Diagnostic value of combined detection of three gastric functions and Helicobacter pylori typing in chronic gastritis and gastric cancer

Fei Wang *
Department of Hepatobiliary Gastrointestinal Surgery, Changshu Hospital of Traditional Chinese Medicine (New Area Hospital), Changshu, Jiangsu 215500, PR China

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ABSTRACT

This research attempted to clarify the clinical diagnostic value of combined detection of gastric function and Helicobacter pylori (Hp) serotyping in chronic gastritis and gastric cancer (GC). The 80 chronic non atrophic gastritis (CNAG) patients treated in our hospital from October 2021 to October 2022 received selection as the CNAG group. The 96 chronic atrophic gastritis (CAG) patients diagnosed by gastroscopy and pathology in the same period received selection as CAG group. During the same period, 50 patients diagnosed with GC received inclusion in GC group. Pepsin I (PG I), PG II (PG II), gastrin-17 (G-17) and Hp serotyping received detection and comparison in three groups. The diagnostic efficacy of PG I, PG II, G-17, the ratio of serum PG I to PG II (PGR), and Hp serotyping in chronic gastritis and GC received evaluation by receiver operating characteristic (ROC). Relative to in the CNAG group, PG I and PGR levels in the other two groups exhibited depletion (P < 0.05); no statistical significance was observed in the PG II level among the three groups (P > 0.05); relative to the CNAG group, the G-17 level in the other two groups exhibited elevation (P < 0.05). Total Hp positive rate was 61.06 %, among which GC group exhibited the highest positive rate (72.00 %), and type I Hp positive rate also exhibited the highest in GC group (60.00 %). The type II Hp positive rate exhibited the highest in CNAG group (15.00 %). The PG I and PGR levels in type I Hp positive patients exhibited depletion relative to those in type II Hp positive patients, whereas PG II and G-17 levels exhibited elevation. When testing each indicator alone, the area under the curve (AUC) of PG I exhibited the highest in CNAG group, which was 0.874. When testing each indicator alone, AUC of Hp typing exhibited the highest in CAG group, which was 0.515. When testing each indicator alone, AUC of G-17 exhibited the highest in GC group, which was 0.787. The performance of combined detection was better than that of individual detection, with AUCs greater than 0.9 in three groups. In conclusion, changes in PG I, PG II, PGR and G-17 levels and Hp serotyping can receive application as screening indicators for chronic gastritis and GC, which can reflect relevant status of gastric mucosa to varying degrees. Combined detection of indicators has higher diagnostic performance and can receive application as an auxiliary diagnostic indicator in addition to gastroscopy biopsy, providing a reference basis for the formulation of clinical diagnosis and treatment plans.

1. Introduction

Chronic gastritis (GA) is an inflammatory response of gastric mucosa caused by a variety of elements, which is easy to recur and seriously affects patients’ quality of life and is one of the common diseases of digestive system [1,2]. CAG is also listed as a precancerous state by the World Health Organization, and its progression is hidden and difficult to find; those with intestinal metaplasia or atypical hyperplasia are likely to become cancerous [3]. According to literature, CAG incidence in China is approximately 10 %–30 % [4], and 70 %–90 % of patients have Hp infection [5]. The presence of chronic gastritis activity highly suggests Hp infection.

GC is a malignant disease originating from epithelial cells of gastric mucosa, which is one of the common refractory tumors in clinical practice. According to the latest statistics, GC incidence in China ranks the third among all malignancies. Every year, there are nearly 400,000 new cases, nearly 300,000 deaths, and case fatality rate is as high as 72.8 % [6]. Some scholars have revealed that GC occurrence and
development has close relation to Hp infection, that is, Hp infection  
–CNAG - CAG - intestinal metaplasia – dysplasia – gastro-intestinal type  
GC in progressive development [7,8]. In recent years, with development  
of serological markers, three items of gastric functions including serum  
PG I, PG II and G-17 are called “serological biopsy” [9], which can  
predict atrophy degree of gastric mucosa [10]. Meanwhile, Hp sero-  
typing is also a novel indicator for determining types of HP infection.  

