ORIGINAL RESEARCH

Effect of Gastrin G-17 Combined with Pepsinogen PGI and PGII on the Early Screening of Gastric Cancer in the Department of Gastroenterology

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ABSTRACT

Objective • To compare serum levels of pepsinogen I (PGI), pepsinogen II (PGII), and gastrin-17 (G-17) among patients with gastritis, gastric ulcer, and gastric cancer, and to assess the effectiveness of these biomarkers individually and in combination for screening gastric cancer.

Methods • Serum levels of PGI, PGII, and G-17 were measured using enzyme-linked immunosorbent assay (ELISA) in 50 patients with gastric cancer, 60 with chronic gastritis, and 60 with gastric ulcer from February 2020 to June 2021. The diagnostic value of these biomarkers was analyzed through sensitivity, specificity, and ROC curve assessments.

Results • Serum PGI levels were significantly lower in patients with advanced gastric cancer compared to those with early gastric cancer ($P < .05$), while PGII and G-17 levels were significantly higher in advanced-stage patients ($P < .05$). The combined ROC curve analysis of PGI, PGII, and G-17 yielded an area under the curve (AUC) of 0.933, indicating higher diagnostic accuracy than any of the markers alone. Statistically significant differences were noted between the combined and individual tests ($Z = 2.376$, $P < .05$). Patients with PGI levels lower than 17.21 ng/ml had a worse prognosis compared to those with higher levels. Similarly, patients with PGII levels greater than 74.65 ng/ml and G-17 levels greater than 17.03 pmol/L had poorer prognoses. Additionally, higher G-17 levels were associated with significantly lower serum PGI levels.

Conclusions • Patients with low expression of PGI have a poorer prognosis, and those with high expression of PGII and G-17 also have a poor prognosis. Combining the three indicators has clear value for the screening and prognostic evaluation of gastric cancer, making it worthy of clinical promotion and application. (*Altern Ther Health Med.* [E-pub ahead of print.])

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INTRODUCTION

Gastric cancer remains a prevalent and formidable malignancy in China, characterized by significantly disparate outcomes contingent on the stage of detection. The five-year survival rate for early-stage gastric cancer patients exceeds 90%, whereas for those diagnosed at an advanced stage, the survival rate plummets to below 20%. This stark discrepancy underscores the paramount importance of early detection, accurate diagnosis, and timely intervention in enhancing patient prognosis.[1]

Currently, the diagnostic paradigm for early gastric cancer predominantly relies on gastroscopy and pathological biopsy. Despite their diagnostic efficacy, these modalities present notable limitations. Gastroscopy, often perceived as invasive and uncomfortable, suffers from suboptimal patient compliance and necessitates sophisticated technical expertise and equipment, thereby limiting its feasibility for large-scale screening. Gastrointestinal angiography, while useful, is associated with a heightened risk of diagnostic oversight.[2,33]

Given these constraints, there has been a burgeoning interest in serological testing as a viable alternative. Recent advancements have facilitated the clinical integration of serological biomarkers such as pepsinogen I (PGI), pepsinogen II (PGII), and gastrin-17 (G-17) for the preliminary screening of early gastric cancer. These biomarkers offer a non-invasive, cost-effective approach, potentially augmenting early detection rates.[4,5]

This study aims to investigate the combined diagnostic utility of serum PGI, PGII, and G-17 levels in the screening of gastric cancer. By evaluating the synergistic diagnostic performance of these biomarkers, this research seeks to establish a robust, accessible, and effective early screening strategy, thereby improving early detection rates and patient outcomes in the realm of gastric oncology.

PATIENTS AND METHODS

General Information

The study enrolled 50 patients diagnosed with gastric cancer (gastric cancer set) who underwent gastroscopy and

pathological diagnosis between February 2020 and June 2021 at our hospital. All patients had confirmed diagnostic results, had not undergone prior treatment related to gastric cancer, and provided informed consent for participation. Exclusion criteria included individuals with a history of gastric surgery, recent use (within the past week) of proton pump inhibitors, H2 receptor antagonists, or gastric mucosal protectants, and those with severe organ damage such as heart, liver, and kidney disorders.

Gastric Cancer Set: Age: 62.15 ± 12.57 years; Gender: 31 males, 19 females; Gastric Cancer Stage: 30 early gastric cancer, 20 advanced gastric cancer; Tumor Location: 4 multifocal lesions, 10 in gastric body, 36 in gastric antrum.

