https://doi.org/10.22416/1382-4376-2025-35-5-85-99
UDC 616.33-006.6-097

Serological Tests for Detection of Gastric Precancerous Lesions and Gastric Cancer

Natalia S. Sergeeva[1], Valeriia I. Ryabtseva[1], Sergey S. Pirogov[1], Tatiana A. Karmakova[1], Igor I. Alentov[1]*, Nina V. Marshutina[1], Andrey D. Kaprin[1,2,3]

[1] *P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre, Moscow, Russian Federation*
[2] *National Medical Research Radiological Centre, Obninsk, Russian Federation*
[3] *Peoples' Friendship University of Russia named after Patrice Lumumba, Moscow, Russian Federation*

Aim: to present current information on serological screening approaches for precancerous gastric diseases and early gastric cancer.
Key points. Gastric cancer is one of the most common malignant tumors. Advanced stage of the tumor at the time of diagnosis determines an unfavorable prognosis in a significant proportion of patients. A real strategy for reducing both the incidence of gastric cancer and mortality rate is the introduction of cost-effective screening methods for atrophic gastritis associated with *Helicobacter pylori* (*H. pylori*) as a precancerous condition of the stomach. As an alternative to endoscopic examination of the stomach, approaches based on the evaluation of serological markers associated with *H. pylori* infection and reflecting the state of the gastric mucosa are currently proposed for laboratory screening: serum levels of antibodies to *H. pylori*, pepsinogen I, pepsinogen II and gastrin 17. Tests combining these markers, GastroPanel®, ABC and New ABC methods, as well as some of their modifications, are currently being widely studied as a tool for atrophic gastritis or gastric cancer risk group selection for further endoscopic examination.
Conclusion. An ensemble of serological markers, pepsinogen I, pepsinogen II, gastrin 17, and antibodies to *H. pylori,* allows for identifying atrophic gastritis with relatively high reliability, and considering additional factors, a high-risk group for the presence of gastric cancer. To achieve optimal medical and economic efficiency, it is necessary to improve the criteria for interpreting test results and including subjects in screening programs.
Keywords: gastric cancer, chronic atrophic gastritis, serological markers
Conflict of interest: the authors declare no conflict of interest.

For citation: Sergeeva N.S., Ryabtseva V.I., Pirogov S.S., Karmakova T.A., Alentov I.I., Marshutina N.V., Kaprin A.D. Serological Tests for Detection of Gastric Precancerous Lesions and Gastric Cancer. Russian Journal of Gastroenterology, Hepatology, Coloproctology. 2025;35(5):85–99. https://doi.org/10.22416/1382-4376-2025-35-5-85-99

Серологические тесты для выявления предраковых заболеваний и рака желудка

Н.С. Сергеева[1], В.И. Рябцева[1], С.С. Пирогов[1], Т.А. Кармакова[1], И.И. Алентов[1]*, Н.В. Маршутина[1], А.Д. Каприн[1,2,3]

[1] *Московский научно-исследовательский онкологический институт им. П.А. Герцена — филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации, Москва, Российская Федерация*
[2] *ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации, Обнинск, Российская Федерация*
[3] *ФГАОУ ВО «Российский Университет дружбы народов им. Патриса Лумумбы», Москва, Российская Федерация*

Цель: представить актуальные сведения о подходах к серологическому скринингу предрака и раннего рака желудка.
Основные положения. Рак желудка — одна из наиболее часто встречающихся злокачественных опухолей. Распространенность опухолевого процесса на этапе первичной диагностики определяет неблагоприятный прогноз у значительной части больных. Реальной стратегией снижения как заболеваемости раком желудка, так и смертности от него является внедрение экономически целесообразных методов скрининга атрофического гастрита, ассоциированного с *Helicobacter pylori* (*H. pylori*), как предракового состояния желудка. В качестве альтернативы эндоскопическому исследованию для лабораторного скрининга атрофического гастрита сегодня предлагаются подходы, основанные на определении серологических маркеров, связанных с хеликобактерной инфекцией и отражающих состояние слизистой оболочки желудка: сывороточного уровня антител к *H. pylori*, пепсиногена I, пепсиногена II и гастрина-17. Комплексные тесты, включающие эти маркеры, — «ГастроПанель®», методы ABC и New ABC, а также некоторые их модификации в настоящее

время широко исследуются как инструмент формирования группы риска наличия атрофического гастрита и рака желудка для дальнейшего эндоскопического обследования.
Заключение. Ансамбль из серологических маркеров (пепсиноген I, пепсиноген II, гастрин-17, антитела к *H. pylori*) позволяет со сравнительно высокой достоверностью выявлять хронический атрофический гастрит, а с учетом дополнительных факторов — группу высокого риска наличия рака желудка. Для достижения оптимальной медицинской и экономической эффективности необходимо совершенствование критериев интерпретации результатов тестов и включения обследуемых лиц в скрининговые программы.
Ключевые слова: рак желудка, хронический атрофический гастрит, серологические маркеры
Конфликт интересов: авторы заявляют об отсутствии конфликта интересов.

Для цитирования: Сергеева Н.С., Рябцева В.И., Пирогов С.С., Кармакова Т.А., Алентов И.И., Маршутина Н.В., Каприн А.Д. Серологические тесты для выявления предраковых заболеваний и рака желудка. Российский журнал гастроэнтерологии, гепатологии, колопроктологии. 2025;35(5):85–99. https://doi.org/10.22416/1382-4376-2025-35-5-85-99

Introduction

Gastric cancer (GC) is the sixth most prevalent form of cancer in Russia and worldwide. The 5-year survival rate of patients diagnosed with gastric cancer in most countries is less than 20 % [3]. This is attributable to the late detection of cancer, with more than one third of cases being first diagnosed at stages III–IV of the tumor process [1].

The principal risk factor for the development of intestinal-type GC, the predominant tumour variant among neoplasms of this localization, is chronic atrophic gastritis (AG), a disease characterised by inflammation of the mucosa leading to gastric gland atrophy. The identification and treatment of chronic AG has been identified as a viable method of reducing both the incidence and mortality of GC. Japan, a country with an extremely high prevalence of cancer, provides a pertinent case study. Between 1975 and 2005, the implementation of total endoscopic control of precancerous lesions resulted in a 50 % reduction in mortality from this specific type of tumour in male patients [4]. In Japan, the proportion of early-stage cancer cases that can be treated by minimally invasive endoscopic techniques with a favourable long-term prognosis and good quality of life is 70 % [5], whereas in most other countries it does not exceed 20 % [6, 7].

However, the use of gastroscopy as a reliable method of early diagnosis of gastric precancerous conditions necessitates modern equipment and highly qualified specialists, incurring significant costs even for developed countries with a high incidence of GC. This requires the exploration of cost-effective diagnostic methodologies for the detection of precancerous lesions and/or early-stage GC.

It is widely accepted that chronic *Helicobacter pylori* (*H. pylori*) infection is a primary contributing factor to chronic AG [8]. The cytotoxins produced by the bacterium are responsible for the death of the epithelial cells, the destruction of the epithelial layer, and the subsequent inflammatory reaction. Proinflammatory cytokines have been demonstrated to activate signaling pathways in epithelial cells, resulting in increased division intensity, suppression of apoptosis, and induction of epithelial-mesenchymal transition [9]. Oxidative stress and virulence factors of *H. pylori* have been demonstrated to directly lead to cellular DNA damage and genomic instability [9]. The hypoacidic state of the stomach, resulting from glandular atrophy and urease activity of *H. pylori*, has been shown to stimulate gastrin 17 (G-17) secretion. This, in turn, has been demonstrated to influence the pathogenesis of stomach cancer [10].

Serological markers associated with these pathological conditions, in various combinations, are now proposed for laboratory screening of *H. pylori* infection and atrophic gastritis as a precancerous gastric condition. The aforementioned markers encompass antibodies to *H. pylori*, as well as blood levels of pepsinogen I (PGI), pepsinogen II (PGII) and gastrin 17 (G-17).

Serologic laboratory tests for the detection of atrophic gastritis

Antibodies to Helicobacter pylori

The prolonged persistence of *H. pylori* in the gastric mucosa has been well-documented as a risk factor for the development of noncardiac intestinal-type GC [11]. However, *H. pylori* does not act as a direct carcinogen, since the eradication of long-term persistent *H. pylori* does not reduce the probability of developing gastric cancer [12]. IgG antibodies to *H. pylori* serve as an indicator of current or past *H. pylori* infection.

The *H. pylori* antibody test system, used in serological tests, in particular, GastroPanel® (see below), demonstrates 91–99.9 % coincidence with histological conclusions about the presence of the pathogen [13–15]. The area under the curve (AUC) when compared with histology is 0.993 [15].

Pepsinogen I

PGI is a proteolytic enzyme, a precursor of pepsin, which is synthesized by the chief and neck cells of the glands of the stomach floor and body. Most of this substance is excreted into the gastric lumen, where it undergoes conversion to pepsin in the presence of hydrochloric acid. It has been determined that only a negligible proportion of PGI is released into circulation [13]. The correlation between the amount of PGI in the blood and the number of principal cells in the gastric mucosa is significant. During the development of *H. pylori*-associated AG, the concentration of PGI in the circulation decreases linearly [16]. Furthermore, the level of PGI in blood is influenced by ulcerogenic agents such as aspirin and smoking [17].

