

## EVALUATION OF THE GASTROINTESTINAL MUCOSA BY THE OLGA SYSTEM IN CHRONIC ATROPHIC GASTRITIS

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### Abstract

The aim of the study was to study the endoscopic and morphological features of the mucous membrane of the stomach and intestines using the OLGA system in chronic atrophic gastritis. The study included 180 patients with dyspepsia symptoms ranging in age from 18 to 80 years old, who were diagnosed with H.pylori - associated gastritis during endoscopic examination with a quick urease test. Neatrophic fundus gastritis was detected in 99 patients (55.0%), mild atrophy of the mucous membrane of the stomach body was detected in 19 patients (10.56%), moderate atrophy in 36 patients (20.0%) and severe atrophy in 26 patients (14.44%). Depending on the presence and severity of multifocal atrophy of the gastric mucosa (simultaneous presence of atrophic changes in the body and antrum), the studied patients were distributed as follows (table 2): lack of multifocal atrophy - 39 patients (21.7%), a weak degree of multifocal atrophy was detected in 46 patients (25.5%), moderate degree of atrophy in 64 patients (35.6%) and severe multifocal atrophy in 31 patients (17.2%). Thus, our data show that the stage of atrophy, established by the OLGA system, generally corresponds to the stage of atrophy, determined by the visual-analogue scale of the Houston modification of the Sydney system.

**Key words:** chronic atrophic gastritis, intestinal metaplasia, morphology, gastric mucosa, H. pylori.

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### INTRODUCTION

Atrophic gastritis is an urgent problem of modern gastroenterology in our country and around the world, in connection with the transformation into gastric cancer.

Atrophic gastritis is understood as a progressive inflammatory process of the gastric mucosa, characterized by the loss of gastric glands. The clinical and morphological feature of atrophic gastritis is a decrease in the number of specialized glandulocytes that provide secretory function of the stomach, and their replacement with simpler cells, including those that produce mucus. Extensive atrophy of the mucous membrane of the body of the stomach, as a rule, is associated with hyposecretion of hydrochloric acid and impaired pepsinogen production.

Helicobacter pylori infection (HP) and autoimmune gastritis are recognized as the most common etiological factors causing atrophic gastritis. Moreover, the occurrence of the vast majority of atrophic gastritis is associated with H. pylori. The bacteria H. pylori, persisting on the gastric epithelium, cause chronic Helicobacter pylori gastritis. Long-existing superficial Helicobacter pylori gastritis is transformed into atrophic without appropriate treatment.

Atrophic gastritis clinically, as a rule, does not manifest itself for a long time, therefore, the diagnosis of chronic gastritis is more morphological than clinical.

Gastric cancer (GC) is a global health burden and the fourth most common cause of cancer death in the world. A sequential histopathology cascade for the development of gastric adenocarcinoma of the intestinal type - from normal gastric epithelium to chronic gastritis, chronic atrophic gastritis (CAG) and intestinal metaplasia (IM), followed by dysplasia and, finally, RG. Patients with precancerous diseases, such as CAG or dysplasia, have a significant risk of developing cancer, and early detection of these lesions is important for screening for cancer.

For CAG population screening, the endoscopic mass screening program has been shown to be effective in countries with a predominant GC, such as Korea and Japan. Overview of modern concepts of gastric metaplasia and gastric cancer. An endoscopic screening program reduced mortality associated with cancer by 47% as part of a case-control study in Korea. The effectiveness of the Korean National Cancer Program in reducing stomach cancer mortality.

The aim of the study was to study the endoscopic and morphological features of the mucous membrane of the stomach and intestines using the OLGA system in chronic atrophic gastritis.

