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Original Article

Diagnostic efficacy of gastrin 17, serum pepsinogen and chromoendoscopy for gastric cancer

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Abstract: Objective: To investigate the diagnostic efficacy of gastrin and serum pepsinogen combined with chromoendoscopy for gastric cancer. Methods: A total of 122 patients with gastric mucosal lesions in our hospital were selected as the study subjects. Among them, 60 patients diagnosed with gastric cancer by pathological diagnosis were placed into the malignant group. Sixty-two patients with benign gastric mucosal lesions were placed into the benign group. During the corresponding period, 60 normal people who came to our hospital for physical examination were placed into the control group. Gastrin 17 (G-17) and serum pepsinogen (PGI and PGII) were detected by ELISA and their expression differences were compared. Gastric cancer in the patients in study group was diagnosed by pigmentation endoscopy (i-scan). The diagnostic efficacy of serum PG, G-17 and i-Scan for gastric cancer were analyzed. Results: The serum levels of PGII and G-17 in the malignant group were the highest, followed by the benign group and then the control group ($P<0.05$). The serum level of PGI in the control group was the highest, followed by the benign group and then the malignant group ($P<0.05$). The diagnostic AUC for gastric cancer was 0.619 in serum PGI, 0.866 in PGII, and 0.694 in G-17. The single diagnosis sensitivity, diagnostic coincidence rate and negative predictive value of serum PGI, PGII, G-17 and i-Scan for gastric cancer were less than those of the combined diagnosis of all of PGI, PGII, G-17 and i-Scan. The diagnostic specificity and positive predictive value of serum PGI were less than those of PGII, G-17, i-Scan, and combined diagnosis of the four indexes. The positive rate of combined detection was higher than that of single detection. Whether serum PGI, PGII, G-17 and i-Scan were used alone or in combination, the positive rate of stage III~IV gastric cancer was higher than that of stage I~II. Conclusion: Serum PG, G-17 and i-Scan have diagnostic value for gastric cancer. The diagnostic performance of combined detection for gastric cancer is higher than that of single diagnosis.

Keywords: Gastrin, serum pepsinogen, magnifying chromoendoscopy, gastric cancer

Introduction

As one of the most common malignant tumors in the digestive system worldwide, gastric cancer has an incidence and mortality that ranks high in malignant tumors [1]. In recent years, with the changes in people's social environment and dietary structure, the incidence of gastric cancer keeps on increasing [2]. Studies have shown that if timely and effective intervention can be performed early in gastric cancer, the patient's 5-year survival rate can be greater than 90%. Nonetheless, once the gastric cancer continues to progress, the 5-year survival rate will drop sharply to less than 15% [3]. Gastric cancer has always been diagnosed by gastroscopy and histopathological biopsy [4]. However, both methods are traumatic, and many patients find these methods difficult to accept [5]. Therefore, finding a diagnosis method that can effectively diagnose early gastric cancer and can be accepted by patients is a problem that needs to be solved in clinical practice.

Serum pepsinogen (PG) belongs to a member of cysteinyl aspartate specific protease. Although it is not active by itself, it can be converted to pepsin when PG is in an acidic environment. Moreover, pepsin is biologically active and is a factor closely related to tumor growth. As the precursor of pepsin, PG is divided into PGI and PGII and the level of PG can reflect the function and morphology of the different parts

of the gastric mucosa [6, 7]. Some studies suggest that when gastric cancer occurs, the production of PGI by gastric mucosa will be reduced. But the production site of PGII is mature adenocytes, whose production and secretion levels are basically unaffected by cancer cells and carcinogenic factors, so there were no significant changes of the level of PGII [8].

Studies have shown that PG levels are differentially expressed in gastric mucosal diseases, which can be used to screen the high-risk groups of gastric cancer and precancerous lesions [9]. Gastrin-17 (G-17) is a polypeptide hormone derived from G cells of the gastrointestinal tract. It has a stimulating effect on the secretion of gastric acid and the nutrition of the gastrointestinal mucosa [10]. In recent years, studies have found that G-17 has a positive effect on the occurrence and development of gastric cancer. Its increased level has a very important impact on the growth of cancer cells [11]. Chromoendoscopy (i-Scan) is a new intelligent staining method that has been gradually promoted in recent years. It can make the color of the lesion more prominent by staining, which is beneficial for visual observation of the mucosa and diagnosis [12]. Although these three methods have been applied in the diagnosis of gastric cancer [13], there are few studies on the combined detection in the early diagnosis of gastric cancer.