Pepsinogen II

PGII is produced by chief and neck gland cells of the body and antral glands of the stomach, as well as by Brunner's gland cells of the proximal duodenum. PGII, as well as PGI, is activated by hydrochloric acid [13]. Serum levels of PGII have been shown to be elevated in gastritis of various etiologies, including infectious (e.g. *H. pylori*), parasitic, and biliary (with biliary reflux), which is also implicated in the pathogenesis of intestinal-type GC [18].

As the progression of AG occurs, the PGI/II ratio decreases linearly [19].

Gastrin 17 (G-17)

Gastrin is a peptide hormone produced by G-cells in the pyloric portion of the stomach, duodenum and pancreas. Its main function is to stimulate the secretion of hydrochloric acid by the parietal cells of the glands of the gastric body. In addition, gastrin partially stimulates the production of pepsinogens by the parietal cells of the gastric glands [16, 20]. A mixture of different molecular weight gastrins is released from the G-cells into the circulation, including G-71, -52, -34, -17, -14, and -6, which are formed as a result of post-translational modification of pre-progastrin. In healthy humans, gastrin 17 (G-17) predominates in plasma [10, 18, 21].

The target of G-17 in the stomach are enterochromaffin-like cells, which have cholecystokinin receptors (CCK2R) that bind gastrin. In response to gastrin stimulation, enterochromaffin-like cells produce and release histamine into the circulation, which binds to its receptors on parietal cells and activates their secretion of hydrochloric acid [10, 20].

One of the main reasons for increased circulating G-17 levels is insufficient hydrochloric acid secretion, especially in cases of *H. pylori*-associated AG. This condition is characterised by the death of both parietal and principal cells and is often accompanied by an antacid ('acid-free') stomach [10, 15, 18, 20]. Additionally, high G-17 levels may result from autoimmune AG.

Low G-17 levels may indicate the presence of AG in the antral region when *H. pylori* is detected or increased hydrochloric acid secretion in the absence of *H. pylori*, which is associated with an increased risk of peptic ulcer disease and Barrett's oesophagus [10, 16, 20, 22].

Serological tests in the detection of gastric precancerous conditions

The GastroPanel® (Biohit Oyj, Finland) [21] is a complex of four markers, mainly used in European studies.

Serological laboratory tests are designed to detect gastric mucosal atrophy, which is a precursor of intestinal-type GC. The aim is to identify patients with precancerous lesions and monitor them for early-stage GC diagnosis and treatment, which could reduce mortality in this category of cancer patients.

Based on the analysis results, the software of the above-mentioned manufacturer issues one of the eight conclusions listed and corresponding recommendations. These recommendations are based on stochastic algorithms and the use of certain discriminatory levels of four markers (Table 1).

Serological laboratory tests distinguish 8 profiles of gastric mucosa condition (five main and

Table 1. Diagnostic levels of biomarkers
Таблица 1. Диагностические уровни маркеров

Biomarker ***Маркер***	**Unit of measurement** ***Единица измерения***	**Normal values** ***Норма***	**Abnormal values** ***Не норма***
Antibodies to *H. pylori* *Антитела к H. pylori*	EIU	≤30	>30
PGI	μg/L / *мкг/л*	30–160	<30
PGII	μg/L / *мкг/л*	3–15	<3
PGI/PGII	rel. units / *отн. ед.*	3–20	<3
G-17b	pmol/L / *пмоль/л*	1–7	<1, >7

Table 2. Diagnostic categories of test results (adap. from [13, 18])
Таблица 2. Диагностические категории результатов тестов (адапт. по [13, 18])

GastroPanel® biomarkers ***Маркеры «ГастроПанели®»***				**Conclusion on the gastric mucosa condition** ***Заключение о состоянии слизистой оболочки желудка***	**Recommendations** ***Рекомендации***
H. pylori	**PGI**	**PGI/PGII**	**G-17**		
–	N	N	N	Healthy mucosa (no atrophy, no *H. pylori* infection) *Здоровая слизистая оболочка (без атрофии и H. pylori)*	–
+	N	N	N	*H. pylori*-associated gastritis *Хеликобактерный гастрит*	· *H. pylori* eradication is recommended *Рекомендуется эрадикация H. pylori* · Gastroscopy at physician's discretion *Гастроскопия — по усмотрению врача*
+/–	Below N *Ниже N* and/or *и/или*	Below N *Ниже N*	Above N *Выше N*	Atrophic gastritis of the corpus and antrum. Hypochlorhydria or achlorhydria of the stomach *Атрофический гастрит тела и дна желудка. Гипохлоридный или ахлоридный желудок*	· High risk of gastric cancer *Высокий риск развития рака желудка* · Gastroscopy is recommended *Рекомендуется гастроскопия*
–	N	N	Below N *Ниже N*	Atrophic gastritis of the antrum or hydrochloric acid hypersecretion *Атрофический гастрит антрального отдела или повышенная секреция соляной кислоты*	· High risk of gastric cancer and gastric/duodenum ulcer *Высокий риск развития рака желудка и язвы желудка/двенадцатиперстной кишки* · Gastroscopy is recommended *Рекомендуется гастроскопия*
+/–	Below N *Ниже N* and/or *и/или*	Ниже N *Below N*	Below N *Ниже N*	Atrophic pangastritis *Атрофический пангастрит*	· High risk of gastric cancer *Высокий риск развития рака желудка* · Gastroscopy is recommended *Рекомендуется гастроскопия*
–	N or above N *N или повышен*	N	Below N *Ниже N*	Decreased hydrochloric acid secretion (for example, due to taking PPI) *Пониженная секреция соляной кислоты (например, на фоне ИПП)*	· Gastroenterologist consultation *Консультация гастроэнтеролога*
–	N	N	Below N *Ниже N*	Increased hydrochloric acid secretion *Повышенная секреция соляной кислоты*	· Gastroenterologist consultation *Консультация гастроэнтеролога*
–	Above N *Выше N*	N	Above N *Выше N*	Short break (4–10 days) in PPIs taking *Краткий перерыв (4–10 дней) в приеме ИПП*	–

Notes: *N — norm, PPI — proton pomp inhibitors.*
Примечание: *N — норма, ИПП — ингибиторы протонной помпы.*

three additional) according to the morphological classification of gastritis USS (Update Sydney System) [13, 18, 23]. The main diagnostic categories are as follows: 1) mucosa without atrophy or *H. pylori* infection; 2) non-atrophic *H. pylori* gastritis; 3) AG of the gastric body and fundus (including autoimmune AG); 4) antral AG or increased hydrochloric acid secretion; and 5) atrophic pangastritis. To identify the autoimmune nature of AG (Group 3), antibodies to parietal cells, Castle's intrinsic factor [10, 16, 21] and (in some studies) antibodies to thyroid peroxidase and the level of vitamin B_{12} are assessed in the blood serum [24, 25].

Based on conclusions 3–5, a risk group for the development of GC is formed, requiring further investigation (upper endoscopy) and subsequent monitoring (Table 2).

The three additional diagnostic categories of serological markers are increased and decreased hydrochloric acid secretion, and a profile of markers characteristic of a short-term interruption to proton pump inhibitors intake (Table 2).

According to the meta-analysis by R.M. Zagari et al. [26], the sensitivity of serological laboratory tests in detecting AG in asymptomatic individuals is 74.7 %, with a specificity of 95.6 % and a negative predictive value of 91 %. Data systematised by M. Romańczyk et al. [27] show that the sensitivity achieved in detecting AG varies significantly across studies from different countries using identical marker threshold levels: from 39.9 % with a specificity of 93.4 % in France (a country with a low incidence of AG) to 80.6 % with a specificity of 48.8 % in Taiwan (a country with a high incidence of AG). It should be noted that the meta-analyses [21, 27] included studies in which the authors used the recommended discriminatory levels of markers, whereas the systematic review discusses studies in which the authors used different discriminatory levels based on the objectives of the study and the results of the receiver operating characteristic (ROC) analysis [27].

A meta-analysis and a systematic review by K. Syrjänen et al. [18, 21] showed that GastroPanel® is more effective at detecting gastric body AG than antral AG. The sensitivity and specificity of GastroPanel® for gastric body AG were 70.2 and 93.9 % respectively, and for antral AG they were 51.6 and 84.1 %. These results are as expected since the antral AG marker profile (low G-17 with normal values for the other markers) is also observed in a hyperacidic stomach without antral atrophy (Table 2).

It should be emphasized that the conclusion based on the results of serological testing about the absence of atrophy and *H. pylori* has high sensitivity and specificity — 89–94 % and 92–95 % respectively [19, 29].

Results of the assessment in asymptomatic populations

According to the results of a study using serological tests in asymptomatic populations of people in the United States concluded that screening for gastric precancerous lesions reduces gastric cancer mortality by 27 %, with the same effectiveness as mammography in women aged 50–59 (cit. from [30]).

