Analysis of Lyon consensus 2.0 statements.

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Abstract

This study is devoted to the analysis of the so-called Lyon consensus 2.0. It is a continuation of the scientific analysis of the current state of gastroenterology, which proved the fallacy of 13 hypotheses on which it is based. It has been shown that pH monitoring was developed with major violations of the methodology, because of which it detects only severe forms of GERD. Twenty practitioners who used different models of pH monitoring, including long-term wireless pH monitoring, and pH-impedance monitoring, were selected to participate because pre-meetings and agreements indicated support for the organizers' ideas. Based on the voting, statements were published that received agreement from at least 80% of participants. The consensus solution is presented as an improvement in the diagnosis of different phenotypes of gastroesophageal reflux disease (GERD), which allows individual therapy to be prescribed in each case. However, the etiology and pathogenesis of GERD are the same for all patients. Despite the diversity of the clinical picture in the process of ontogenesis, it is the disease that needs to be treated, not the symptoms. The authors argue that prescribing PPI for up to 8 weeks is optimal. If this treatment does not lead to improvement in symptoms and/or endoscopic appearance, then we are talking about refractory GERD, which is the basis for offering surgical treatment. However, mildly acidic refluxant also damage the esophagus. Therefore, comprehensive treatment is optimal, which prevents or reduces episodes of reflux, protects the mucosa from refluxant, and restores evacuation from the esophagus and stomach. Therefore, lifestyle changes combined with drug treatment are preferable to surgery in most patients with GERD. In the diagnostic algorithm, the authors propose three types of pH monitoring, which is based on the false assumption of the possibility of physiological reflux. This error arose from improper selection of control subjects to determine the normal boundary. Meanwhile, it is known that more than 30% of patients with GERD consider themselves healthy. It follows from this that the use of equipment for pH monitoring, which detects only severe forms of GERD, is pointless and dangerous, since in many patients the diagnosis of GERD is unreasonably denied, and they do not receive pathogenetic treatment. For example, in case of heartburn, where pH <4, a diagnosis of esophageal hypersensitivity was invented, and patients are denied treatment for GERD. Lyon consensus 2.0. in fact, it is an advertisement for expensive but unsafe equipment for patients, which practitioners who are not prepared for scientific work present as scientific work.

Keywords: gastroesophageal reflux disease; pH monitoring; proton pump inhibitor; Lyon consensus 2.0.; critical analysis.

Introduction. This study is devoted to the analysis of the so-called Lyon consensus 2.0. [1]. It is a continuation of the scientific analysis of the current state of gastroenterology, which proved the fallacy of 13 hypotheses on which it is based [2]. It has been shown that pH monitoring was developed with major violations of the methodology, because of which it detects only severe forms of GERD [2]. In order not to repeat the evidence base, I will only address the analysis of statements that contradict common sense.

The stated goal of the Lyon consensus is to improve the diagnosis of GERD. For many decades, GERD was viewed as a disease whose symptoms varied as LES function worsened. However, the authors state "that many presentations of GERD represent distinct phenotypes with unique predisposing cofactors and pathophysiology outside of this paradigm". “For example, patients with reflux hypersensitivity may have normal LES function yet abnormalities of peripheral and/or central sensory processing. In contrast, patients with BE (Barrett's esophagus) may have a relative esophageal hyposensitivity” [1]. (1) The diagnosis of reflux hypersensitivity is based on AET (acid exposure time) < 4%. However, the idea that acid that breaks down proteins does not cause damage to the esophagus, which does not have the same protection as the stomach and duodenum, is counterintuitive. (2) Currently, there is no research method that accurately determines the function of the LES. This could be judged by the histological determination of the length of the cardiac epithelium using the method of Prof. Parakrama Chandrasoma, but the authors did not use it. (3). The statement that patients’ complaints of heartburn may be due to a disruption in communication with the brain has no scientific evidence and is contrary to common sense. It follows from this that an erroneous refusal to diagnose GERD and a delay in pathogenetic treatment in a patient at the initial stage of the disease, when the progression of the disease can be prevented, will worsen the prognosis of the disease. (4) Barrett's esophagus is an advanced stage of GERD. The absence or weakness of pain is due to the destruction of sensitive elements in the wall of the esophagus under the influence of hydrochloric acid and pepsin. However, both GERD with severe pain at the onset of the disease and GERD with mild pain require the same intensive treatment. Thus, the authors unreasonably violate the basic principle of medicine: treat the disease, not the symptoms.