Therefore, in order to provide more diagnostic approaches for the diagnosis of early gastric cancer, the diagnostic value of PG, G-17 and i-Scan for early gastric cancer was explored by single and combined detection. The specific operation was as follows.

Materials and methods

General information

A total of 122 patients with gastric mucosal lesions in our hospital were selected as the study subjects of the study group, including 71 male patients and 51 female patients. The average age was (46.45±5.39) years. Among them, 60 patients were diagnosed with gastric cancer by pathological diagnosis were placed into malignant group. Sixty-two patients with benign gastric mucosal lesions were placed into the benign group. During the corresponding period, 60 normal people who came to our hospital for physical examination were placed into the control group. Inclusion and exclusion criteria: Inclusion criteria: patients diagnosed with early gastric cancer by pathological diagnosis in the malignant group, and patients diagnosed with benign gastric mucosal lesions by pathological diagnosis in the benign group. Exclusion criteria: patients with other malignant tumors; patients with severe cardiovascular and cerebrovascular diseases; patients receiving digestive system treatment or taking any medicine in the past month before the study; patients with severe liver or kidney dysfunction; patients with communication impairment or cognitive dysfunction; patients showing no cooperation for treatment. All patients and subjects in the control group and their families agreed to participate in the experiment and signed the informed consent form. This experiment has been approved by the Inner Mongolia Hohhot First Hospital ethics committee.

Experimental reagents and instruments

Serum PG and G-17 were detected by the ELISA method, serum PGI (Cat no. Tw038347), PGII (Cat no. Tw038347) and G-17 (Cat no. Tw039509) ELISA kits were all purchased from Shanghai Tongwei biotechnology co., LTD.

Detection method

Detection of serum PG and G-17: Five ml of venous blood was collected from all subjects in the morning, and was centrifuged at 2000 r/min. After centrifugation, serum PGI, PGII and G17 was detected by ELISA. The detection procedure was carried out in strict accordance with the Elisa kit.

i-Scan detection: i-Scan was conducted on all patients of the study group after the detection of serum PG and G-17. Before i-Scan, all patients were subjected to fasting for 8 hours. The specific detection procedure was: fresh water was used to aspirate the suspicious lesion area first. When the aspiration was finished, the 0.2% indigo carmine solution + 0.5% methylene blue stain were mixed. The suspicious lesion and its surrounding mucosa were sprayed and stained. The surface morphology of the gastric mucosa and changes of microvascular structure after 5 minutes of staining

were observed. Corresponding diagnosis were performed [14]. After the end of the detection, the residual staining solution in the stomach was washed.

Outcome measures

(1) Serum PGI, PGII, and G-17 levels were compared between the 3 groups. (2) Serum PGI, PGII, G17 and i-Scan were compared for the diagnostic value of gastric cancer and early gastric cancer by single or combined diagnosis.

Statistical methods

In this experiment, SPSS 19.0 (Shanghai Yuchuang Network Technology Co., Ltd.) statistical software was used to analyze and process the data. The enumeration data was compared between the groups by χ^2 test. The measurement data was compared between the groups was by independent t test. One-way ANOVA was used for comparison among multiple groups, Bonferroni test was used for the post hoc pairwise comparison. The ROC curve was plotted by Graphpad 6 software and compared between groups by the Medcalc software. The cut-offs indicated by the ROC curve were used to measure the combined diagnosis for gastric cancer. P<0.05 suggested a statistical difference.

Results

General information

There were no significant differences in gender, age, BMI and history of smoking among the 3 groups (P<0.05). The number of helicobacter pylori infections in the benign and malignant groups was significantly higher than that in the control group (P<0.05) (**Table 1**).