The frequency of detection of gastric body AG using laboratory tests confirmed by upper endoscopy and morphological studies of biopsy specimens, according to the results of meta-analysis by K. Syrjänen et al., is 0.3 %, while antral AG detection is 0.2 % [21]. In Russia, the detection rates were 7.5 % for gastric body AG, 23 % for antral AG and 1 % for atrophic pangastritis, with an overall concordance rate with upper endoscopy of 82.5 % [31]. Other Russian researchers found that the laboratory tests conclusion about the presence of AG coincided with the morphological conclusion in 95.2 % of cases [25].

Overall, all authors agree that the GastroPanel® is an effective method for detecting AG in asymptomatic populations. However, the low frequency of AG makes it necessary to clarify the inclusion criteria for asymptomatic individuals in screening programmes for economic reasons.

Results of the study in populations of subjects with dyspepsia

As expected, the frequency of AG detection was higher in patients with dyspepsia than in asymptomatic populations, ranging from 10.2 % in Finland to 65 % in Romania. Approximately half of those examined patients were infected with *H. pylori* (Table 3). All cases of AG identified were confirmed morphologically using biopsy specimens taken during EGDS. The diagnostic characteristics of available serological laboratory tests (sensitivity, specificity, positive and negative predictive values, and the area under the curve for individual markers) vary greatly between studies. According to the authors, this is related to the qualifications and equipment of endoscopists and morphologists. Table 3 summarizes a few typical studies. Most authors conclude that serological testing is an excellent tool for examining patients with dyspepsia, as the results allow for the selection of a risk group for referral for an upper endoscopy. In this regard, the results of

Table 3. Detection rate of atrophic gastritis in the population of patients with dyspepsia
Таблица 3. Частота выявления атрофического гастрита в популяции пациентов с диспепсией

Source ***Источник***	**Country** ***Страна***	**AG detection rate, %** ***Частота АГ, %***	**HP detection rate, %** ***Частота HP+, %***	**Additional information** ***Дополнительная информация***
[15]	Finland *Финляндия*	10.2 %		Match with histology / *Совпадение с гистологией* — 92.4 % AUC for PGI / *AUC для PGI* — 0.952 AUC for PGI/PGII / *AUC для PGI/PGII* — 0.998 AUC for HP+ / *AUC для HP+* — 0.993
[29]	Italy *Италия*	16 % (AGC / *АГТ* — 10 %, AGA / *АГА* — 3.6 %, panAG / *панАГ* — 2.4 %)		Match with histology for AGC / *Совпадение с гистологией для АГТ* — 94 % Sensitivity / *Чувствительность* — 80 % Specificity / *Специфичность* — 96 %
[32]	Mexico *Мексика*	14 %	49.6 %	–
[33]	Romania *Румыния*	65 %	51 %	Sensitivity / *Чувствительность* — 50 % Specificity / *Специфичность* — 80 % PPV / *ППЗ* — 25 %, NPV / *ОПЗ* — 92 %
[34]	Spain *Испания*	6 %		Sensitivity / *Чувствительность* — 87.5 % Specificity / *Специфичность* — 100 %
[35]	Spain *Испания*	17 % (AGC / *АГТ* — 6 %, AGA / *АГА* — 7 %, panAG / *панАГ* — 4 %)	51 %	No differences in PGI and PGI/PGII in the presence or absence of AG / *Нет различий PGI и PGI/PGII при наличии и отсутствии АГ* Sensitivity / *Чувствительность* — 50 % Specificity / *Специфичность* — 80 % PPV / *ППЗ* — 25 %, NPV / *ОПЗ* — 92 %

Notes: *AG — atrophic gastritis, AGA — atrophic gastritis of gastric antrum, AGC — atrophic gastritis of gastric corpus, panAG — atrophic pangastritis, NPV — negative prognostic value, PPV — positive prognostic value, HP — Helicobacter pylori.*
Примечания: *АГ — атрофический гастрит, АГА — атрофический гастрит антрального отдела, АГТ — атрофический гастрит тела желудка, панАГ — атрофический пангастрит, ОПЗ — отрицательная прогностическая значимость, ППЗ — положительная прогностическая значимость, HP — Helicobacter pylori.*

L. Lombardo et al. [29] are noteworthy, as they found atrophic pangastritis in individuals under 30 years of age (12 % of all patients with atrophic pangastritis), which could lower the recommended minimum age for the use of laboratory testing (usually over 40 years). However, in individual studies from Spain [35] and Iran [36], the authors concluded that laboratory diagnostics using markers PGI, PGII, G-17, and antibodies to *H. pylori* do not accurately predict the presence of AG. In particular, PGI, PGII and PGI/PGII levels were not significantly different in the presence or absence of AG.

Serological diagnostics using markers of PGI, PGII, G-17, antibodies to H. pylori in the detection of gastric mucosal atrophy of varying severity

The question of whether it is possible to differentiate between AG of varying severity using serological laboratory testing is a natural one, as its solution will allow for the identification of a group of subjects with an extremely high risk of developing GC, for the purpose of conducting a precision endoscopic examination and subsequent monitoring. Nevertheless, the question remains unresolved. So, M.C.F. Coelho et al. (Brazil) [37] stratified 41 patients with AG detected by laboratory screening according to the severity of atrophy as per the OLGA and OLGIM (morphological classification) systems into the groups of low and high risk of gastric cancer development. The authors concluded that biomarkers PGI, PGII, G-17 and antibodies to *H. pylori* do not distinguish between these groups. The concordance of OLGA and OLGIM conclusions in this study was 85.4 %. A Romanian study of patients with dyspepsia yielded similar results, with 65 % of subjects diagnosed with AG [33]. The authors found no differences in the levels of PGI, PGII, G-17 and antibodies to *H. pylori* at different locations of atrophy, as well as in the presence and absence of intestinal metaplasia.

At the same time, according to a study conducted in France [28], it was found that serological

laboratory testing has almost twice the sensitivity in diagnosing severe atrophy compared to mild atrophy (61.0 % vs. 39.9 %). Furthermore, an analysis of Finnish authors revealed that the area under the curve (AUC) for differentiating moderate and severe dysplasia by PGI levels was 0.952 (95 % CI: 0.891–1.000), and by PGI/PGII levels was 0.998 (95 % CI: 0.996–1.000) [15]. It is evident that the serological panel is capable of distinguishing between varying degrees of dysplasia with a high level of confidence. The data of D. Ogutmen Koc and S. Bektas [38] demonstrated an inverse and significant correlation between PGI and PGI/PGII, and the severity of atrophy in the stomach. The authors hypothesize that the combined use of serum pepsinogen determination and OLGA/OLGIM staging can provide useful information for differential diagnosis and risk assessment of gastric cancer.

Study using serological laboratory tests in patients with gastroesophageal reflux disease

U. Peitz et al. [39] examined the blood serum of GERD patients enrolled in the ProGERD program. They found a significant negative correlation between PGI levels and gastric body AG presence, though no antral AG cases were identified in this patient group. Overall, serological testing had a sensitivity of 32 % and a specificity of 70 % in identifying AG in GERD patients, leading the authors to conclude that its use in this category of patients is inappropriate.

Study using serological laboratory tests in patients with gastric cancer

To identify additional applications for the serological testing, several authors have studied its use in patients with GC.

A.V. Belkovets et al. (Russia) [40] examined markers of PGI, PGII, G-17 and antibodies to *H. pylori* in 85 cancer patients and demonstrated that, according to serological test results, fundal atrophy occurred in 43.2 % of cases. Meanwhile, the average marker values in this cancer patient group were within the reference intervals. The authors found no differences in the test results between groups differing in tumor morphology, differentiation degree, stomach location and disease stage.

Similar data were obtained by E. Gašenko et al. (Latvia) [41] in a study of 481 patients with GC, in which the serological testing was used. The values of PGI, PGII, G-17 and antibodies to *H. pylori* markers were assessed using a cut-off developed for the detection of AG. Of the examined patients, 74 % were *H. pylori*-positive, 32.4 % had PGI/PGII <3.0, 12.2 % had a G-17 level <1.0 pg/mL, and only 1.2 % had abnormal values for all three markers. No correlation was found between abnormal values and the histological type of tumor (intestinal or diffuse) or its anatomical localization in the stomach. The authors concluded that most GC patients have normal levels of pepsinogen and G-17, and that these markers are not useful for GC screening in the European population. In our opinion, however, these data require verification because, at least in the case of small diffuse-type GC that has developed against a background of significant atrophic changes, the results of serological laboratory tests should indicate the presence of chronic atrophic gastritis.

Researchers in Spain compared the results of the serological test in patients with dyspepsia (n = 47) and gastric cancer (n = 9). AG was more prevalent among GC patients than among dyspepsia patients (56 % vs. 6 %). The sensitivity and specificity of the serological test for detecting AG were 87.5 % and 100 %, respectively. PGI, PGII, G-17 and antibodies to *H. pylori* markers remained normal in four out of nine cases of GC that were not related to AG. This is to be expected, since these markers are primarily sensitive to atrophic mucosal changes and are not designed to detect GC.