About the methodology. An international working group (20 voting members) was assembled in January 2023, selected based on expertise in GERD diagnosis and management. All authors used the entire arsenal of expensive equipment produced for examining the esophagus. You can guess about the organizers of the conference, who selected members based on availability for virtual and in-person meetings. Since consensus decisions were determined by voting, if

the agreement between members exceeded 80%, these decisions cannot be considered scientific, i.e. correct.

GERD definition. In 2006, the Montreal Consensus, using a modified Delphi process, adopted the following definition of GERD: - «GERD was defined as a condition that develops when the reflux of stomach contents causes troublesome symptoms and/or complications» [3]. This definition shows that voting in science is not acceptable because it was contrary to scientific evidence. Firstly, it is known that GERD can occur and progress without clinical manifestations in more than 30% of patients [2]. Secondly, patients with minimal atypical and extra-esophageal symptoms, as well as patients without symptoms, fell out of sight of doctors using this classification, i.e., did not receive pathogenetic treatment on time. The accepted Lyon consensus 2.0. definition of GERD "requires conclusive evidence of reflux-related pathology on endoscopy and/or abnormal reflux monitoring (using Lyon consensus thresholds) in the presence of compatible troublesome symptoms" [1]. This definition includes information about the "presence of compatible troublesome symptoms", which, as shown above, has no scientific basis, as well as the need to use a wide range of diagnostic equipment, however, there is no reference to the etiology and pathogenesis that always determine the disease.

PPI testing. The authors recommend the use of antisecretory therapy as a diagnostic test. Relief of typical symptoms by PPI is considered evidence of GERD, and lack of effect can be considered either a denial of GERD in the absence of typical symptoms, or evidence of refractory GERD. This recommendation has no pathophysiological basis. First, if typical symptoms are present, there is no need for further diagnostic tests. Secondly, with weak LES, reflux of gastric juice into the esophagus in a horizontal position against the background of esophagitis cannot significantly affect the symptoms for any acidity. Reflux of chyme with "normal" acidity, which denatures food proteins, causes pain reactions in the same range as with hypersecretion of HCl. Thirdly, based on the lack of response to PPI treatment, it is impossible to claim refractory GERD, since antisecretory therapy is only a small part of the comprehensive treatment of GERD. If the patient continues to consume food that provokes hypersecretion of hydrochloric acid, goes to bed with food in the stomach, eats large amounts of food at the same time, especially meat and fats, and does not fight from esophagitis, which impairs esophageal emptying, then he will have no chance get rid of symptoms.

Symptoms of GERD. The description of esophageal symptoms that have high, intermediate, and low likelihood of association with reflux episodes has no practical significance, since it is

contrary to medical ethics. All symptoms that can be observed with GERD are a reason for examination, except for typical symptoms (heartburn and regurgitation), which have diagnostic status. If the doctor does not initiate an examination of patients with complaints of belching, putrid mouth, sinusitis, chronic cough, small gas bubble of the stomach, anemia, hoarseness, globus, nausea, abdominal pain, and other dyspeptic symptoms in combination or separately, his patients risk not receive pathophysiological treatment for GERD. Moreover, the degree of probability is determined incorrectly, since due to the low diagnostic accuracy of pH monitoring, GERD was not diagnosed in many patients with atypical symptoms.

Objective endoscopic findings of GERD

As the authors show, "the initial study indicated that LA grade A esophagitis had higher acid exposure time (AET) than non-erosive reflux disease (NERD) (9.3% vs 6.7%, respectively). Later studies have demonstrated grade A esophagitis in 5%–7.5% of healthy subjects. In healthy subjects LA grades B, C and D esophagitis are highly uncommon ."First, subsequent studies did not change the difference in acid exposure time in esophagitis A compared with NERD. Secondly, the presence of esophagitis in so-called healthy subjects convincingly indicates that they are not healthy. The authors of all cited articles selected supposedly healthy individuals as controls, not understanding the scientific significance of accurately identifying individuals in whom pathology of the esophagogastric junction would be excluded based on manometric, endoscopic, histological, and radiological methods. Any scientific physicist, chemist, biologist, etc. will confirm that all studies based on such selection of the control have no scientific significance. The authors do not recommend routine standard biopsy, without even mentioning the simple and scientifically proven Chandrosoma method. Instead, they suggest provoking inflammation to increase the chances of detecting esophagitis during endoscopy. “To maximize the diagnostic yield, endoscopy should be performed 2–4 weeks after discontinuation of antisecretory therapy in unproven GERD” [1].