Additionally, 60 patients with chronic gastritis (gastritis set) and 60 patients with gastric ulcer (gastric ulcer set) were included as comparative study subjects.

Gastritis Set: Age: 59.08 ± 8.92 years; Gender: 38 males, 22 females.

Gastric Ulcer Set: Age: 55.01 ± 9.96 years; Gender: 40 males, 20 females.

All participants provided informed consent, and the therapeutic and diagnostic procedures employed in the study were established safe practices in clinical settings. The demographic and clinical data collected were solely utilized for research purposes and not for any other intents.

Research Methods

Serum Collection and Biomarker Analysis. In each of the three patient groups, 5 ml of fasting venous blood was collected into a procoagulation tube and immediately subjected to gentle mixing. Following collection, the blood samples underwent centrifugation at 3000 rpm for 10 minutes to separate the serum. The serum was then carefully transferred into labeled storage tubes and promptly stored at -20°C until further analysis.

Enzyme-Linked Immunoassay (ELISA) Methodology. Serum levels of PGI, PGII, and G-17 were quantified using commercially available ELISA kits from reputable manufacturers, PGI and PGII: Human Pepsinogen I ELISA Kit (Catalog No. E-EL-H0811) and Human Pepsinogen II ELISA Kit (Catalog No. E-EL-H0812) from Elabscience; G-17: Human Gastrin-17 ELISA Kit (Catalog No. E-EL-H1295) from Elabscience.

These assays were performed in strict accordance with the manufacturers' instructions to ensure consistency and accuracy. The kits used are validated for their sensitivity and specificity in detecting each biomarker, thereby enhancing the methodological rigor of the study.

Handling Procedures and Quality Control. Post-centrifugation, stringent protocols were followed to maintain the integrity of the serum samples. This included immediate storage at -20°C to prevent degradation of the biomarkers. All handling procedures, from sample collection to analysis, adhered meticulously to standardized protocols to minimize variability and ensure reproducibility of results.

The enzyme-linked immunosorbent assays were conducted using an FC microplate reader, calibrated according to the specifications provided by the kit manufacturers. This meticulous approach not only standardized the analytical process but also ensured that the results obtained were reliable and comparable across the different patient cohorts.

Statistical Methods

All data collected in this study were compiled into a structured database and analyzed using SPSS 26.0 software. Continuous variables were expressed as mean ± standard deviation (SD) and assessed for normality using appropriate statistical tests. Normally distributed data were analyzed using parametric tests such as analysis of variance (ANOVA) for comparisons among multiple groups and independent sample *t* tests for comparisons between two groups. Paired sample *t* tests were employed for within-group comparisons. Non-normally distributed data were analyzed using the Mann-Whitney U test. Categorical data were presented as percentages and analyzed using the chi-square (χ^2) test. To explore relationships between serum biomarkers (PGI, PGII, and G-17) and gastric cancer, Pearson correlation coefficients were calculated. The diagnostic performance of PGI and PGII compared to G-17 was evaluated using receiver operating characteristic (ROC) curves, with significance set at $P < .05$.

RESULTS

Baseline data comparison

There were no statistically significant differences in baseline characteristics such as age and gender among the gastric cancer, gastritis, and gastric ulcer groups ($P > .05$). Detailed demographic data are presented in Table 1.

Comparison of Serum PGI, PGII, and G-17 Levels Across Groups

Serum PGI levels were significantly lower in the gastric cancer group compared to both the gastritis and gastric ulcer groups ($P < .05$). Conversely, PGII and G-17 levels were significantly higher in the gastric cancer group compared to the gastritis and gastric ulcer groups ($P < .05$). Refer to Table 2 for comprehensive results.

Table 1. The contrast of serum PGI, PG, and G-17 levels in the three sufferer sets

set	G-17 (pmol/L)	PGI (ng/ml)	PGII (ng/ml)
Gastritis set (n=60)	13.26±3.55	113.16±10.58	14.69±3.78
Gastric ulcer set (n=60)	16.89±4.59[a]	99.63±9.82[a]	16.08±3.99
Gastric cancer set (n=50)	17.10±6.04[a,b]	63.63±12.85[a,b]	17.67±4.65[a,b]
F	11.578	286.895	7.118
P value	<.001	<.001	<.001

[a]Represents that, when contrast to the gastritis set
[b]$P < .05$ contrast to the gastric ulcer set.