In a study byG. Dondov et al. (Mongolia) [42], which included 40 patients with GC, 40 patients with AG and 40 control cases, the authors demonstrated that patients with GC have lower PGI and PGI/PGII values than patients with AG. Evaluating the combination of these values using the discriminatory levels calculated by the authors (PGI <35.25 ng/mL and PGI/PGII <5.27) enabled patients with GC to be distinguished with a sensitivity of 77.7 % and a specificity of 60.5 %.

Authors from Iran attempted to answer the question of whether intestinal-type AG and GC could be discriminated using the serological laboratory tests [43]. They also modified the recommended discriminatory levels and found that reduced PGI (<80 ng/mL) and PGI/PGII (<10) values could differentiate between AG and GC with high accuracy (AUC — 0.83 and 0.78, respectively).

Thus, the limited available data does not yet allow us to draw a definitive conclusion about the diagnostic potential of serological diagnostics in relation to GC. Nevertheless, the correlation between marked atrophy of the gastric mucosa and low PGI and PGI/PGII values provides a basis for using these markers, either on their own or in combination with *H. pylori* antibody levels, to assess the risk of GC development. For

example, a Russian prospective study involving 9,360 individuals showed that patients with GC, which was identified over an 8-year follow-up period (n = 52), had significantly lower mean PGI levels (65.5 μg/L vs. 94.5 μg/L) and lower PGI/PGII values (3.7 vs. 6.3) than the control group (n = 104; matched for age, sex, follow-up duration, etc.). The threshold levels of atrophy indices for GC risk assessment exceeded those recommended by the manufacturer (PGI <55 μg/L; PGI/PGII <5.0) and varied according to the subjects' sex. In a multivariate analysis, only the PGI/PGII ratio demonstrated reliable predictive power (OR = 3.3; 95 % CI: 1.5–7.3). The prognostic significance of low blood pepsinogen levels as an indicator of AG associated with a high risk of GC development is confirmed by other independent studies [45].

Laboratory screening systems for gastric cancer and precancerous diseases of the stomach in East Asian countries

The incidence of gastric cancer in East Asian countries — Japan, China and South Korea — is the highest in the world [4]. Furthermore, in Japan and South Korea, early gastric cancer accounts for 70 % and 50 %, respectively, of the primary gastric neoplasms detected, whereas in China the proportion of such cases does not exceed 10 % [5, 46, 47]. These differences are due to the fact that in Japan and South Korea screening with gastroscopy is mandatory for all persons over 40 years of age. While this approach ensures a high rate of early cancer detection, it places a heavy burden on the health care system, requires specialists and expensive equipment, and is invasive with insufficient patient compliance. In China, a country with a high population density, total endoscopic screening is not performed for the above reasons.

These circumstances justify investigating the possibility of using laboratory tests to form a risk group for the presence of GC for further endoscopic screening. The laboratory tests used for this purpose are the same as those used in the GastroPanel®, but differ in the manufacturer of the test kits, the recommended discriminatory levels values, the original combinations of tests and the interpretation of the data.

ABC method

K. Miki et al. [48] suggested using three serological tests for GC screening: PGI, PGII and antibodies against *H. pylori* and to classify PGI ≤70 pg/mL and PGI/PGII ≤3 as PG-positive cases (PG^+) and antibody titer against *H. pylori* ≥10 U/mL as positive cases (HP^+). All results were divided into four groups: Group A: PG^-HP^-; Group B: PG^-HP^+; Group C: PG^+HP^+; Group D: PG^+HP^-. Based on the data of the subsequent endoscopy of the subjects, the authors justified the following interpretation of the results: Group A — uninfected; Group B — active *H. pylori* infection, no or weak AG; Group C — chronic AG with chronic *H. pylori* infection; Group D — severe chronic AG with spontaneous eradication of *H. pylori*. Groups C and D were considered high-risk cases of GC requiring careful endoscopic follow-up. Group B was classified as having a moderate risk of GC. Group A, which included 50–70 % of the subjects, could be excluded from further surveillance by the authors if they had no clinical symptoms and were not taking proton pump inhibitors [48].

Over the last 15 years, a number of screening programmes using the ABC method have been carried out in different categories of subjects.

Firstly, Group A was found to give false-negative results in patients after previous eradication of persistent *H. pylori*, thus missing severe chronic AG and GC [49–51]. According to these investigators, the ABC panel is not informative in this category of individuals and screening for GC should begin with gastroscopy. Furthermore, it has been shown that elderly patients with severe AG often fall into Group A; therefore, for this category of subjects it is necessary to select specific discriminatory levels of all three markers to exclude false-negative results [52, 53].

Japanese authors believe that a fourth marker — G-17 — should be added to the ABC panel to improve its diagnostic properties. N. Nagasaki et al. [54] in a study of 1507 people (ABC method + upper endoscopy), although they showed the absence of GC in Group A, but revealed the absence of differences in the frequency of GC in Groups B, C and D (a total of 24 cases of GC were revealed), which, in our opinion, confirms the need to improve the diagnostic characteristics of the ABC method. At the same time, D.Q. Ni et al. [55] analyzed the screening results of 30,126 individuals and found a significantly higher incidence of GC in Group D compared to Groups B and C (4.1 % vs. 1.68 % and 1.38 %, respectively). Y. Yamaguchi et al. [56] believe that the ABC method is a good way to divide subjects into high and low GC risk groups: screening of 36,628 subjects resulted in 65 GC diagnoses, 52 (80 %) of which were early GC.

S.M. Baek et al. [57] from South Korea investigated the results of the ABC method in patients with proven GC (n = 1124), with dysplasia (n = 353) and in control subjects (n = 1463). They

found that a PGI/PGII <3 was characteristic for dysplasia and for disseminated intestinal-type GC, and the combination of PGII ≥20 ng/mL with *H. pylori* was characteristic for early diffuse GC in patients younger than 40 years.

H. Kishikawa et al. [49] justified the periodicity of gastroscopy in subjects using the ABC method; for Group B — every 3 years, for Group C — every 2 years, for Group D — annually. For patients in Group A, after eradication of *H. pylori*, an individual choice of gastroscopy intervals is necessary, taking into account the duration of persistence of infection.

ABC tests are included in the National Clinical Guidelines of the People's Republic of China 2024 for screening for GC in people over 40 years of age with certain risk factors (smoking, family history of GC, etc.) [58].

New ABC method

The New ABC method is an examination of the serum levels of three markers — PGI, PGII and G-17 [59, 60]. This means that the panel does not include an assessment of *H. pylori* infection. Cases with PGI < 70 ng/mL and PGI/PGII <3 are considered positive (PG^+); cases with G-17 >2 pmol/L are also considered positive ($G\text{-}17^+$). The authors suggest dividing all the patients studied into four groups: Group A — $PG^-G\text{-}17^-$; Group B — $PG^-G\text{-}17^+$; Group C — $PG^+G\text{-}17^-$; Group D — $PG^+G\text{-}17^+$. According to the risk of having GC, subjects in Group A have a low risk of having GC, those in Group B have a moderate risk, and those in Groups C and D have a high risk of having GC.

M.Y. Li et al. [61] concluded from a direct comparison study that the New ABC method was more sensitive and specific in detecting GC, including early GC, but less sensitive than ABC in detecting precancerous lesions — AG. Thus, the sensitivity and specificity of the ABC method for AG were 75.8 and 36 %, and of the New ABC they were 62.1 and 75 %, respectively. At the same time, the sensitivity and specificity of New ABC for early GC were higher than those of ABC: 92.5 and 54.46 % vs. 90.74 and 29.46 %, respectively.

D.Q. Ni et al. [55], who analyzed the results of GC screening in 30,126 individuals using ABC, New ABC and subsequent gastroscopy, suggested introducing another parameter into the calculations — the PGI to G-17 ratio (PGR) with a discriminatory level of 4.135, which improved the diagnostic performance of laboratory screening. Using this approach, the authors were able to identify 22 cases of PGR, 19 of which were early.

X.M. Liu et al. [62] performed a detailed study of the diagnostic performance of the New ABC method in a cohort of 702 subjects, using upper endoscopy with narrow-band imaging (NBI) and chromoendoscopy as reference methods, assessing gastric mucosal status according to the Kyoto Classification of Gastritis. The incidence of AG, intestinal metaplasia and intestinal-type GC, including early GC, was assessed in low, intermediate and high-risk GC groups (according to the New ABC). Based on the totality of the data obtained, the authors concluded that the New ABC is not suitable for screening for precancerous conditions, but in countries with high population density and high incidence of GC, it is applicable for screening to select a population at high risk of GC for gastroscopy [63]. Unfortunately, the proportion of early cancers among primary detected cases was very low.

H. Tu predictive model ("Tu's score") for identifying the risk group of gastric cancer

Prediction model proposed in 2016 by H. Tu et al. [16] is based on the analysis of the results of the Zhuangue Gastric Diseases Screening Programme. It included 12,112 people who had blood serum levels of four markers — PGI, PGII, antibodies to *H. pylori* and G-17 — tested and then underwent upper endoscopy. In analyzing the results, the authors divided the markers levels into ranges and calculated the odds ratio (OR) of having GC in each range, on the basis of which they assigned scores to each range (Table 4). The incidence of GC increased with increasing total score: from 24.1 cases per 100,000 person-years with a score ≤2 to 122.7 cases per 100,000 person-years with a score ≥14. According to these results, criteria for low risk of GC (≤2 points), intermediate risk (3–13 points) and high risk (≥14 points) were established. The AUC of this model was 0.803 (95% CI: 0.789–0.816) based on ROC analysis.

