties, including gastroenterologists, otorhinolaryngologists, pulmonologists, and allergists. Although researchers publish papers on laryngopharyngeal reflux every year, the current difficulty in managing patients with laryngopharyngeal symptoms is



due to the lack of a gold standard for diagnosing and treating such patients. It is worth noting that patients with laryngopharyngeal reflux require an integrated approach when examining with the participation of physicians in related specialties, performing laryngoscopy, esophagogastroduodenoscopy. The diagnostic method that allows one to directly visualize reflux into the larynx is the hypopharyngeal-esophageal multichannel intraluminal 24-hour pH-impedance monitoring using a special probe catheter. The new

technology, which includes a practical diagnostic algorithm (Fig. 2) and, for the first time in Russia, a developed and constructed laryngopharyngeal probe, opens up wide diagnostic possibilities for qualitative and quantitative assessment of high laryngopharyngeal reflux and differential diagnosis between laryngopharyngeal reflux disease and gastroesophageal reflux disease with extraesophageal manifestations. To date, the question of the reference values of laryngopharyngeal reflux in pH-impedance monitoring remains open, which requires further research.

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