Comparison of serum PGI, PGII and G-17 expression in three groups of subjects

The expression levels of serum PGII and G-17 in the malignant group were higher than those in the benign group and in the control group. The expression level of serum PGI was lower than that in the benign group and the control group (P<0.05). The expression levels of PGII and G-17 in the control group were lower than those in the benign group. The expression level of serum PGI was higher than that in the benign group (P<0.05) (**Table 2**; **Figure 1**).

Diagnostic values of serum PGI, PGII and G-17 for gastric cancer

The diagnostic AUC for gastric cancer was 0.619 in serum PGI, 0.866 in PGII, and 0.694 in G-17. The AUC area of serum PGII for gastric cancer diagnosis was greater than that of serum PGI and G-17. The sensitivity of serum PGI and PGII for gastric cancer were higher than that of serum G-17. The diagnostic specificity of serum PGI for gastric cancer was lower than that of serum PGII and G-17 (**Table 3**; **Figures 2**-**4**).

Detection rates of serum PGI, PGII, G-17 and i-Scan for gastric cancer by single and combined diagnosis

The sensitivity, specificity, diagnostic coincidence rate, positive predictive value and negative predictive value of serum PGI for the diagnosis of gastric cancer were 75.00%, 48.39%, 63.11%, 60.00% and 68.09%, respectively. The sensitivity, specificity, diagnostic coincidence rate, positive predictive value and negative predictive value of serum PGII for the diagnosis of gastric cancer were 76.67%, 77.42%, 77.05%, 76.67% and 77.42%, respectively. The sensitivity, specificity, diagnostic coincidence rate, positive predictive value and negative predictive value of serum G-17 for diagnosis of gastric cancer were 63.33%, 79.03%, 71.31%, 74.51%, and 69.01%, respectively. The sensitivity, specificity, diagnostic coincidence rate, positive predictive value and negative predictive value of i-Scan for the diagnosis of gastric cancer were 71.67%, 72.58%, 72.13%, 71.67%, and 72.58%, respectively. The sensitivity, specificity, diagnostic coincidence rate, positive predictive value, and negative predictive value of the combined detection of these four methods for gastric cancer diagnosis were 91.67%, 69.35%, and 80.33%, 74.32% and 89.58%, respectively. The single diagnosis sensitivity, diagnostic coincidence rate and negative predictive value of serum PGI, PGII, G-17 and i-Scan for gastric cancer were less than those of the combined diagnosis. The diagnostic specificity and positive predictive value of serum PGI were less than those of PGII, G-17, i-Scan, and combined diagnosis (**Table 4**).

Table 1. General information table

Project	Malignant group n=60	Benign group n=62	Control group n=60	X^2	P
Gender				0.055	0.973
Male	35 (58.33)	36 (58.06)	36 (60.00)		
Female	25 (41.67)	26 (43.33)	24 (40.00)		
Ages				0.616	0.735
≤46	34 (56.67)	35 (56.45)	35 (58.33)		
>46	26 (43.33)	27 (43.55)	25 (41.67)		
BMI (kg/m^2)				0.048	0.976
≤22	32 (53.33)	33 (53.23)	33 (55.00)		
>22	28 (46.67)	29 (46.77)	27 (45.00)		
Pathological staging					
I~II	45 (75.00)	-	-		
III~IV	15 (25.00)	-	-		
Pathological typing					
Adenosquamous carcinoma	13 (21.67)	-	-		
Squamous cell carcinoma	15 (25.00)	-	-		
Chorionic epithelial carcinoma	17 (28.33)	-	-		
Undifferentiated carcinoma	12 (20.00)	-	-		
Drinking history				0.103	0.950
Yes	41 (68.33)	43 (69.35)	40 (66.67)		
No	19 (31.67)	19 (30.65)	20 (33.33)		
Family history				0.042	0.979
Yes	17 (28.33)	17 (27.42)	16 (26.67)		
No	43 (71.67)	45 (72.58)	44 (73.33)		
Helicobacter pylori Infection				0.001	0.976
Yes	35 (58.33)	36 (58.06)			
No	25 (41.67)	26 (41.94)			
History of smoking				0.039	0.981
Yes	41 (68.33)	42 (67.74)	40 (66.67)		
No	19 (31.67)	20 (32.26)	20 (33.33)		
High salt diet				0.103	0.950
Yes	40 (66.67)	43 (69.35)	41 (68.33)		
No	20 (33.33)	19 (30.65)	19 (31.67)		