Predictive model Li ("Li's score") for identifying the risk group of gastric cancer

In 2019, the results of a multicenter screening-type study conducted in China to identify the risk group for GC were published, which included 14,929 participants [64]. To identify serological markers, a set of PGI, PGII, G-17, antibodies to *H. pylori* with an original division of marker levels into ranges was used. All subjects underwent gastroscopy. In addition, the authors analyzed the contribution of age, gender and dietary patterns to GC risk. This analysis led to the development of a predictive model (Table 5) which allows subjects to be classified into three groups

Table 4. System for assessing the risk of having gastric cancer using a predictive model "Tu's score" [16]
Таблица 4. Система оценки риска наличия рака желудка по предсказательной модели «Tu's score» [16]

Risk factors, biomarkers *Факторы риска, маркеры*	**Gastric cancer risk (OR, 95% CI)** *Риск наличия рака желудка (ОШ, 95% ДИ)*	**Gastric cancer risk score** *Баллы, соответствующие степени риска наличия рака желудка*
PGI, ng/mL */нг/мл*		
>70	ref. value / *реф. зн.*	0
30–70	0.92 (0.8–1.05)	0
<30	1.21 (0.76–1.93)	1
PGII, ng/mL */нг/мл*		
Q_1 (≤6.0)	ref. value / *реф. зн.*	0
Q_2 (6.01–9.73)	1.17 (1.02–1.35)	1
Q_3 (9.74–16.78)	1.82 (1.53–2.14)	3
Q_4 (≥16.78)	3.22 (2.50–4.15)	6
PGI/PGII		
>7	ref. value / *реф. зн.*	0
3–7	2.10 (1.73–2.54)	4
<3	2.44 (1.58–3.77)	4
Antibodies to *H. pylori*, EIU ***Антитела к H. pylori, EIU***		
Seronegative / *Серонегативные* (<34)	ref. value / *реф. зн.*	0
Seropositive / *Серопозитивные* (≥34)	3.76 (3.27–4.32)	7
G-17, pmol/L / *пмоль/л*		
Q_1 (≤0.5)	1.27 (1.11–1.47)	1
Q_2 (0.51–2.0)	ref. value / *реф. зн.*	0
Q_3 (2.01–4.8)	1.33 (1.14–1.55)	1
Q_4 (>4.8)	1.75 (1.49–2.06)	3

Note: *OR — odds ratio, ref. value — within reference values, 95% CI — 95 % confidence interval, EIU — enzyme immunounits.*
Примечание: *ОШ — отношение шансов, 95% ДИ — 95%-ный доверительный интервал, реф. зн. — в пределах референсных значений, EIU (enzyme immunounits) — иммуноферментные единицы.*

according to their risk of developing GC: low (0–11 points), intermediate (12–16 points) and high (17–25 points), depending on the number of points scored. The authors have shown that all the risk indicators in the table are independent, which justifies the possibility of grouping them together. It is noteworthy that the highest odds ratio was observed in the age group >69 years (OR = 8.67; 9 points), with G-17 >5.7 pmol/L (OR = 2.87; 4 points) and male sex (OR = 2.52; 4 points).

In a screening program involving 25,194 individuals, higher odds ratios (OR) of having GC were obtained for age (5.934), male sex (5.721) and high dietary salt (2.877), as well as a protective effect of green vegetable consumption (0.388) [62]. In the same work, the diagnostic parameters of Li's score in the detection of GC were evaluated: sensitivity was 81.5 %, specificity was 77.8 % and AUC was 0.817 (0.721–0.913). The frequency of GC was 0 % in the low-risk group, 1.63 % in the intermediate risk group and 9 % in the high-risk group.

Y. Hu et al. [60], by analyzing the results of 9754 people by ROC analysis, found that Li's score has a significant advantage in its ability to discriminate the risk group of early and prevalent GC compared with ABC, New ABC and Tu's score methods. According to D.Q. Ni et al. [55], the frequency of detected GC in the medium and high-risk groups was higher with the Li's score than with the ABC and New ABC methods.

Conclusion

The development of a range of tests suitable for the detection of the main precursor of gastric cancer of the intestinal type — atrophic gastritis — is based on the fundamental findings of oncology regarding the mechanisms of carcinogenesis and the stages of tumour development in the gastric mucosa.

Table 5. System for assessing the risk of having gastric cancer using a predictive model "Li's score" [64]
Таблица 5. Система оценки риска наличия рака желудка по предсказательной модели «Li's score» [64]

Risk factors, biomarkers *Факторы риска, маркеры*	Gastric cancer risk (OR, 95% CI) *Риск наличия рака желудка (ОШ, 95% ДИ)*	Gastric cancer risk score *Баллы, соответствующие степени риска наличия рака желудка*
Age, years / *Возраст, годы*		
40–49	ref. value / *реф. зн.*	0
50–59	2.77 (1.72–4.47)	4
60–69	4.31 (2.69–6.89)	6
>69	8.67 (5.32–14.13)	9
Gender / *Пол*		
female / *женский*	ref. value / *реф. зн.*	0
male / *мужской*	2.52 (1.92–3.30)	4
Pickled vegetables in the diet ***Маринованные овощи в рационе питания***		
rarely / *редко*	ref. value / *реф. зн.*	0
regularly / *регулярно*	1.49 (1.1–2.01)	2
Fried food / *Жареная еда*		
rarely / *редко*	ref. value / *реф. зн.*	0
regularly / *регулярно*	1.71 (1.15–2.54)	2
Antibodies to *H. pylori*, EIU ***Антитела к H. pylori, EIU***		
Seronegative / *Серонегативные* (<34)	ref. value / *реф. зн.*	0
Seropositive / *Серопозитивные* (≥34)	1.26 (1.12–1.62)	1
PGI/PGII		
≥3.89	ref. value / *реф. зн.*	0
<3.89	2.02 (1.41–2.9)	3
G-17, pmol/L / *пмоль/л*		
≤1.49	ref. value / *реф. зн.*	0
1.5–5.7	2.01 (1.33–3.0)	3
>5.7	2.84 (1.93–4.17)	4

Note: *OR — odds ratio, ref. value — within reference values, 95% CI — 95 % confidence interval, EIU — enzyme immunounits.*
Примечание: *ОШ — отношение шансов, 95% ДИ — 95%-ный доверительный интервал, реф. зн. — в пределах референсных значений, EIU (enzyme immunounits) — иммуноферментные единицы.*

The collected data allow us to draw a clear conclusion that the ensemble of four serological markers (PGI, PGII, G-17, antibodies to *H. pylori*) makes it possible to detect gastric precancerous lesions (chronic atrophic gastritis) with relatively high reliability and, taking into account such individual characteristics as age, sex, bad habits and dietary peculiarities, to identify the group of people with a high risk of developing gastric cancer (Li's score predictive model).

The range of clinical studies performed allows us to conclude that the marker complex "PGI, PGII, G-17, antibodies to *H. pylori*" is adequate for the detection of atrophic gastritis of the body and antral part of the stomach associated with *H. pylori* mucosal infection. The serological testing is currently recommended by the US Food and Drug Administration (FDA) for the detection of *H. pylori* infection and atrophic gastritis. Variations in the diagnostic performance, as demonstrated by data from different authors, are most likely due to differences in the qualifications of endoscopists, morphologists and the equipment of endoscopy departments in different countries.

At the same time, not all questions regarding various aspects of the use of the serological laboratory testing for such a task have been resolved. For example, to achieve optimal medical and economic efficiency, it is necessary to develop criteria for the inclusion of subjects in screening programs (asymptomatic persons, patients with dyspepsia, age, including gender), which may differ in regions with high and low gastric cancer incidence, as well as in countries with different levels of economic development. Thus, especially for countries combining high population density, high gastric cancer incidence and not the highest standard of living, the detection of severe atrophic gastritis with intestinal metaplasia and early gastric cancer may be most relevant. The capabilities and limitations of the serological laboratory testing in this regard are not yet fully understood.