Stopping PPI leads to a sharp increase in the secretion of hydrochloric acid, which is called rebound acid hypersecretion. Gastric acid rebound hypersecretion following PPI therapy induces reflux-like symptoms post-treatment in asymptomatic volunteers [4]. This provocation of increased secretion of hydrochloric acid not only intensifies the inflammatory process in the esophagus, but also provokes pain. The authors proceed from a false understanding of the etiology, pathophysiology, and pathogenesis of GERD, which were proposed based on improper selection of control (non-healthy) individuals and a false hypothesis about the

possibility of physiological reflux, i.e., the reflux, that does not damage the function of the LES and esophagus. Although we do not know whether each episode of reflux leaves its mark on the weakening of the antireflux function of the LES and disruption of the structure and function of the esophageal wall, the goal of treatment is to prevent reflux itself, and reduce the aggressiveness of the gastric juice. Stopping PPI for 4 weeks is unacceptable from the point of view of medical ethics, as it causes suffering to the patient and damages the function of the esophagus and LES, while alternative and safe methods for diagnosing GERD are available.

Most of the article is devoted to advertising equipment for diagnosing GERD, including the boundaries between normality and disease.

1. For **pH monitoring, including extended wireless pH monitoring,** the following limits have been established.

A). AET (acid exposure time) <4.0% on all days of wireless pH monitoring with negative reflux-symptom association excludes GERD.

B). AET>6.0% for ≥2 days is diagnostic of GERD and supports treatment for GERD.

C). AET<4.0% on all days with positive reflux-symptom association meets criteria for reflux hypersensitivity.

D). Total AET >6% off PPI on ambulatory pH monitoring is diagnostic of GERD and supports treatment for GERD.

These recommendations are dangerous because patients with GERD who are outside the erroneous standards do not receive pathogenetic treatment, because of which their disease progresses. For example, in patients with atypical symptoms with AET <4.0% (A), GERD cannot be excluded. Those patients (C) who suffer from heartburn, but with an acid reflux rate of < 4%, are mistakenly diagnosed with esophageal hypersensitivity and they do not receive pathogenetic treatment. In patients with AET<6.0% (B, D), GERD is unreasonably excluded and treatment for GERD is not supported.

2. pH-impedance monitoring.

The authors state that ambulatory pH-impedance monitoring off antisecretory therapy has diagnostic value in unproven GERD when typical reflux symptoms are associated with excessive belching, when rumination is suspected, and when pulmonary symptoms are being evaluated for association with GERD. The following are the boundaries.

a). Total reflux episodes <40/day is adjunctive evidence for absence of pathological GERD.

b). Total reflux episodes 40–80/day off PPI is inconclusive evidence for GERD as a standalone metric.

c). Total reflux episodes >80/day is adjunctive evidence for objective GERD.

d). Combination of AET>4% and >80 reflux episodes on an optimized antisecretory regimen is evidence for actionable refractory GERD.

These recommendations are erroneous because they are based on the false assumption that reflux can be physiological and not damage the esophagus and LES. After examining patients with GERD who considered themselves healthy, the authors came to the false conclusion that recurring belching can occur in healthy people.

Baseline impedance of <1500 ohms is adjunctive evidence for GERD, while baseline impedance >2500 ohms is evidence against pathological GERD.

The interval between <1500 and >2500 is too large to consider this method diagnostic.

Thus, the use of pH-impedance monitoring, the assessment of which requires special skills, makes no sense and is dangerous, since it diagnoses only very severe forms of GERD. This begs the question, why do the authors not use a simple, cheap, and very accurate method for diagnosing GERD by the presence and length of the cardiac epithelium between the gastric and esophageal epithelium? [5] (**Figure 1**).