Table 2. Comparison of serum PGI, PGII and G-17 expression in three groups of subjects

Project	Malignant group n=60	Benign group n=62	Control group n=60	F	P
PGI (μg/L)	54.31±22.19*,#	70.13±21.95*	113.95±10.19	159	<0.001
PGII (μg/L)	21.06±3.88*,#	16.19±2.33*	13.04±3.15	97.19	<0.001
G-17 (pmol/L)	16.59±9.12*,#	10.35±6.93*	8.98±2.37	22.06	<0.001

Note: * represent the comparison with Control group (P<0.05). # represent the comparison with Benign group (P<0.05).

Comparison of the diagnostic positive rates of serum PGI, PGII, G-17 and i-Scan for different stages of gastric cancer by single and combined diagnosis

In patients with stage I~II gastric cancer, the positive rate of serum PGI was 73.33%, the positive rate of PGII was 75.56%, the positive rate of G-17 was 60.00%, the positive rate of i-Scan was 71.11%, and the positive rate of combined detection was 91.11%. In patients with stage III~IV gastric cancer, the positive rate of serum PGI was 80.00%, the positive rate of PGII was 80.00%, the positive rate of

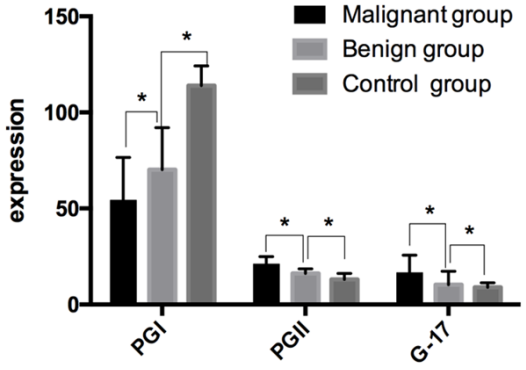

Figure 1. Expression comparison of serum PGI, PGII and G-17 in three groups of subjects. The expression levels of serum PGII and G-17 in the malignant group were higher than that in the benign group and in the control group. The expression level of serum PGI was lower than that in the benign group and the control group (P<0.05). The expression levels of PGII and G-17 in the control group were lower than those in the benign group. The expression level of serum PGI was higher than that in the benign group (P<0.05). Note: * indicates P<0.05.

Table 3. Diagnostic values of serum PGI, PGII and G-17 for early stage of gastric cancer

Diagnostic value	PGI	PGII	G-17
Sensitivity	75.00%	76.67%	63.33%
Specificity	48.39%	77.42%	79.03%
AUC	0.619*	0.866	0.694*
Threshold	66.160	18.180	11.720
P			

Note: * represents the comparison with PGII (P<0.05).

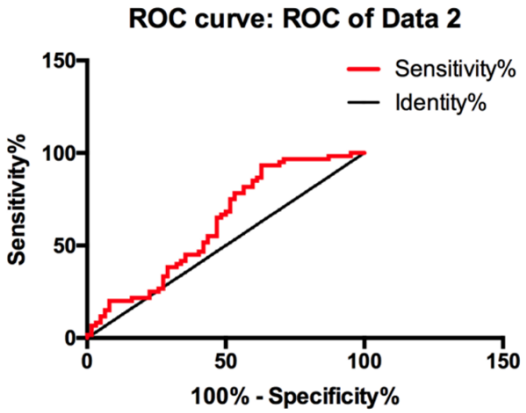

Figure 2. ROC curve of serum PGI for gastric cancer diagnosis. The diagnostic sensitivity, specificity, AUC and diagnostic threshold of serum PGI for gastric cancer were 75.00%, 48.39%, 0.619 and 66.160 μg/L, respectively.