This research observed changes in three items of gastric functions  
and positive rates of different types of Hp infection in chronic gastritis  
and GC, and clarified clinical diagnostic value of combined detection  
of gastric function and Hp serotyping in chronic gastritis and gastric cancer, in order to determine whether these indicators can be used as non-  
invasive auxiliary diagnostic indicators for chronic gastritis and GC except for endoscopic biopsy, which may provide more clinical basis for  
early screening diagnosis of CAG and GC.

2. Materials and methods

2.1. General data

From October 2021 to October 2022, all patients admitted to our hospital underwent upper gastrointestinal endoscopy to obtain patho-  
diagnosis. According to the histopathological type, the subjects were divided into GC group, CAG group, and CNAG group. Among them,  
there were 80 cases in the CNAG group, 96 patients with CAG and 50  
patients with GC in the same period. Demographic data such as age and  
gender were recorded, Helicobacter pylori serotyping was analyzed, and  
those with acute and chronic infectious diseases; 3) primary and sec-  
dary severe organ damage; 4) those who did not cooperate with ex-  
trausal biopsy within 2 weeks. Exclusion criteria: 1) Those with other tumors; 2)  
steroidal drugs, antibiotics, proton pump inhibitors received applica-  
tion, in order to determine whether these indicators can be used as non-  
invasive auxiliary diagnostic indicators for chronic gastritis and GC except for endoscopic biopsy, which may provide more clinical basis for  
early screening diagnosis of CAG and GC.

2.2. Methods

(1) Three items of gastric function (PG I, PG II, G-17). The 3 mL of  
venous blood on an empty stomach in the morning of admission  
received collection from all subjects, followed by centrifugation at  
4000 r/min for 15 min, and serum received separation for testing. The MAGLUMI 2000 plus fully automatic luminescence  
instrument and its supporting reagents (Shenzhen New Industries  
Biomedical Engineering Co., Ltd) received application for mea-  
surement, and ratio of serum PG I to PG II (PGR) received calculation.

(2) Measurement of Hp infection: The status of H. pylori infection was verified by 13C-urea breath test (UBT) (HY-IREX II channel;  
Huayou Mingkang Photoelectric Technology Co., Ltd, Guangzhou, China) and serological H. pylori antibody test (HEL-p  
TEST™ II, AMRAD Biotech, Australia). When both tests are negative, the patient is considered uninfected. When a positive  
result is observed in one test, but not both, they have no inclusion  
criteria to avoid false positive or negative results. When both tests are  
positive, the patient is considered infected.

(3) Hp serotyping. A 5 ml fasting venous blood sample was collected  
from the patient. All samples are centrifuged at 1500 × g for 5  
in minutes and analyzed within 2 h after blood collection. The virulence  
the factors CagA, VacA and UreA received determination through the  
AFS2000 A multi-channel dry fluorescent immune analyzer and its  
supporting reagents (Chongqing ISIA Bio-technology Co., Ltd), and  
results were semi quantitative. CagA and/or VacA positive strains are type I Hp strains; both CagA and VacA are negative, and  
UreA positive strains are type II Hp strains.

2.3. Statistical analysis

SPSS 27.0 software received application for data analysis. All data  
were tested for normal distribution by Kolmogorov-Smirnov test. We  
performed Bonferroni correction for multiple comparisons to control for  
type I error. The levels of gastric function indicators received expression  
as mean ± standard deviation, with intergroup comparisons through  
Kruskal Wallis or t-test. The Hp antibody typing and counting data  
received expression in [n (%)], with intergroup comparisons through  
Chi-square test. The diagnostic efficacy of PG I, PG I, G-17, PGR, and Hp  
serotyping in chronic gastritis and GC received evaluation by receiver  
operating characteristic (ROC). P < 0.05 indicated a statistically sig-  
nificant difference.

3. Results

3.1. Comparison of general data among three groups

The 80 CNAG patients treated in our hospital from October 2021 to  
October 2022 were allocated into the CNAG group, including 47 males  
and 33 females, aged 14-78 years old, with mean age of 50.5 ± 12.6  
years. The 96 CAG patients diagnosed by gastroscopy and pathology in  
the same period were allocated into the CAG group, including 52 males  
and 44 females, aged 21-77 years old, with mean age of 52.0 ± 12.8  
years. During the same period, 50 patients diagnosed with GC were  
allocated into the GC group, including 28 males and 22 females, aged  
29–81 years old, with mean age of 52.8 ± 13.2 years. No statistical  
significance in general data exhibited among three groups (P > 0.05;  
Table 1), indicating comparability.