### MATERIAL AND RESEARCH METHODS

The study included 180 patients with dyspepsia symptoms ranging in age from 18 to 80 years old, who were diagnosed with H.pylori - associated gastritis during endoscopic examination with a quick urease test. Men accounted for 33.89% of the respondents (61 people), women - 66.11% (119 people). Prior to the endoscopic examination, none of the patients took drugs from the groups of proton pump inhibitors or non-steroidal anti-inflammatory drugs. The study did not include patients with concomitant diseases that affect the course of the underlying disease (pathology of the central nervous system, organic diseases of the endocrine glands, kidney diseases, cholelithiasis, symptomatic gastric and duodenal ulcers, diseases requiring the use of antibacterial or anti-inflammatory drugs).

The control group consisted of HP-negative volunteers aged 17 to 45 years, in whom there was no history of gastrointestinal tract diseases and gastroduodenal mucosa was assessed as practically unchanged with endoscopy.

The average age of the studied patients was  $43.3 \pm 7.4$  years, while the greatest number of them belonged to the age groups of 31-40 years and 41-59 years.

In accordance with the tasks, endoscopic endoscopy was performed with multiple biopsies (2 biopsy samples from the body and antrum of the stomach and one biopsy from the angle of the stomach, taking into account the requirements of the modified Sydney system) with histological study of biopsy samples. The revealed changes were classified depending on the stage of development of atrophy and the degree of inflammatory infiltration in accordance with the visual-analogue scale of the Houston modification of the Sydney system, as well as according to the OLGA system.

Histological examination was carried out in the pathoanatomical department of Gastroenterology of republican specialized scientific and practical medical center therapies and medical rehabilitation in Tashkent. Biopsies were fixed in 10% neutral formalin buffered according to Lilly, after which the material was subjected to standard histological processing with filling in Histomix paraffin medium. The resulting paraffin blocks were subjected to cutting on a rotary microtome to obtain serial sections with a thickness of 5 µm.

To assess the general pathological changes in the mucous membrane, the sections were stained with hematoxylin-eosin and picrofuxin according to Van Gieson; the state of the glandular apparatus of the mucous membrane was assessed by staining with Alcian blue at pH 2.5 (detection of sialomucins) and at pH 1.0 (detection of sulfomucins) in combination with the SHIK reaction; additional morphological verification of the presence of *H. pylori* in biopsy specimens was carried out by staining the sections according to the modified Giemsa method with azurII-eosin and studying the preparations under immersion increase.

Statistical processing of the obtained data was carried out according to the generally accepted technique in accordance with the monograph of S. Glanz "Biomedical statistics" using the computer program StatPlus 2008 Professional 5.3.5.0. The results were considered reliable when the error probability was  $P < 0.05$ , which is generally accepted in medical research. A comparative analysis of qualitative features — morphological changes in the coolant: pylorization of the body glands, intestinal metaplasia, epithelial dysplasia, atrophy of the gastric mucosa — was performed using Fisher's exact test, criterion  $\chi^2$ , and nonparametric criterion  $x^2$ .

**RESEARCH RESULTS**

In all studied patients, histological examination revealed the presence of chronic gastritis, expressed to varying degrees. Depending on the presence, nature and severity of inflammatory infiltration of the gastric mucosa, we analyzed the degree of gastritis activity and the severity of mononuclear infiltration of the gastric mucosa lamina propria. The degree of gastritis activity was evaluated in the antrum and in the stomach in accordance with the severity of infiltration of the lamina propria with polymorphonuclear (neutrophilic) leukocytes. *H. pylori*-associated chronic gastritis of a moderate degree of activity developed more often in the body of the stomach, and chronic gastritis of a high degree of activity developed in the antrum. A comparative analysis of the obtained data revealed significant differences between the frequency of development of gastritis of moderate and high degree of activity in the antrum and the body of the stomach ( $P < 0.05$ ).

Depending on the presence and severity of atrophy in the stomach, patients were divided as follows. Nonatrophic fundus gastritis was detected in 99 patients (55.0%), mild atrophy of the mucous membrane of the stomach body was detected in 19 patients (10.56%), moderate atrophy in 36 patients (20.0%) and severe atrophy in 26 patients (14.44%).