References / Литература

1. *Каприн А.Д., Старинский В.В., Шахзадова А.О. (ред.).* Злокачественные новообразования в России в 2023 году (Заболеваемость и смертность). М.: МНИОИ им. П.А. Герцена — филиал ФГБУ «НМИЦ радиологии» Минздрава России, 2024. [*Kaprin A.D., Starinskij V.V., Shakhzadova A.O. (eds).* Malignant neoplasms in Russia in 2023 (incidence and mortality). Moscow: P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre of the Ministry of Health of the Russian Federation, 2024. (In Russ.)].
2. *Bray F., Laversanne M., Sung H., Ferlay J., Siegel R.L., Soerjomataram I., et al.* Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin*. 2024;74(3):229–63. DOI: 10.3322/caac.21834
3. *Karimi P., Islami F., Anandasabapathy S., Freedman N.D., Kamangar F.* Gastric cancer: Descriptive epidemiology, risk factors, screening, and prevention. *Cancer Epidemiol Prevent Biomarkers*. 2014;23(5):700–13. DOI: 10.1158/1055-9965.EPI-13-1057
4. *Hamashima C.* Current issues and future perspectives of gastric cancer screening. *World J Gastroenterol*. 2014;20(38):13767–74. DOI: 10.3748/wjg.v20.i38.13767
5. *Higashi T., Machii R., Aoki A., Hamashima C., Saito H.* Evaluation and revision of checklists for screening facilities and municipal governmental programs for gastric cancer and colorectal cancer screening in Japan. *Jpn J Clin Oncol*. 2010;40(11):1021–30. DOI: 10.1093/jjco/hyq091
6. *Каприн А.Д., Старинский В.В., Шахзадова А.О. (ред.).* Состояние онкологической помощи населению России в 2023 году. М.: МНИОИ им. П.А. Герцена — филиал ФГБУ «НМИЦ радиологии» Минздрава России, 2024. [*Kaprin A.D., Starinskij V.V., Shakhzadova A.O. (eds).* The state of oncology care in Russia in 2023. Moscow: P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre of the Ministry of Health of the Russian Federation; 2024. (In Russ.)].
7. *Chiarello M.M., Fico V., Pepe G., Tropeano G., Adams N.J., Altieri G., et al.* Early gastric cancer: A challenge in Western countries. *World J Gastroenterol*. 2022;28(7):693–703. DOI: 10.3748/wjg.v28.i7.693
8. *Moss S.F.* The clinical evidence linking *Helicobacter pylori* to gastric cancer. *Cell Mol Gastroenterol Hepatol*. 2016;3(2):183–91. DOI: 10.1016/j.jcmgh.2016.12.001
9. *Duan Y., Xu Y., Dou Y., Xu D. Helicobacter pylori* and gastric cancer: Mechanisms and new perspectives. *J Hematol Oncol*. 2025;18(1):10. DOI: 10.1186/s13045-024-01654-2
10. *Waldum H., Mjønes P.* The central role of gastrin in gastric cancer. *Front Oncol*. 2023;13:1176673. DOI: 10.3389/fonc.2023.1176673
11. *Correa P., Piazuelo M.B.* The gastric precancerous cascade. *J Dig Dis*. 2012;13(1):2–9. DOI: 10.1111/j.1751-2980.2011.00550.x
12. *Shichijo S., Uedo N., Michida T.* Detection of early gastric cancer after *Helicobacter pylori* eradication. *Digestion.* 2022;103(1):54–61. DOI: 10.1159/000519838
13. *Loor A., Dumitraşcu D.L. Helicobacter pylori* infection, gastric cancer and Gastropanel. *Rom J Intern Med*. 2016;54(3):151–6. DOI: 10.1515/rjim-2016-0025
14. *Mäki M., Söderström D., Paloheimo L., Hendolin P., Suovaniemi O., Syrjänen K. Helicobacter pylori* (Hp) IgG ELISA of the new-generation GastroPanel® is highly accurate in diagnosis of Hp-infection in gastroscopy referral patients. *Anticancer Res*. 2020;40(11):6387–98. DOI: 10.21873/anticanres.14660
15. *Koivurova O.P., Koskela R., Blomster T., Ala-Rämi A., Lumme H., Kettunen O., et al.* Serological biomarker panel in diagnosis of atrophic gastritis and *Helicobacter pylori* infection in gastroscopy referral patients: Clinical validation of the new-generation GastroPanel® test. *Anticancer Res*. 2021;41(11):5527–37. DOI: 10.21873/anticanres.15366
16. *Tu H., Sun L., Dong X., Gong Y., Xu Q., Jing J., et al.* A serological biopsy using five stomach-specific circulating biomarkers for gastric cancer risk assessment: A multi-phase study. *Am J Gastroenterol*. 2017;112(5):704–15. DOI: 10.1038/ajg.2017.55
17. *Lee S.Y., Ahn Y.S., Moon H.W.* Comparison between the GastroPanel test and the serum pepsinogen assay interpreted with the ABC method-A prospective study. *Helicobacter*. 2024;29(1):e13056. DOI: 10.1111/hel.13056
18. *Syrjänen K., Eskelinen M., Peetsalu A., Sillakivi T., Sipponen P., Härkönen M., et al.* GastroPanel® biomarker assay: The most comprehensive test for *Helicobacter pylori* infection and its clinical sequelae. A critical review. *Anticancer Res*. 2019;39(3):1091–104. DOI: 10.21873/anticanres.13218
19. *Storskrubb T., Aro P., Ronkainen J., Sipponen P., Nyhlin H., Talley N.J., et al.* Serum biomarkers provide an accurate method for diagnosis of atrophic gastritis in a general population: The Kalixanda study. *Scand J Gastroenterol*. 2008;43(12):1448–55. DOI: 10.1080/00365520802273025
20. *Duan S., Rico K., Merchant J.L.* Gastrin: From physiology to gastrointestinal malignancies. *Function (Oxf)*. 2021;3(1):zqab062. DOI: 10.1093/function/zqab062
21. *Syrjänen K.* A panel of serum biomarkers (GastroPanel®) in non-invasive diagnosis of atrophic gastritis. Systematic review and meta-analysis. *Anticancer Res*. 2016;36(10):5133–44. DOI: 10.21873/anticanres.11083
22. *Xu Y., Miremadi A., Link A., Malfertheiner P., Fitzgerald R.C., Bornschein J.* Feasibility of combined screening for upper gastrointestinal adenocarcinoma risk by serology and Cytosponge testing: The SUGAR study. *J Clin Pathol*. 2019;72(12):825–9. DOI: 10.1136/jclinpath-2019-205700
23. *Paloheimo L., Tiusanen T., Suovaniemi O., Syrjänen K.* Serological biomarker test (GastroPanel®) in the diagnosis of functional gastric disorders, *Helicobacter pylori* and atrophic gastritis in patients examined for dyspeptic symptoms. *Anticancer Res*. 2021;41(2):811–9. DOI: 10.21873/anticanres.14833
24. *Белковец А.В., Курилович С.А., Решетников О.В., Рагино Ю.И., Щербакова Л.В.* Распространенность и особенности фундального атрофического гастрита в популяции с высоким уровнем *Helicobacter pylori*-инфекции. *Экспериментальная и клиническая гастроэнтерология*. 2016;9:8–13. [*Belkovets A.V., Kurilovich S.A., Reshetnikov O.V., Ragino Yu., Scherbakova L.V.* Prevalence and peculiarity of corpus atrophic gastritis in population with high level of *Helicobacter pylori* infection. *Experimental & Clinical Gastroenterology*. 2016;9:8–13 (In Russ.)].
25. *Bakulina N., Tikhonov S., Malkov V., Vorobyev S., Belyakov I., Peshkova N., et al.* Non-invasive screening of autoimmune atrophic gastritis in asymptomatic subjects by serological biomarker test (GastroPanel®). *Anticancer Res*. 2022;42(3):1517–26. DOI: 10.21873/anticanres.15624
26. *Zagari R.M., Rabitti S., Greenwood D.C., Eusebi L.H., Vestito A., Bazzoli F.* Systematic review with meta-analysis: Diagnostic performance of the combination of pepsinogen, gastrin-17 and anti-*Helicobacter pylori* antibodies serum assays for the diagnosis of atrophic gastritis. *Aliment Pharmacol Ther*. 2017;46(7):657–67. DOI: 10.1111/apt.14248
27. *Romańczyk M., Osmola M., Link A., Druet A., Hémont C., Martin J., et al.* Non-invasive markers for the detection of gastric precancerous conditions. *Cancers (Basel)*. 2024;16(12):2254. DOI: 10.3390/cancers16122254
28. *Chapelle N., Petryszyn P., Blin J., Leroy M., Le Berre-Scoul C., Jirka I., et al.* A panel of stomach-specific biomarkers (GastroPanel®) for the diagnosis of atrophic gastritis: A prospective, multicenter study in a low gastric cancer incidence area. *Helicobacter*. 2020;25(5):e12727. DOI: 10.1111/hel.12727
29. *Lombardo L., Leto R., Molinaro G., Migliardi M., Ravarino N., Rocca R., et al.* Prevalence of atrophic gastritis

