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## **Significance of pH-impedancemetry and manometry in the management of patients with refractory gastroesophageal reflux disease**

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**Abstract.** Gastroesophageal reflux disease (GERD) is a widespread disease that has a significant impact on the quality of life of patients and is a leading risk factor for the development of esophageal adenocarcinoma. Currently, proton pump inhibitor therapy (PPI) is the basic treatment for patients with GERD, but 1/3 of patients show resistance to the prescribed therapy.

Currently, 24-hour pH-impedancemetry and high-resolution esophageal manometry are the most informative diagnostic methods in patients resistant to PPI therapy. These methods allow timely recognition of the causes of the refractory course of GERD, differential diagnosis with other nosologies, timely correction administer therapy individually for each patient.

**Keywords:** gastroesophageal reflux disease, proton pump inhibitors, refractoriness, pH-impedancemetry, high resolution manometry.

**Introduction.** The study of gastroesophageal reflux disease (GERD) has a long history. The first description of inflammatory changes in the esophagus belongs to Claudius Galen, who in the 2nd century AD noted that damage to the organ may be accompanied by heartburn and pain when swallowing. A more complete presentation of the clinical picture of GERD, which included symptoms such as heartburn, belching of sour and bitter, can be found in the writings of Avicenna [1].

Currently, two forms of GERD are distinguished [4]: non-erosive reflux disease (NERD), accounting for 60–65% of all cases, and erosive RE, detected in 30–35% of patients. For RE, it is recommended to use the classification adopted at the X World Congress of Gastroenterologists (Los Angeles, 1994) [7].

The clinical significance of GERD (especially over the past 10 years) determine its high prevalence among chronic diseases of the gastrointestinal tract and the continuing increase in the incidence even in those geographical areas where previously this pathology was rarely detected. In this regard, the statement that “the 20th century is the century of peptic ulcer disease, and the 21st century is the century of GERD” is relevant, which was proposed at the VI Joint Gastroenterological Week in Birmingham in 1997 [8].

An analysis of epidemiological studies conducted to assess the prevalence of the disease demonstrates significant geographical differences (Table 1), and only the East Asian region has consistently relatively low rates, not exceeding 10% [9]. Distributed in Russia GERD incidence averages 13.3% [10], however, in the Moscow region it reaches 23.6%, which is one of the highest rates among the Western population [11].

Refractory course of GERD. Currently for diagnostic In addition to non-invasive methods (using the GERD Q questionnaire) [12], a whole arsenal of modern instrumental studies is widely used in GERD, including esophagogastroduodenoscopy with esophageal biopsy and histological examination of biopsy specimens, intraesophageal 24-hour pH impedancemetry, and high-

resolution intraesophageal manometry. In addition, approaches to the treatment of patients with GERD are constantly being improved, among which the leading positions are firmly assigned to proton pump inhibitors (PPIs) [5].

Despite the large number of studies on GERD, many issues of diagnosis and treatment remain controversial and need further study. Among them, a special place is occupied by refractory GERD, which is observed on average in 30% of patients [13].

Over the past decade, predictors have been actively studied: development of GERD resistance to PPIs. It is known that the nature of refractory GERD is multifactorial.

One of the GERD refractoriness factors is non-compliance by patients with the prescribed treatment regimen, which includes a number of subjective reasons for the ineffectiveness of therapy: non-compliance with the frequency, time and duration of PPI intake, replacement of expensive drugs with more affordable ones, and often the lack of clear medical recommendations for treatment [21, 22].

Regarding the phenomenon of "night acid breakthrough" and its contribution to the development of the refractory form of GERD, studies are few and their results are contradictory. "Nocturnal acid breakthrough" is defined as a period of decrease in pH in foodwater  $<4$  at night lasting  $>1$  h, including in patients taking PPIs 2 times a day [23]. According to the study by A. Bredenoord et al. [24], this phenomenon cannot be considered a key one in the pathogenesis of the refractory form of GERD.