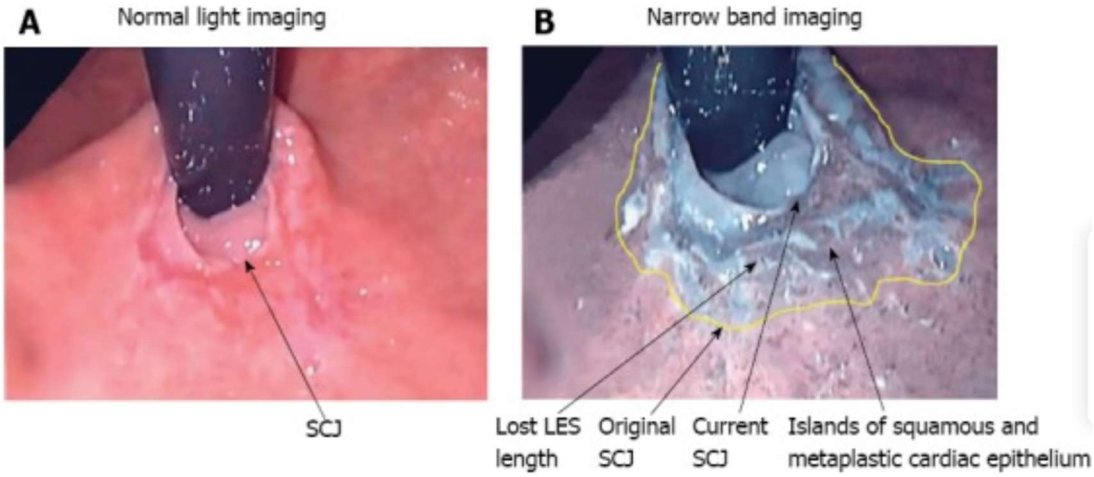

Figure 1. From the article by Labenz et al. [5]. Retroflex endoscopic view of the squamocolumnar junction in advanced gastroesophageal reflux disease. A: Normal white light image displays a slightly irregular SCJ with normal squamous epithelium extending up the

esophagus; B: Narrow band image shows multiple islands of squamous epithelium below the SCJ, surrounded by newly formed metaplastic cardiac epithelium. The splayed out original SCJ (indicated by the yellow line), and damaged portion of the LES between the original SCJ and the current SCJ, take on the appearance of stomach. Loss of esophageal muscle due to inflammation results in a reduction in the abdominal length of the LES and loss of the LES barrier function.

For several decades, no one has denied the reliability of this method, which means the correctness of the scientific concept. The rejection of a simpler and more accurate method for diagnosing GERD is due, firstly, to the fact that this concept reveals the falsity of the concept on which modern gastroenterology is built. Secondly, it becomes obvious that the second, unstated goal of the Lyon Consensus is the advertising of diagnostic equipment.

Conclusion

Gastroesophageal reflux disease is caused by hypersecretion of hydrochloric acid. Triggers of hypersecretion are food ingredients, one of which is lactose (**etiology**). Based on physiological and pathological studies, the concept was proposed that GERD begins at the squamo-columnar junction (SCJ). In the absence of squamous epithelial injury, the SCJ and the gastroesophageal junction are concordant. With injury to squamous epithelial hydrochloric acid, metaplastic cardiac epithelium forms and the SCJ separates from the gastroesophageal junction and moves upwards into the esophagus. This process causes damage to the LES, resulting in greater esophageal exposure to acid and bile [5] (**Pathogenesis**). Damage to the wall of the esophagus by hydrochloric acid, pepsin and bile causes expansion of the lumen, especially often the supradiaphragmatic part (**phrenic ampulla**). Fibrous changes occur in the wall of the esophagus, and the space between the mucosal cells increases. Peptic lesions and luminal narrowing may occur. All this leads to disruption of the motor function of the esophagus and LES, as well as to a decrease in sensitivity. These changes depend on the duration of the disease, lifestyle, immunological reactivity of the body and genetic factors. (**Pathophysiology**). In the process of **ontogenesis**, following changes in the pathophysiology the symptoms of the disease change.

GERD is a chronic, progressive disease. Treatment of GERD should be aimed at preventing (as much as possible reducing) episodes of reflux, reducing the aggressiveness of gastric contents, and protecting the mucosa from damage by the refluxant. Treatment of symptoms,

i.e., phenotypes, as suggested by the consensus participants, rather than diseases contradicts the methodology of science.

The authors voted for two statements, (1) that the persistence of inflammatory and/or fibrotic mucosal lesions despite optimized PPI therapy is indicative of refractory GERD, regardless of whether patients are symptomatic or not. (2) that the combination of AET>4% and >80 reflux episodes/day on an optimized antisecretory regimen is evidence for actionable refractory GERD. Two definitions follow from the text: (1). Optimized PPI therapy is the use of 20 or 40 mg PPI twice a day for 8 weeks. (2). Refractory GERD is an indication for surgery. However, mildly acidic refluxant also damage the esophagus. Therefore, comprehensive treatment is optimal, which prevents or reduces episodes of reflux, protects the mucosa from refluxant, and restores evacuation from the esophagus and stomach. Therefore, lifestyle changes combined with drug treatment are preferable to surgery in most patients with GERD.

Thus, the stated goal, to improve the diagnosis of GERD, was initially impossible because it was based on false hypotheses. Another, unstated purpose of the so-called Lyon Consensus is to advertise expensive diagnostic equipment. The purpose of this analysis is to show that, from the point of view of science and common sense, the advertised equipment should not be used in gastroenterology.

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