in dyspeptic patients in Piedmont. A survey using the GastroPanel test. *Clin Chem Lab Med*. 2010;48(9):1327–32. DOI: 10.1515/CCLM.2010.256
30. *Tu H., Sun L., Dong X., Gong Y., Xu Q., Jing J., et al.* Temporal changes in serum biomarkers and risk for progression of gastric precancerous lesions: A longitudinal study. *Int J Cancer*. 2015;136(2):425–34. DOI: 10.1002/ijc.29005
31. *Roman L.D., Lukyanchuk R., Sablin O.A., Araslanova E.I., Eklund C., Hendolin P., et al.* Prevalence of *H. pylori* infection and atrophic gastritis in a population-based screening with serum biomarker panel (GastroPanel®) in St. Petersburg. *Anticancer Res.* 2016;36(8):4129–38.
32. *Sánchez-López J.Y., Díaz-Herrera L.C., Rizo-de la Torre L.D.C.* Pepsinogen I, pepsinogen II, gastrin-17, and *Helicobacter pylori* serological biomarkers in the diagnosis of precursor lesions of gastric cancer. *Arch Med Sci*. 2024;20(3):1016–21. DOI: 10.5114/aoms/189971
33. *Grad C., Pop A., Gaborean E., Grad S., Dumitrascu D.* Value of GastroPanel in the diagnosis of atrophic gastritis. *Exp Ther Med*. 2021;22(5):1347. DOI: 10.3892/etm.2021.10782
34. *Valle Muñoz J., Artaza Varasa T., López Pardo R., Rodríguez Merlo R., Pérez Grueso M.J., Martín Escobedo R., et al.* Serological diagnosis of atrophic gastritis with a combination of pepsinogen I and II, gastrin-17 and anti-*Helicobacter pylori* antibodies. *Gastroenterol Hepatol*. 2007;30(10):567–71. (In Spanish). DOI: 10.1157/13112584
35. *McNicholl A.G., Forné M., Barrio J., De la Coba C., González B., Rivera R., et al.; Helicobacter pylori Study Group of Asociación Española de Gastroenterología (AEG).* Accuracy of GastroPanel for the diagnosis of atrophic gastritis. *Eur J Gastroenterol Hepato*l. 2014;26(9):941–8. DOI: 10.1097/MEG.0000000000000132
36. *Taniyama Y., Katanoda K., Charvat H., Hori M., Ohno Y., Sasazuki S., et al.* Estimation of lifetime cumulative incidence and mortality risk of gastric cancer. *Jpn J Clin Oncol*. 2017;47(11):1097–102. DOI: 10.1093/jjco/hyx128
37. *Coelho M.C.F., Ribeiro H.G., Gomes C.G.O., Marinho F.P., Barbosa A.J.A., Coelho L.G.V. Helicobacter pylori* chronic gastritis on patients with premalignant conditions: OLGA and OLGIM evaluation and serum biomarkers performance. *Arq Gastroenterol.* 2021;58(1):39–47. DOI: 10.1590/S0004-2803.202100000-08
38. *Ogutmen Koc D., Bektas S.* Serum pepsinogen levels and OLGA/OLGIM staging in the assessment of atrophic gastritis types. *Postgrad Med J*. 2022;98(1160):441–5. DOI: 10.1136/postgradmedj-2020-139183
39. *Peitz U., Wex T., Vieth M., Stolte M., Willich S., Labenz J., et al.* Correlation of serum pepsinogens and gastrin-17 with atrophic gastritis in gastroesophageal reflux patients: A matched-pairs study. *J Gastroenterol Hepatol*. 2011;26(1):82–9. DOI: 10.1111/j.1440-1746.2010.06413.x
40. *Белковец А.В., Курилович С.А., Рагино Ю.И., Щербакова Л.В., Черемисина О.В., Чердынцева Н.В. и др.* Биомаркеры желудочной атрофии у пациентов с раком желудка. *Российский журнал гастроэнтерологии, гепатологии, колопроктологии*. 2018;28(2):24–32. [*Belkovets A.V., Kurilovich S.A., Ragino Yu.I., Scherbakova L.V., Cheremisina O.B., Cherdyntseva N.V., et al.* Biomarkers of gastric atrophy at stomach cancer. *Russian Journal of Gastroenterology, Hepatology, Coloproctology*. 2018;28(2):24–32. (In Russ.)]. DOI: 10.22416/1382-4376-2018-28-2-24-32
41. *Gašenko E., Bogdanova I., Sjomina O., Aleksandraviča I., Kiršners A., Ancāns G., et al.* Assessing the utility of pepsinogens and gastrin-17 in gastric cancer detection. *Eur J Cancer Prev*. 2023;32(5):478–84. DOI: 10.1097/CEJ.0000000000000791
42. *Dondov G., Amarbayasgalan D., Batsaikhan B., Badamjav T., Batbaatar B., Tuvdenjamts B., et al.* Diagnostic performances of pepsinogens and gastrin-17 for atrophic gastritis and gastric cancer in Mongolian subjects. *PLoS One*. 2022;17(10):e0274938. DOI: 10.1371/journal.pone.0274938
43. *Nejadi-Kelarijani F., Roshandel G., Semnani S., Ahmadi A., Faghani B., Besharat S., et al.* Diagnostic values of serum levels of pepsinogens and gastrin-17 for screening gastritis and gastric cancer in a high risk area in northern Iran. *Asian Pac J Cancer Prev*. 2014;15(17):7433–6. DOI: 10.7314/apjcp.2014.15.17.7433
44. *Kurilovich S., Belkovets A., Reshetnikov O., Openko T., Malyutina S., Ragino Y., et al.* Stomach-specific iomarkers (GastroPanel) can predict the development of gastric cancer in a Caucasian population: A longitudinal nested case-control study in Siberia. *Anticancer Res*. 2016;36(1):247–53.
45. *Terasawa T., Nishida H., Kato K., Miyashiro I., Yoshikawa T., Takaku R., et al.* Prediction of gastric cancer development by serum pepsinogen test and *Helicobacter pylori* seropositivity in eastern Asians: A systematic review and meta-analysis. *PLoS One*. 2014;9(10):e109783. DOI: 10.1371/journal.pone.0109783
46. *Kim G.H., Bang S.J., Ende A.R., Hwang J.H.* Is screening and surveillance for early detection of gastric cancer needed in Korean Americans? *Korean J Int Med*. 2015;30(6):747–58. DOI: 10.3904/kjim.2015.30.6.747
47. *Chen W., Zheng R., Baade P.D., Zhang S., Zeng H., Bray F., et al.* Cancer statistics in China, 2015. *CA Cancer J Clin*. 2016;66(2):115–32. DOI: 10.3322/caac.21338
48. *Miki K.* Gastric cancer screening by combined assay for serum anti-*Helicobacter pylori* IgG antibody and serum pepsinogen levels – "ABC method". *Proc Jpn Acad Ser B Phys Biol Sci*. 2011;87(7):405–14. DOI: 10.2183/pjab.87.405
49. *Kishikawa H., Kimura K., Takarabe S., Kaida S., Nishida J. Helicobacter pylori* antibody titer and gastric cancer screening. *Dis Markers*. 2015;2015:156719. DOI: 10.1155/2015/156719
50. *Kishino T., Oyama T., Tomori A., Takahashi A., Shinohara T.* Usefulness and limitations of a serum screening system to predict the risk of gastric cancer. *Intern Med*. 2020;59(12):1473–80. DOI: 10.2169/internalmedicine.3521-19
51. *Kishikawa H., Nakamura K., Takarabe S., Katayama T., Sasaki A., Miura S., et al.* Clinical characteristics of patients with previous *Helicobacter pylori* infection-induced atrophic gastritis. *Cureus*. 2024;16(6):e63368. DOI: 10.7759/cureus.63368
52. *Kotachi T., Ito M., Yoshihara M., Boda T., Kiso M., Masuda K., et al.* Serological evaluation of gastric cancer risk based on pepsinogen and *Helicobacter pylori* antibody: Relationship to endoscopic findings. *Digestion*. 2017;95(4):314–8. DOI: 10.1159/000477239
53. *Cho J.H., Jin S.Y., Park S.* Scoring model for discriminating gastric cancer risk in patients with negative serum pepsinogen and anti-*Helicobacter pylori* antibody results. *J Gastroenterol Hepatol*. 2021;36(12):3345–53. DOI: 10.1111/jgh.15630
54. *Nagasaki N., Ito M., Boda T., Kotachi T., Takigawa H., Oka S., et al.* Identification of Helicobacter pylori-related gastric cancer risk using serological gastritis markers and endoscopic findings: A large-scale retrospective cohort study. *BMC Gastroenterol*. 2022;22(1):299. DOI: 10.1186/s12876-022-02381-z
55. *Ni D.Q., Lyu B., Bao H.B., Jin H.F., Zhao J., Xu Y., et al.* Comparison of different serological methods in screening early gastric cancer. *Zhonghua Nei Ke Za Zhi*. 2019;1;58(4):294–300. [In Chinese]. DOI: 10.3760/cma.j.issn.0578-1426.2019.04.011
56. *Yamaguchi Y., Nagata Y., Hiratsuka R., Kawase Y., Tominaga T., Takeuchi S., et al.* Gastric cancer screening by combined assay for serum anti-*Helicobacter pylori* IgG antibody and serum pepsinogen levels – The ABC method. *Digestion*. 2016;93(1):13–8. DOI: 10.1159/000441742
57. *Baek S.M., Kim N., Kwon Y.J., Lee H.S., Kim H.Y., Lee J., et al.* Role of serum pepsinogen II and *Helico-*