To the factors that may affect the lack of response to antisecretory therapy for GERD or insufficient relief of symptoms, also include the presence of non-acid reflux in the patient, impaired motor activity of the thoracic esophagus, an increase in the number and duration of periods of transient relaxation of the lower esophageal sphincter, HH. It should be noted that when making a diagnosis of refractory GERD, it is necessary not only to analyze the possible factors causing it, but also to take into account the likelihood of erroneous definition of GERD as refractory and, moreover, an erroneous diagnosis of GERD itself.

Modern possibilities of diagnostics of refractory GERD. In modern clinical practice, the use of 24-hour pH-impedancemetry and high-resolution intraesophageal manometry allows answering many of the above questions. pH-impedance monitoring is indispensable for the detection of non-acid refluxes, esophageal manometry helps in diagnosis of motor disorders of the esophagus. In addition, these methods sometimes make it possible to correct the diagnostic concept of refractory GERD, demonstrating results that make it possible to exclude the diagnosis of GERD and establish a different nosological form or identify the intersection of GERD and other functional disorders [35].

24-hour pH-impedancemetry. The method is a combination of pH meters and multichannel impedancemetry. In this case, catheters having both impedance sensors and one or more pH sensors are used. At the same time, the presence of reflux is judged by a change in the impedance curve, while pH sensors make it possible to characterize the refluxate chemically by pH values (acidic, slightly acidic, slightly alkaline, alkaline), as well as to evaluate the chemical clearance of foodwater [36].

Impedancemetry allows not only determining episodes of reflux, but also their physical state (gas, liquid) and bolus clearance. In the absence of sips or refluxes, the

impedancena curve is a basal line with a level of  $Z=800-2400$  Ohm. When swallowing or refluxing liquid contents, the conductivity of which is significantly higher than the conductivity of the walls of the esophagus, the impedance between adjacent electrodes of the measuring segment decreases and the impedance curve drops below the basal level. Thus, the wide diagnostic capabilities of 24-hour pH-impedancemetry make it possible to maximally individualize the approach to each patient and choose the most rational way for further therapy.

High resolution manometry. In development refractory In GERD, factors such as impaired motor activity of the thoracic esophagus, an increase in the number and duration of periods of transient relaxation of the LES, the presence of HH are often important, which can be detected by intraesophageal manometry. High-Resolution Manometry is a high-tech multi-probe method that allows detailed assessment of the motor function of the esophagus throughout its entire length, including the upper esophageal sphincter, thoracic esophagus, and LES.

Methodology the study is based on the fact that the patient drinks 10 sips of water, 5 ml each, then, based on the polychrome image of areas with different pressure levels, an automatic calculation of the parameters for each sip (IRP, DCI, CDP, DL, Break ) is performed, followed by evaluation as each individual pharynx, and all sips in general. Currently, the assessment of high-resolution manometry results is based on the Chicago Classification III revision (2015), which allows you to determine the presence or absence of motor disorders of the esophagus [48].

The Chicago Classification covers primary esophageal motility disorders, including esophageal motility disorders (achalasia, gastroesophageal junction obstruction), major motility disorders (diffuse esophagospasm, absent peristalsis, and jackhammer type esophagus) and minor peristaltic disorders (minor disorders of peristalsis — inefficient motility) [48]. Among them, the so-called inefficient motility (weak or fragmented peristalsis) is of particular importance in cases of refractory GERD, when, with normal functioning, NES (IRNPS is normal)  $\geq 50\%$  of all sips are ineffective positive, as evidenced by a DCI value of  $< 450$  mm Hg cm s. Thus, we can judge the violation of the clearance of the esophagus, which is one of the common causes of stenting of patients with GERD to treatment.

## Conclusion

Thus, at present, 24-hour pH-impedancemetry and high-resolution esophageal manometry are the most informative diagnostic methods in patients resistant to standard doses of PPI. These methods allow timely recognition of the causes of refractory GERD, differential diagnosis with other nosologies, timely adjustment of therapy individually for each patient, and determination of indications for antireflux surgical treatment. The diagnostic capabilities of these methods determine their relevance and the need for a wider introduction of high-resolution 24-hour pH-impedance and high-resolution esophageal manometry into clinical practice.

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