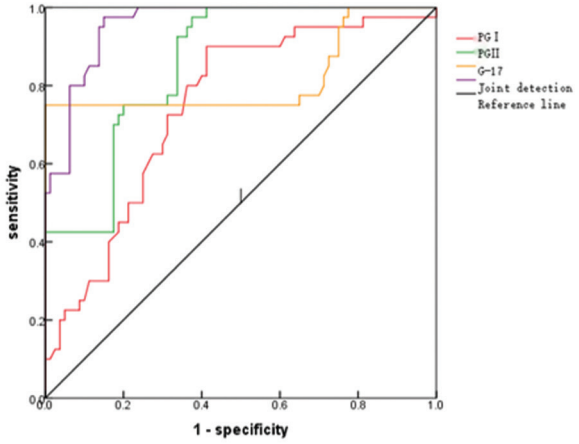
Table 2. Contrast of serum PGI, PG, and G-17 levels in gastric cancer sufferers at different periods

Set	G-17 (pmol/L)	PGI (ng/ml)	PGII (ng/ml)
Early-stage gastric cancer (n=30)	15.26±5.71	70.63±10.28	16.13±3.29
Advanced gastric cancer (n=20)	19.86±6.33	53.15±8.49	19.96±5.47
t	-2.672	6.300	-3.094
P value	.010	<.001	.003

Table 3. Analyzes the value of the combined detection of PGI, PG, and G-17 for the diagnosis of gastric cancer

Metric	Sensitivity	Specificity	Cutoff value	AUC	Youden index
PGI	70.50	75.50	17.21ng/ml	0.725 (0.638~0.799)	0.460
PGII	75.00	76.00	74.65ng/ml	0.759 (0.662~0.838)	0.510
G-17	75.00	73.00	17.03pmol/L	0.740 (0.662~0.845)	0.480
Joint detection	95.00	94.00	/	0.933 (0.901~0.973)	0.890

Figure 1. Analyzes the ROC curve of the combined value of PGI, PG, and G-17 for the diagnosis of gastric cancer



Comparison of Serum PGI, PGII, and G-17 Levels in Different Stages of Gastric Cancer

Among gastric cancer patients, PGI levels were notably lower in advanced stages than in early stages ($P < .05$). In contrast, PGII and G-17 levels were notably higher in advanced stages compared to early stages ($P < .05$). Detailed comparisons can be found in Table 3.

Analysis of Diagnostic Value of PGI, PGII, and G-17 in Gastric Cancer

Combined analysis of PGI, PGII, and G-17 yielded an AUC of 0.933 in ROC curve analysis for diagnosing gastric cancer, indicating high specificity and sensitivity. This combined AUC was significantly higher than that of individual biomarkers ($P < .05$). Refer to Figure 1 for detailed statistical analysis.

Prognostic Correlations with Different Levels of PGI, PGII, and G-17 in Gastric Cancer Patients

Correlation of PGI Levels with Prognosis: Patients with PGI < 17.21 ng/ml had significantly poorer prognoses compared to those with PGI ≥ 17.21 ng/ml ($P < .05$). See Figure 2 for graphical representation.

Correlation of PGII Levels with Prognosis: Patients with PGII > 74.65 ng/ml showed significantly worse prognoses than those with PGII ≤ 74.65 ng/ml ($P < .05$). Detailed results are presented in Figure 3.

Correlation of G-17 Levels with Prognosis: Patients with G-17 > 17.03 pmol/L exhibited significantly poorer prognoses compared to those with G-17 ≤ 17.03 pmol/L ($P < .05$). Refer to Figure 4 for graphical representation.

Figure 2. Analysis of the expression of different PGI levels and the prognosis of gastric cancer sufferers

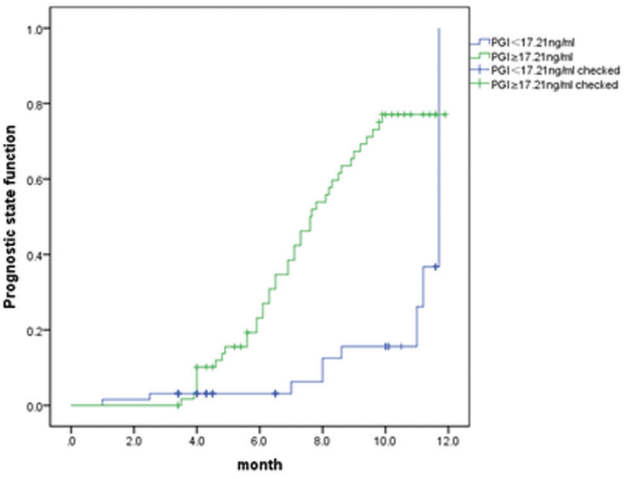


Figure 3. Analysis of different PG expression levels and the prognosis of GC sufferers