3.2. Comparison of serum PG I, PG II, PGR and G-17 levels among three  
groups

Th statistical significance exhibited in PG I, PGR, and G-17 levels among  
CNAG, CAG, and GC groups (P < 0.05); relative to in CNAG  
group, PG I and PGR levels in the other two groups exhibited depletion,  
in descending order of CNAG group > CAG group > GC group, indi-  
cating statistical significance (P < 0.05); no statistical significance in PG  
II level exhibited among three groups (P > 0.05). Relative to CNAG  
group, G-17 level in the other two groups exhibited elevation, with  
upward order of CNAG group < CAG group < GC group, indicating  
statistical significance (P < 0.05; Fig. 1).

3.3. Comparison of Hp positive rates and Hp typing among three groups

A total of 226 patients received inclusion in this research, of which  
138 were Hp positive, with a positive rate of 61.06 %. The Hp positive  
rates in CNAG, CAG and GC groups were 52.50 %, 62.50 %, and 72.00  
%, respectively. The statistical significance exhibited between GC and  
CNAG groups (P < 0.05); no difference in Hp positive rate exhibited  
between CNAG and CAG groups (P > 0.05); no difference in Hp positive  
rate exhibited between CAG and GC groups (P > 0.05). The type I Hp  
positive rate exhibited the highest in GC group (60.00 %), and type I Hp  
positive rate in CAG and GC groups exhibited elevation relative to that in  
CNAG group, indicating statistical significance (P < 0.05); no difference

Table 1

<table>
<thead>
<tr>
<th>Groups</th>
<th>N</th>
<th>Gender [n (%)]</th>
<th>Age (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>CNAG group</td>
<td>80</td>
<td>47 (58.75)</td>
<td>33 (41.25)</td>
</tr>
<tr>
<td>CAG group</td>
<td>96</td>
<td>52 (54.17)</td>
<td>44 (45.83)</td>
</tr>
<tr>
<td>GC group</td>
<td>50</td>
<td>28 (56.00)</td>
<td>22 (44.00)</td>
</tr>
<tr>
<td>χ²/H</td>
<td></td>
<td>0.515</td>
<td>3.056</td>
</tr>
<tr>
<td>P</td>
<td>0.773</td>
<td>0.217</td>
<td></td>
</tr>
</tbody>
</table>


in type I Hp positive rate exhibited between CAG and GC groups \((P > 0.05)\). The CagA + VacA positive rate exhibited the highest in GC group (40.00 %) and exhibited statistical significance relative to CNAG and CAG groups \((P < 0.05)\); no statistical significance exhibited between CNAG and CAG groups \((P > 0.05)\). The CagA or VacA positive rate exhibited the highest in CAG group (28.12 %), whereas no statistical significance exhibited between groups \((P > 0.05)\). The type II Hp positive rate exhibited the highest in CNAG group (15 %), whereas no statistical significance exhibited between groups \((P > 0.05)\; \text{Table 2} \). 

### 3.4. Comparison of serum PGI, PGII, PGR and G17 levels in patients with different types of Hp infection

There were 138 Hp positive patients, of which 110 type I Hp positive patients and 28 type II Hp positive patients in this research. The PG I and PGR levels in type I Hp positive patients exhibited depletion relative to those in type II Hp positive patients, whereas PG II and G-17 levels exhibited elevation. The statistical significance in four indicators exhibited between type I and type II Hp positive patients \((P < 0.05; \text{Fig. 2})\).