Depending on the presence and severity of atrophy of the mucous membrane of the antrum, the studied patients were divided as follows: non-atrophic gastritis was detected in 12 patients (6.67%), mild atrophy of the gastric mucosa in 35 patients (19.44%), moderate atrophy - in 69 patients (38.33%) and severe atrophy - in 64 patients (35.56%).

When comparing the results of the diagnosis of atrophy in the antrum and in the body of the stomach (table 1), we revealed significant differences: in the body of the stomach, significantly more significant non-atrophic gastritis was detected, and in the antrum - significantly more often than in the body, any degree of atrophy of the gastric mucosa developed (in all cases,  $P < 0.05$ ). Such differences are probably due to the fact that HP-associated gastric damage begins in the antrum, and by the time clinical manifestations develop, when the patient undergoes a biopsy of the mucous membrane, changes in the antrum are more pronounced due to their longer duration.

**Table 1. Statistical analysis of the incidence of atrophy of the mucous membrane in the antrum and body of the stomach**

Degree of atrophy	Atrophy detection rate (%)		P
	Body	Antrum	
Non atrophic gastritis	55,0	6,67	<0,05
Mild atrophy	10,56	19,44	<0,05
Moderate atrophy	20,0	38,33	<0,05
Severe atrophy	14,44	35,56	<0,05

**Table 2. Statistical analysis of the incidence of mucosal atrophy in multifocal and focal chronic gastritis**

Stage of atrophy	Atrophy detection rate (%)			P <sub>1-3</sub>	P <sub>2-3</sub>
	1. Corpus dominant atrophy	2. Antrum dominant atrophy	3. Multifocal atrophy		
Nonatrophic gastritis	55,0	6,67	21,7	<0,05	<0,05
Mild atrophy	10,56	19,44	25,5	<0,05	>0,05
Moderate atrophy	20,0	38,33	35,6	<0,05	>0,05
Severe atrophy	14,44	35,56	17,2	>0,05	<0,05

Depending on the presence and severity of multifocal atrophy of the gastric mucosa (simultaneous presence of atrophic changes in the body and antrum), the studied patients were distributed as follows (table 2): lack of multifocal atrophy - 39 patients (21.7%), a weak degree of multifocal atrophy was detected in 46 patients (25.5%), moderate degree of atrophy in 64 patients (35.6%) and severe multifocal atrophy in 31 patients (17.2%).

When comparing the results of the diagnosis of multifocal atrophy with the frequency of detecting atrophy in the antrum and in the body of the stomach, we obtained the following results: non-atrophic multifocal gastritis occurred significantly more often than corpus dominant gastritis, but at the same time, significantly less often than non-atrophic antrum-dominant gastritis. In the case of the development of a mild to moderate degree of multifocal atrophy, its frequency was significantly higher than for corpus-dominant gastritis and did not significantly differ from the frequency of antrum-dominant

atrophic gastritis. With a pronounced degree of multifocal atrophy of the gastric mucosa, an inverse relationship was observed: an unreliable difference from the frequency of the corpus dominant atrophic gastritis and a significant difference from the frequency of the antrum-dominant atrophic gastritis. The results can be interpreted as follows: the initial development of atrophy of the gastric mucosa is carried out more intensively in the antrum of the stomach, where under natural conditions the degree of contamination of *H. pylori* predominates - the main cause of the development of chronic gastritis; further progression of inflammatory damage in the proximal direction leads to an increase in corpus dominating atrophy, including with the development of pseudopyloric metaplasia, and at the stage of development of severe multifocal atrophy of the mucous membrane, its severity is largely determined by damage to the fundus of the stomach.

The development of intestinal metaplasia in our observations was detected in 89 out of 180 patients (49.4%) and was accompanied by a local disappearance of *H. pylori* contamination in the metaplasia zones and a decrease in the activity of the inflammatory reaction. Most often, full small bowel metaplasia was found in the preparations, characterized by the presence of absorbent epithelial cells, goblet cells containing sialomucins, and Panet cells. Less often, incomplete small intestinal metaplasia was detected, characterized by the presence of goblet cells containing sialomucins among the integumentary-fossa epithelium of the gastric type. Finally, in a number of cases, we revealed foci of large intestinal metaplasia with the presence of goblet cells separated by high prismatic epithelial cells with an abundant content of sulfomucins.