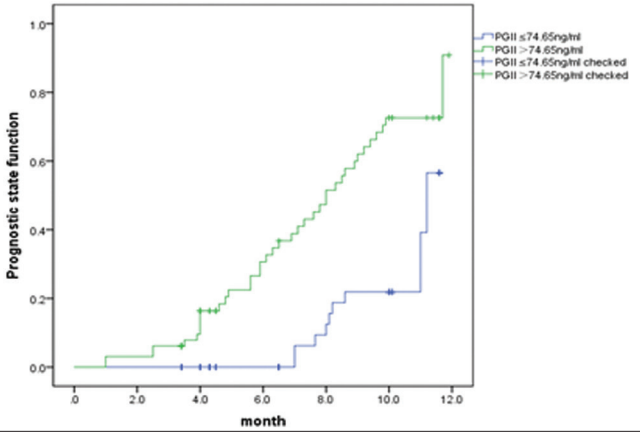
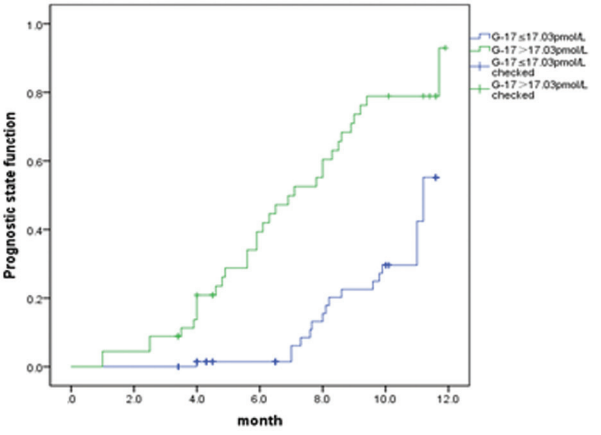


Figure 4. Analysis of different G-17 expression levels and the prognosis of gastric cancer sufferers



DISCUSSION

Gastric cancer remains a formidable challenge in oncology, characterized by its silent progression in early stages and the stark contrast in prognosis between early and advanced disease. Early detection strategies are crucial to

improving outcomes and reducing mortality rates. This study contributes valuable insights into the role of serum biomarkers—PGI, PGII, and G-17—in enhancing the detection and management of gastric cancer.

Importance of Early Detection

The asymptomatic nature of early gastric cancer often delays diagnosis until advanced stages, when treatment options are limited and prognosis is poor. Most early gastric cancer cases are asymptomatic or present with non-specific dyspeptic symptoms, often leading to delayed diagnosis and low detection rates. The five-year survival rate for early gastric cancer can exceed 95% with prompt treatment, underscoring the critical importance of effective screening strategies aimed at high-risk populations. Early detection not only improves prognosis but also significantly reduces mortality rates associated with this malignancy. [6,7]

Current Screening Challenges and Limitations

Currently, screening techniques for gastric cancer include gastroscopy, barium meal imaging tests, and serological tests. Barium meal imaging is prone to missing flat and non-concave lesions and cannot provide a qualitative diagnosis, resulting in low sensitivity and specificity, and has gradually lost its advantage in early gastric cancer screening. Gastroscopic pathological examination of the gastric mucosa is the gold standard for gastric cancer diagnosis, offering higher sensitivity than barium meal imaging. Despite the rapid development and promotion of digestive endoscopy technology making gastroscopy feasible for mass screening, it remains an invasive examination that most sufferers find painful and have poor compliance with. Moreover, gastroscopy is relatively time-consuming and requires significant manpower and resources, making it impractical for extensive-scale population screening.[8]

The Role of Serum Markers in Screening

Serological testing of PGs and G-17 offers advantages such as being non-invasive, simple, and cost-effective. Serological testing can be used to screen high-risk groups for gastroscopy. Countries like Japan and Finland have begun to investigate the early diagnosis of gastric cancer using combined serum gastrin and PG tests.