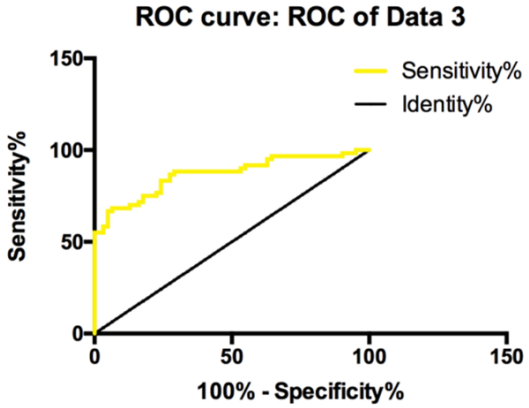

Figure 3. ROC curve of serum PGII for gastric cancer diagnosis. The diagnostic sensitivity, specificity, AUC and diagnostic threshold of serum PGII for gastric cancer were 76.67%, 77.42%, 0.866 and 18.180 μg/L, respectively.

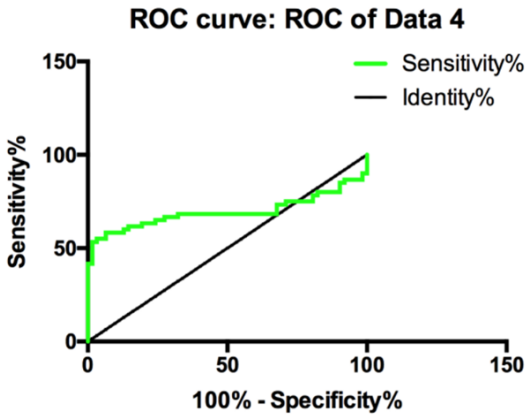

Figure 4. ROC curve of serum G-17 for gastric cancer diagnosis. The diagnostic sensitivity, specificity, AUC and diagnostic threshold of serum G-17 for gastric cancer were 63.33%, 79.03%, 0.694 and 11.720 pmol/L, respectively.

G-17 was 73.33%, the positive rate of i-Scan was 73.33%, and the positive rate of combined detection was 93.33%. The positive rate of combined detection was higher than that of single detection, the detection positive rate of stage III~IV gastric cancer was higher than that of stage I~II gastric cancer (**Table 5**).

Discussions

As a clinically common malignant tumor, gastric cancer has a relatively complicated pathogenesis. Its incidence is caused by various factors such as environmental factors and genetic fac-

Table 4. Diagnostic value of serum PGI, PGII, G-17 and i-Scan for gastric cancer by single and combined detection [n (%)]

Factor	PGI	PGII	G-17	i-Scan	Joint diagnosis
Sensitivity	45 (75.00)*	46 (76.67)*	38 (63.33)*	43 (71.67)*	55 (91.67)
Specificity	30 (48.39)	48 (77.42)	49 (79.03)	45 (72.58)	43 (69.35)
Diagnostic compliance rate	77 (63.11)*	94 (77.05)*	87 (71.31)*	88 (72.13)*	98 (80.33)
Positive predictive value	45 (60.00)	46 (76.67)	38 (74.51)	43 (71.67)	55 (74.32)
Negative predictive value	32 (68.09)*	48 (77.42)*	49 (69.01)*	45 (72.58)*	43 (89.58)

Note: * represents the comparison with joint diagnosis (P<0.05).

Table 5. Positive rates in diagnosis of different stages of gastric cancer by serum PGI, PGII, G-17 and i-Scan alone or in combination [n (%)]

Factor	PGI	PGII	G-17	i-Scan	Combined diagnosis
I~II (n=45)	33 (73.33)*	34 (75.56)*	27 (60.00)*	32 (71.11)*	41 (91.11)
III~IV (n=15)	12 (80.00)*,#	12 (80.00)*,#	11 (73.33)*,#	11 (73.33)*,#	14 (93.33)#

Note: * represents the comparison with joint diagnosis (P<0.05). # represents the comparison with I~II (P<0.05).

tors [15]. The hidden symptoms of gastric cancer in the early stage are often ignored by patients. Once diagnosed, patients are often in the middle or late stages and patients will miss the best treatment opportunity [16, 17]. Therefore, for patients with gastric cancer, early diagnosis and timely treatment are clinically important for improving their survival rate. At present, gastric cancer screening is mainly carried out by gastroscope combined with pathological diagnosis. However, gastroscopy or pathological biopsy is traumatic and poorly tolerated in patients with gastric cancer [18].