bacter pylori status in the detection of diffuse-type early gastric cancer in young individuals in South Korea. *Gut Liver*. 2020;14(4):439–49. DOI: 10.5009/gnl19091
58. *Li P., Li Z., Linghu E., Ji J.; Society of Digestive Endoscopy of the Chinese Medical Association, Colorectal Surgery Group of the Chinese Medical Association, Chinese Association of Gastroenterologists & Hepatologists, National Clinical Research Center for Digestive Diseases, Chinese Medical Journal Clinical Practice Guideline Collaborative.* Chinese national clinical practice guidelines on the prevention, diagnosis, and treatment of early gastric cancer. *Chin Med J (Engl).* 2024;137(8):887–908. DOI: 10.1097/CM9.0000000000003101
59. *Chinese Society of Digestive Endoscopy.* Consensus on screening and endoscopic diagnosis and treatment of early gastric cancer in China (Changsha, 2014). *Zhong hua Xiao Hua Nei Jing Za Zhi.* 2014;31(7):361–77.
60. *Hu Y., Bao H., Jin H., Zhao J., Xu Y., Huang X., et al.* Performance evaluation of four prediction models for risk stratification in gastric cancer screening among a high-risk population in China. *Gastric Cancer.* 2021;24(6):1194–202. DOI: 10.1007/s10120-021-01204-6
61. *Li M.Y., Zhang D.Q., Lu X., Chen W.C.* Comparison of two serological methods in screening gastric cancer and its precancerous condition. *Zhonghua Nei Ke Za Zhi.* 2018;57(12):907–11. [In Chinese]. DOI: 10.3760/cma.j.issn.0578-1426.2018.12.006
62. *Liu X.M., Ma X.Y., Liu F., Liu Z.L., Tang X.Y., Ji M.Z., et al.* Gastric cancer screening methods: A comparative study of the Chinese New Gastric Cancer Screening Score and Kyoto classification of gastritis. *Gastroenterol Res Pract*. 2022;2022:7639968. DOI: 10.1155/2022/7639968
63. *Cai Q., Zhu C., Yuan Y., Feng Q., Feng Y., Hao Y., et al.; Gastrointestinal Early Cancer Prevention & Treatment Alliance of China (GECA).* Development and validation of a prediction rule for estimating gastric cancer risk in the Chinese high-risk population: A nationwide multicentre study. *Gut*. 2019;68(9):1576–87. DOI: 10.1136/gutjnl-2018-317556
64. *Li L., Ni J., Sun S., Zha X., Li R., He C.* Clinical applicability of a new scoring system for population-based screening and risk factors of gastric cancer in the Wannan region. *BMC Gastroenterol*. 2022;22(1):306. DOI: 10.1186/s12876-022-02384-w

Information about the authors

Natalia S. Sergeeva — Dr. Sci. (Biol.), Professor, Head of the Department of Prediction of the Effectiveness of Conservative Treatment, P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre.
Contact information: prognoz.01@mail.ru;
125284, Moscow, 2nd Botkinsky lane, 3.
ORCID: https://orcid.org/0000-0001-7406-9973

Valeriia I. Ryabtseva — Clinical Resident at the Endoscopy Department, P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre.
Contact information: valeryappv@gmail.com;
125284, Moscow, 2nd Botkinsky lane, 3.
ORCID: https://orcid.org/0000-0003-3174-7695

Sergey S. Pirogov — Dr. Sci. (Med.), Head of the Endoscopy Department, P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre.
Contact information: pirogov@mail.ru;
125284, Moscow, 2nd Botkinsky lane, 3.
ORCID: https://orcid.org/0000-0002-8101-2155

Tatiana A. Karmakova — Dr. Sci. (Biol.), Leading Researcher of the Department of Prediction of the Effectiveness of Conservative Treatment, P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre.
Contact information: kalmar123@yandex.ru;
125284, Moscow, 2nd Botkinsky lane, 3.
ORCID: https://orcid.org/0000-0002-8017-5657

Сведения об авторах

Сергеева Наталья Сергеевна — доктор биологических наук, профессор, заведующая отделением прогноза эффективности консервативного лечения, Московский научно-исследовательский онкологический институт им. П.А. Герцена — филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации.
Контактная информация: prognoz.01@mail.ru;
125284, г. Москва, 2-й Боткинский пр., 3.
ORCID: https://orcid.org/0000-0001-7406-9973

Рябцева Валерия Игоревна — клинический ординатор отдела эндоскопии, Московский научно-исследовательский онкологический институт им. П.А. Герцена — филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации.
Контактная информация: valeryappv@gmail.com;
125284, г. Москва, 2-й Боткинский пр., 3.
ORCID: https://orcid.org/0000-0003-3174-7695

Пирогов Сергей Сергеевич — доктор медицинских наук, заведующий отделом эндоскопии, Московский научно-исследовательский онкологический институт им. П.А. Герцена — филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации.
Контактная информация: pirogov@mail.ru;
125284, г. Москва, 2-й Боткинский пр., 3.
ORCID: https://orcid.org/0000-0002-8101-2155

Кармакова Татьяна Анатольевна — доктор биологических наук, ведущий научный сотрудник отделения прогноза эффективности консервативного лечения, Московский научно-исследовательский онкологический институт им. П.А. Герцена — филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации.
Контактная информация: kalmar123@yandex.ru;
125284, г. Москва, 2-й Боткинский пр., 3.
ORCID: https://orcid.org/0000-0002-8017-5657

Igor I. Alentov* — Cand. Sci. (Biol.), Senior Researcher of the Department of Prediction of the Effectiveness of Conservative Treatment, P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre.
Contact information: igoralentov@gmail.com;
125284, Moscow, 2nd Botkinsky lane, 3.
ORCID: https://orcid.org/0000-0002-5920-5823

Нина V. Marshutina — Cand. Sci. (Biol.), Researcher of the Department of Prediction of the Effectiveness of Conservative Treatment, P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre.
Contact information: nin.mars@mail.ru;
125284, Moscow, 2nd Botkinsky lane, 3.
ORCID: https://orcid.org/0000-0003-2997-4936

Andrey D. Kaprin — Dr. Sci. (Med.), Professor, Academician of Russian Academy of Sciences, Academician of the Russian Academy of Education, Director, P. Hertsen Moscow Oncology Research Institute — Branch of the National Medical Research Radiological Centre; General Director, National Medical Research Radiological Centre; Head of the Department of Oncology and Roentgenology named after V.P. Kharchenko, Peoples' Friendship University of Russia named after Patrice Lumumba.
Contact information: kaprin@mail.ru;
249036, Obninsk, Koroleva str., 4.
ORCID: https://orcid.org/0000-0001-8784-8415

Алентов Игорь Игоревич* — кандидат биологических наук, старший научный сотрудник отделения прогноза эффективности консервативного лечения, Московский научно-исследовательский онкологический институт им. П.А. Герцена — филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации.
Контактная информация: igoralentov@gmail.com;
125284, г. Москва, 2-й Боткинский пр., 3.
ORCID: https://orcid.org/0000-0002-5920-5823

Маршутина Нина Викторовна — кандидат биологических наук, научный сотрудник отделения прогноза эффективности консервативного лечения, Московский научно-исследовательский онкологический институт им. П.А. Герцена — филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации.
Контактная информация: nin.mars@mail.ru;
125284, г. Москва, 2-й Боткинский пр., 3.
ORCID: https://orcid.org/0000-0003-2997-4936

Каприн Андрей Дмитриевич — доктор медицинских наук, профессор, академик РАН и РАО, директор, Московский научно-исследовательский онкологический институт им. П.А. Герцена — филиал ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации; генеральный директор, ФГБУ «Национальный медицинский исследовательский центр радиологии» Министерства здравоохранения Российской Федерации; заведующий кафедрой онкологии и рентгенорадиологии им. В.П. Харченко, ФГАОУ ВО «Российский университет дружбы народов».
Контактная информация: kaprin@mail.ru;
249036, г. Обнинск, ул. Королева, 4.
ORCID: https://orcid.org/0000-0001-8784-8415

Authors' contributions

Concept and design of the study: Sergeeva N.S., Pirogov S.S., Kaprin A.D.
Collection and processing of the material: Sergeeva N.S., Ryabtseva V.I., Pirogov S.S., Karmakova T.A., Marshutina N.V.
Writing of the text: Sergeeva N.S., Ryabtseva V.I., Karmakova T.A., Alentov I.I.
Editing: Sergeeva N.S., Kaprin A.D.
Proof checking and approval with authors: Pirogov S.S., Marshutina N.V.

Вклад авторов

Концепция и формулирование обзора литературы: Сергеева Н.С., Пирогов С.С., Каприн А.Д.
Сбор и обработка материалов: Сергеева Н.С., Рябцева В.И., Пирогов С.С., Кармакова Т.А., Маршутина Н.В.
Написание текста: Сергеева Н.С., Рябцева В.И., Кармакова Т.А., Алентов И.И.
Редактирование: Сергеева Н.С., Каприн А.Д.
Проверка верстки и ее согласование с авторским коллективом: Пирогов С.С., Маршутина Н.В.

Submitted: 27.05.2025 Accepted: 26.08.2025 Published: 31.10.2025
Поступила: 27.05.2025 Принята: 26.08.2025 Опубликована: 31.10.2025

* Corresponding author / Автор, ответственный за переписку