In all cases, the presence of intestinal metaplasia was accompanied by atrophic changes in the gastric mucosa, expressed to one degree or another. In antrum-dominant chronic atrophic gastritis, intestinal metaplasia of the gastric epithelium was histologically detected in 84 (50%) of 168 patients. In this case, a weak and moderate prevalence of intestinal metaplasia prevailed.

In the group of patients with corpus dominant chronic atrophic gastritis, we identified 33 cases of the development of intestinal metaplasia of gastric epithelium (40.74%) out of 81 patients. Moreover, as in the case of antrum dominant chronic atrophic gastritis, a weak and moderate degree of prevalence of intestinal metaplasia predominated.

In addition to intestinal metaplasia, in patients with corpus dominant atrophic gastritis, we recorded the presence of pseudopyloric metaplasia, or "anthralization," of the gastric mucosa. At the same time, two main localizations of the development of pseudopyloric metaplasia were distinguished: in the area of the actually large curvature of the stomach body and in the area of angular incision of the stomach, where the main gastric glands normally prevail. Pseudo-pyloric mucosal metaplasia in the incision region was detected in 53 of 81

(65.4%) patients with corpus dominant atrophic gastritis, and in the area of great curvature of the body of the stomach, in 10 of 81 (12.3%) patients.

Thus, in the area of incubation, significantly ( $P < 0.05$ ) and significantly more often than in the area of large curvature of the body of the stomach, there was a violation of the differentiation of gastric epithelial elements, which reflects a greater risk of malignancy in this area of the gastric mucosa with *N. pylori*- associated chronic atrophic gastritis.

In the group of patients with multifocal atrophy of the gastric mucosa, we identified 81 cases of the development of intestinal metaplasia of gastric epithelium (57.45%) out of 141 patients.

Thus, intestinal epithelial metaplasia in the gastric mucosa against the background of atrophic gastritis was characterized by a predominance of a weak and moderate degree of prevalence, regardless of the localization of atrophy. Statistical analysis did not reveal significant differences in the frequency of each degree of prevalence of intestinal metaplasia depending on the affected part of the stomach ( $P > 0.05$  in all cases).

For further studies, we used biopsy specimens from 55 patients who were histologically diagnosed with *H. pylori*-associated atrophic gastritis.

In the antrum, atrophic changes of various degrees prevailed in 20 of 55 patients (36.36%), of which a weak degree of atrophy was detected in 5 patients, moderate in 9 patients and severe in 6 patients.

Corpus dominant chronic atrophic gastritis was diagnosed in 16 patients out of 55 (29.09%), of which a weak degree of atrophy was determined in 3 patients, moderate in 6 patients and severe in 7 patients.

We diagnosed multifocal chronic atrophic gastritis in 19 of 55 patients (34.55%), of which a weak degree of atrophy was determined in 6 patients, moderate in 6 patients and severe in 7 patients.

Then, the data obtained during histological verification of the stage of atrophy in accordance with the visual-analogue scale of the Houston modification of the Sydney system were entered into the table of the OLGA system. After distributing the obtained data in the table, according to the OLGA system, the following results were obtained (table 3): cases of a weak degree of atrophy, determined in accordance with the visual-analogue scale, corresponded mainly to the first stage of development of atrophy according to the OLGA system 50%, cases of moderate atrophy corresponded mainly to the second stages of development of atrophy according to the OLGA system 38.1%, cases of severe atrophy corresponded mainly to the fourth stage of development of atrophy according to the OLGA system 40%.