In recent years, studies have suggested that precancerous lesions of gastric cancer can be diagnosed by detecting serum PG and G-17 [19]. Other studies have found that i-Scan plays an important role in diagnosing early gastrointestinal tumors. It can increase the contrast between lesion and normal tissues by staining technology, which is more helpful in distinguishing early cancer tissues from normal tissues [20]. Therefore, in order to find a more accurate diagnostic mode for gastric cancer, the diagnostic value of serum PG, G-17 and i-Scan for gastric cancer was analyzed by single and combined diagnosis. First, the results showed that the expression levels of serum PGII and G-17 in the malignant group were higher than those in the benign group and the control group. The expression level of serum PGI was lower than that of the benign group and the control group. Studies have shown that the serum level of PGI shows an increase and a subsequent decrease as the gastric disease progresses, while the serum level of PGII shows a constant increase and maintains a high level [21]. Such levels of PGI and PGII levels make patients with gastric cancer distinguishable from health people. As a polypeptide hormone, G-17 also plays an important role in regulating digestion and maintaining mucosal integration. It is a good biomarker that can better reflect the state of gastric mucosa [22]. Our results also suggest that serum PG and G-17 are differently expressed in normal people, and patients with benign gastric mucosa lesions and malignant lesions. Previous studies [23] found that serum PG and G-17 in 85 serum samples were differently expressed between normal and gastric cancer patients, which was consistent with our conclusions. Through ROC curve analysis, the diagnostic sensitivity, specificity, and diagnostic threshold of serum PG and G-17 for gastric cancer were 66.16 μg/L, 18.18 μg/L and 11.72 pmol/L, respectively. Then the diagnostic value of serum PGI, PGII, G-17 and i-Scan for gastric cancer by single and combined diagnosis were further compared. The single diagnosis sensitivity, diagnostic coincidence rate and negative predictive value of serum PGI, PGII, G-17. This indicates that the combination of serum PG, G-17 and i-Scan can effectively improve the sensitivity of gastric cancer diagnosis. This has high clinical value. There have been no studies on the combined detection of serum PG, G-17 and i-Scan for the gastric can-

cer diagnosis. There were studies [24] indicating that the diagnostic value of combined detection of serum PG and G-17 was higher than that of single diagnosis. There were also studies [25, 26] indicating that the diagnostic value of combined detection of serum PG and i-Scan was also higher than that of the single diagnosis. All of the above studies can verify our conclusions from the side. Finally, in order to further clarify the diagnostic value of PG, G-17 and i-Scan for gastric cancer, the diagnostic positive rates of serum PG, G-17 and i-Scan for different stages of gastric cancer were compared by single and combined diagnosis. The results showed the positive rate of combined detection was higher than that of single detection, and the combined detection had higher detection positive rate for stage III~IV gastric cancer than for stage I~II gastric cancer. It suggests that the diagnostic classification value of combined detection of serum PG, G-17 and i-Scan for gastric cancer will also increase. It boasts great clinical significance for the diagnosis of gastric cancer in the early stage.

In summary, serum PG, G-17 and i-Scan have a certain diagnostic value for gastric cancer and its diagnostic classification. Moreover, the performance of combined detection for gastric cancer is higher than that of single diagnosis. The diagnostic value can be used as an important means to screen early gastric cancer. However, this study has some limitations. For example, we have not carried out correlation analysis on the expression of serum PG and G-17, which will help us to draw accurate conclusions. Due to the insufficient sample number and the lack of dynamic monitoring of the patient's relevant indicators, the conclusion still needs further confirmation. In the follow-up experiments, we will further increase the sample number and monitor the patient's serum indicators more accurately.

Disclosure of conflict of interest

None.

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