Pepsinogen, the precursor of pepsin, consists of 375 amino acids and has a relative molecular weight of 42 kDa. It is mainly secreted by the gastric mucosa and is divided into two subsets: PGI and PGII. PGI is primarily secreted by gastric fundus gland chief cells and cervical mucus cells, while PG is secreted by these cells as well as gastric antral pyloric glands and proximal duodenal Brunner glands, with minor secretion by the pancreas and prostate. Under normal conditions, most pepsinogen is released into the gastric cavity, with only about 1% entering the bloodstream. [9-13]

Research Findings

The present study found that PGI and PGII levels were significantly lower in advanced gastric cancer sufferers, while G-17 levels were significantly higher in early gastric cancer sufferers, and these levels were also higher in gastric ulcer and gastritis patients (both $P < .05$). PGI levels correlate with gastric acid secretion and decrease with conditions such as gastric mucosa gland atrophy or after gastric resection. PGII, secreted by various glands, maintains a relatively stable secretion volume. Serum PGII levels are associated with factors such as proton pump inhibitors, H2 receptor antagonists, and renal function but are not significantly affected by diet. [14]

G-17 is primarily secreted by gastric antral G cells and regulates gastric acid secretion by interacting with somatostatin cells and enterochromaffin-like cells. G-17 promotes gastric mucosa cell proliferation and differentiation, accelerates gastric mucosa repair, and participates in gastric mucosa inflammation. Its secretion is influenced by various factors, such as G cell number, food intake, gastric pH, vagal nerve stimulation, and gastric antrum stretching.[15,16]

Implications of Research Findings

The study also found that the prognosis for patients with PGI < 17.21 ng/ml is worse than for those with PGI ≥ 17.21 ng/ml; patients with PGII > 74.65 ng/ml have a worse prognosis compared to those with G-17 > 17.03 pmol/L and G-17 ≤ 17.03 pmol/L. In gastritis, PGI decreases due to atrophy of chief cells and cervical mucus cells and impaired secretion function. PG secretion, besides from chief cells and cervical mucus cells, is less affected. Inflammation promotes the development of atrophic lesions, intestinal metaplasia, and dysplasia, further decreasing PGI secretion while increasing PG secretion, leading to a decreased PGI/PGII ratio.

Research has shown that reduced PGI and PGI/PGII levels indicate a high risk of gastric cancer and can serve as early warning signals. G-17 levels, influenced by gastric acidity, diet, and G cell count, can reflect gastric antral mucosa atrophy and function. The combined AUC of PGI, PGII, and G-17 in gastric cancer patients was 0.933, indicating high specificity and sensitivity, and significantly higher than individual markers alone ($Z = 2.376$, $P < .05$). [17-19]

Further research could focus on optimizing cutoff values for PGI, PGII, and G-17 to enhance their diagnostic accuracy across diverse populations and varying risk profiles. Moreover, international studies, particularly from countries like Japan and Finland, have explored the combined use of serum gastrin and PG, reflecting ongoing global efforts to advance early gastric cancer detection strategies. Implementing these serological markers in routine clinical practice could revolutionize gastric cancer screening by enabling timely interventions and potentially reducing the burden of advanced-stage diagnoses.

In conclusion, while gastroscopy remains essential for definitive diagnosis, serological markers offer a promising adjunct for initial screening in high-risk populations. By improving detection rates and facilitating early intervention, these markers contribute significantly to the overarching goal of mitigating gastric cancer-related morbidity and mortality.[20,21]

CONCLUSION

Serum PGI levels are significantly lower in gastric cancer sufferers, while PGII and G-17 levels are notably higher. Patients with low PGI and high PGII and G-17 expressions tend to have poorer prognoses. The combined assessment of these three indexes shows promise for the early diagnosis of gastric cancer and is worthy of clinical application. Integrating these serum markers into screening protocols can enhance early detection, improve patient outcomes, and provide a cost-effective approach for widespread gastric cancer screening and prevention.

CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

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This study did not receive any funding in any form.

AUTHOR CONTRIBUTIONS

HC and HX designed the study and performed the experiments, HC collected the data, HX analyzed the data, and HC and HX prepared the manuscript. All authors read and approved the final manuscript.

ETHICAL COMPLIANCE

This study was approved by the ethics committee of Nanjing Second Hospital. Signed written informed consents were obtained from the patients and/or guardians.

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