### 3.5. Diagnostic value of combined detection of serum PG I, PG II, PGR and G-17 and Hp typing in chronic gastritis and GC

To assess each indicator’s diagnostic performance when evaluated separately and in combination, ROC analysis was conducted for the indicators examined in the CNAG, CAG, and GC groups (Fig. 3). When testing each indicator alone, AUC (95 %CI) of PG I exhibited the highest in CNAG group, which were 0.874. When testing each indicator alone, AUC of Hp typing exhibited the highest in CAG group, which were 0.515. When testing each indicator alone, AUC of G-17 exhibited the highest in GC group, which were 0.787 (Table 3). The performance of combined detection was better than that of individual detection, with

### Table 2

<table>
<thead>
<tr>
<th>Indicators</th>
<th>CNAG (n=80)</th>
<th>CAG (n=96)</th>
<th>GC (n=50)</th>
<th>(\chi^2) (CNAG/CAG)</th>
<th>P (CNAG/CAG)</th>
<th>(\chi^2) (CNAG/GC)</th>
<th>P (CNAG/GC)</th>
<th>(\chi^2) (CAG/GC)</th>
<th>P (CAG/GC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hp positive</td>
<td>42 (52.50)</td>
<td>60 (62.50)</td>
<td>36 (72.00)</td>
<td>2.025</td>
<td>0.155</td>
<td>8.146</td>
<td>0.004</td>
<td>2.11</td>
<td>0.146</td>
</tr>
<tr>
<td>Type I Hp positive</td>
<td>30 (37.50)</td>
<td>50 (52.08)</td>
<td>30 (60.00)</td>
<td>4.2</td>
<td>0.04</td>
<td>10.07</td>
<td>0.002</td>
<td>1.299</td>
<td>0.254</td>
</tr>
<tr>
<td>CagA + VacA positive</td>
<td>12 (15.00)</td>
<td>23 (23.96)</td>
<td>20 (40.00)</td>
<td>2.58</td>
<td>0.108</td>
<td>15.674</td>
<td>&lt;0.001</td>
<td>5.882</td>
<td>0.015</td>
</tr>
<tr>
<td>CagA or VacA positive</td>
<td>18 (22.50)</td>
<td>27 (28.12)</td>
<td>10 (20.00)</td>
<td>0.725</td>
<td>0.394</td>
<td>0.23</td>
<td>0.632</td>
<td>1.754</td>
<td>0.185</td>
</tr>
<tr>
<td>Type II Hp positive</td>
<td>12 (15.00)</td>
<td>10 (10.42)</td>
<td>6 (12.00)</td>
<td>1.143</td>
<td>0.285</td>
<td>0.385</td>
<td>0.535</td>
<td>0.204</td>
<td>0.651</td>
</tr>
</tbody>
</table>
AUCs greater than 0.9 in three groups, even reaching 100% in GC group, making it a good indicator for GC screening and diagnosis.

### 4. Discussion

China is a country with a high incidence of Hp infection, and current virulent strains of Helicobacter pylori, including types I and I, are closely associated with an increased risk of progressive gastric disease [11,12]. Chronic gastritis is one of the most common diseases of the digestive system, including CAG and CNAG, and Hp infection is the main cause of chronic gastritis [13]. The disease is slow-on, recurrent, and difficult to cure [14,15]. Epidemiological investigations suggest that most patients with chronic gastritis are asymptomatic and not easily detected, and it is estimated that the prevalence of chronic gastritis in the local population is roughly parallel to the rate of Hp infection and may be higher or slightly higher than the rate of Hp infection [16]. Without effective treatment, chronic gastritis with precancerous lesions can eventually progress to GC. Repeated or persistent Hp infections and poor dietary habits can exacerbate gastric mucosal atrophy and intestinal metaplasia [17]. GC is not easy to detect in the early stages, has a poor prognosis in the later stages, has no eradication methods, and has a high case fatality rate, which places a huge burden on patients and their families [18]. Therefore, it is urgent to find effective targeted detection indicators.