**Table 3. Stage atrophy in chronic atrophic gastritis according to OLGA systems**

Allstages	Number of patients	St 0	St 1	St 2	St 3	St 4
Atrophy	55	0	19	14	9	13
mild	14	0	7	4	2	1
moderate	21	0	6	8	3	4
severe	20	0	6	2	4	8

Next, we analyzed the prevalence of intestinal metaplasia of the gastric mucosa, depending on the stage of its atrophy according to the OLGA system. As the results showed, a histologically verified weak prevalence of intestinal metaplasia was determined mainly in the first and second stages of atrophy according to the OLGA system, respectively, at 35.29% (table 4).

When analyzing the data obtained, it was found that the presence of inflammatory infiltration of the gastric mucosa in patients with chronic atrophic gastritis corresponded to the

second, third or fourth degree according to the OLGA system, while the "zero" and first degrees were not detected.

Such results can be explained by the predominant development of a more pronounced intensity of the inflammatory reaction in one of the stomach sections (corpus-dominant or antrum-dominant gastritis), which, when distributed according to the OLGA system due to the summation of indicators from the body and antrum, led to a higher degree of inflammatory infiltration than when assessed by a visual analogue scale as a separate indicator for each section of the stomach.

**Table 4. Identification of intestinal metaplasia at different stages of atrophy of the gastric mucosa in chronic atrophic gastritis according to the OLGA system**

Allstages	Number of patients	St 0	St 1	St 2	St 3	St 4
Intestinalmetaplasia	42	0	11	15	12	4
weak	17	0	6	6	5	0
moderate	18	0	5	7	5	1
severe	7	0	0	2	2	3

## DISCUSSION

In the analysis of publications devoted to the assessment of the histological state of the gastric mucosa in relatives of patients with gastric cancer, the results of published studies were systematized and presented in accordance with the following aspects of this problem: H. pylori infection, detection of atrophy and metaplasia, dysplasia, assessment of the gastric mucosa in accordance with the OLGA staging system. It should be noted that most of the publications belong to authors from Asian countries, South America and only a few from European countries (Portugal, Italy). On many issues, research results are quite controversial. Studies evaluating H. pylori infection suggest that in relatives of patients with gastric cancer it is the same as in the general population, or higher. Data on the absence of differences compared with the control group were obtained mainly in studies conducted in regions with a high level of H. pylori infection, reaching 70–90%. Under such conditions, the identification of an increased susceptibility to infection can be difficult. At the same time, in works where the infection rate of the control group was lower, it was possible to identify differences in the frequency of detection of infection. This may be explained by the presence of relatives of individuals with a burdened heredity of genetic features predisposing to infection or environmental conditions common with patients who have developed cancer. In accordance with the results of the only discovered published meta-analysis, atrophy and intestinal metaplasia of the gastric mucosa are detected significantly more often in individuals with heredity burdened by gastric cancer than in the general population. However, there are many individual studies that contradict the results of this publication, as well as each other. Perhaps this is due to differences in the design of studies and sample sizes, insufficient elaboration of approaches to standardize the histological evaluation of precancerous lesions, and a low degree of consistency between researchers when evaluating a symptom such as non-metaplastic atrophy. Data on the incidence of dysplasia in different studies are more consistent and suggest a higher risk of developing dysplasia in relatives of patients with gastric cancer. Despite the fact that the OLGA classification system, aimed at stratifying the risk of cancer, has been used for more than 10 years ago, studies with its use in people with a history of gastric cancer are practically absent. Only two works were found, one of which contains only a small amount of data (48 people), and the other as a main group includes a special category - relatives of patients with stomach cancer that started at a young age.

## CONCLUSION

Thus, our data show that the stage of atrophy, established by the OLGA system, generally corresponds to the stage of atrophy, determined by the visual-analogue scale of the Houston modification of the Sydney system. Moreover, an increase in the stage of atrophy of the gastric mucosa, determined by the OLGA system, is associated with an increase in the severity of preneoplastic changes - intestinal metaplasia and dysplasia, which confirms the known relationship of these morphological changes in the cascade of gastric carcinogenesis. The degree of inflammatory infiltration of the gastric mucosa, determined by the OLGA system, also corresponds to the degree of inflammatory infiltration established during the assessment using a visual-analogue scale.

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