At present, the diagnosis of CAG and GC still relies on endoscopic biopsy sampling, and gastric mucosal lesions have focal distribution characteristics, and there may be missed detection in the biopsy process, which is often affected by the professional level and subjective factors of gastroscopists. Therefore, in recent years, great progress has been made in the study of serological indicators. Serum PG has been shown to reflect the atrophy of the gastric mucosa and contribute to risk stratification in people at high risk of GC, with patients with low PG I/II ratios suggesting a higher risk of GC [19]. G-17 may indicate the degree of gastric mucosal atrophy and the presence of dysplasia [20]. However, to date, the same serological screening protocols applied in different regions have produced different results for a variety of reasons. ABC methods (based on G-17, PG, and PGR) were used in Japan and South Korea to predict the occurrence of gastric tumors [21]. Due to the high incidence of Hp infection in China, new testing methods are needed. Therefore, this study detected the risk of gastric mucosal lesions based on Hp serotyping combined with G-17, PG and PGR.

Studies have shown that the combination of different markers can improve diagnostic efficiency. G-17 and PG [22,23], Both G-17 and PGR [24] can improve the sensitivity, specificity, and diagnostic coincidence rate of the diagnosis of GC. In our study, PG I and PGR levels exhibited...
depletion whereas G-17 level exhibited elevation in CAG and GC groups relative to those in CNAG group. The difference in G-17 between CNAG and CAG groups was not remarkable, but increase was most remarkable in GC group. This is consistent with previous research results. When gastric mucosa atrophies, gastric fundus gland cells exhibit a marked depletion or destruction due to inflammation, which reduces secretion of pepsin and attenuates serum pepsin level; serum pepsin has negative correlation with degree and progression of gastric mucosa atrophy. The increase or decrease in G-17 level has relation to different affected areas of lesion, increasing with gastric atrophy and decreasing with gastric antrum atrophy. In the CNAG group, the ratio of PG I/II (PGR) between the CAG group and the GC group was from high to low, with PG II not showing statistically significant consumption between groups, while PG I showed significant attrition, suggesting that the difference in pg was mainly due to the change in PG I. Moreover, statistical significance in PG I and PGR levels exhibited between CAG and CNAG groups, and statistical significance in PG I, PGR and G-17 levels exhibited between GC group and CAG or CNAG group. This result indicated that PGR and G-17 levels can provide a basis for the diagnostic scoring system of chronic gastritis and GC, but further detection is required.

Herein, total Hp positive rate was 61.06 %, among which GC group exhibited the highest positive rate (72.00 %), and type I Hp positive rate also exhibited the highest in GC group (60.00 %). The type II Hp positive rate exhibited the highest in CNAG group (15.00 %). The PG I and PGR levels in type I Hp positive patients exhibited depletion relative to those in type II Hp positive patients, whereas PG II and G-17 levels exhibited elevation. Previous studies have found that a combination of PG and anti-Hp IgG is helpful in detecting the progression of gastric adenomas to Lauren enterotype GC [25]. In this study, HP serotyping combined with PG and PGR detection was used to provide more diagnostic value for patients.

When testing each indicator alone, AUC of PG I exhibited the highest in CNAG group, which were 0.874. When testing each indicator alone, AUC of Hp typing exhibited the highest in CAG group, which were 0.515. When testing each indicator alone, AUC of G-17 exhibited the highest in GC group, which were 0.787. All in all, this study showed that the performance of combined detection was better than that of individual detection, with AUCs greater than 0.9 in three groups, even reaching 100 % in GC group. Therefore, these results suggest that PG I, PG II, PGR, and G-17 combined with Hp serotyping may be non-invasive indicators for GC screening and diagnosis, providing a basis for non-invasive diagnostic testing in clinical practice and alleviating the pain of patients. Further research is needed to test this indicator because patients have group or regional differences, or perhaps due to changes in the degree of atrophy itself.

5. Conclusion

Changes in PG I, PG II, PGR, and G-17 levels and Hp serotyping can serve as screening indicators for chronic gastritis and GC, which can reflect relevant status of gastric mucosa to varying degrees. Combined detection of indicators has higher diagnostic performance, which can receive application as an auxiliary diagnostic indicator in addition to gastroscopy biopsy, providing a reference basis for formulation of clinical diagnosis and treatment plans.

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Ethical statement

This work was supported by the ethical committee of the Changshu Traditional Chinese Medicine Hospital and was conducted in accordance with Declaration of Helsinki – Version 2008.

CRediT authorship contribution statement

Fei Wang: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

Declaration of competing interest

All authors declare no conflicts of interest.

References