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The serum pepsinogen levels for risk assessment of gastric neoplasms

New proposal from a case–control study in Korea

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Abstract

To decrease the gastric cancer related mortality rate, endoscopic screening is widely performed in Korea. However, a precise method for identifying those at a high risk of gastric neoplasms has not been established. This study aims to evaluate serum pepsinogen (PG) levels for risk assessment of gastric neoplasms. Between August 2014 and March 2016, a total of 398 subjects, including 87 with gastric neoplasms, were enrolled in this study. On the basis of the serum PG I/II ratio, the enrolled subjects were classified into 4 groups: group A, PG I/II ratio >4; group B, >3 and ≤4; group C, >2 and ≤3; group D, ≤2. Compared with group A, a stepwise increase in the risk of gastric neoplasm was observed from group B [odds ratio (OR) = 9.9, 95% confidence interval (95% CI) = 4.0–24.4] to group C (OR = 20.9, 95% CI = 8.7–50.5) to group D (OR = 37.3, 95% CI = 14.3–97.4). The optimal cutoff value of the serum PG I/II ratio for predicting gastric neoplasms was 4.5, with a sensitivity of 97.7% and a specificity of 57.6%. A decrease in the serum PG I/II ratio was strongly associated with an increased risk of gastric neoplasms. The serum PG I/II ratio can be used to identify those at a high risk of gastric neoplasms in Korean population.

Abbreviations: CI = confidence interval, *H pylori* = *Helicobacter pylori*, OR = odds ratio, PG = pepsinogen, ROC = receiver operating characteristic, SD = standard deviation.

Keywords: atrophy, gastric neoplasm, *Helicobacter pylori*, pepsinogen, risk

1. Introduction

Gastric cancer is highly prevalent in Asian countries.[1] In Korea, gastric cancer is the most common cancer in males and the fourth most common in females.[2] The age-standardized mortality rate for gastric cancer was 10.5 per 100,000 in 2013, ranking third after lung and liver cancers. In Korea, the National Cancer Screening Program was introduced to decrease the gastric cancer related mortality rate.[3] An upper gastrointestinal series or endoscopy is provided biennially to all populations aged 40 years or older.

Helicobacter pylori has been recognized as a major pathogen in gastric carcinogenesis.[4] In the *H pylori* infected stomach, chronic active inflammation becomes persistent, leading to mucosal atrophy with destruction of gastric glands.[5] Gastric atrophic changes are related to secretion of pepsinogen (PG), a proenzyme of pepsin, by chief and mucous neck cells in the gastric mucosa.[6,7] On the basis of the source of secretion, PGs are subdivided into 2 types: PG I and II. PG I is only secreted from the fundic glands in the corpus of the stomach, whereas PG II is secreted from the corpus, as well as the pyloric glands in the antrum and proximal duodenum. PG is excreted mainly into the stomach lumen, but approximately 1% diffuses into the blood stream.[8] A previous study reported that serum PG was significantly related to extensive chronic gastritis.[9] For this reason, measurement of the serum PG level was introduced in gastric cancer screening programs in Japan.[10]

Atrophic gastritis and intestinal metaplasia are well-known risk factors for gastric neoplasms including dysplasia.[11] To identify these premalignant gastric conditions, histological biopsy or image-enhanced endoscopy is performed. However, a precise method for determining the risk of gastric neoplasms has not been proposed in Korea. Serum PG measurements could provide a simple and noninvasive method for screening gastric neoplasms. In this study, we aimed to evaluate serum PG levels for risk assessment of gastric neoplasms and to determine the optimal cutoff value for mass screening.

2. Methods

2.1. Study population

Between August 2014 and March 2016, subjects were enrolled in a single academic hospital. All subjects underwent gastroscopy for gastric cancer screening or further evaluation of biopsy-proven gastric neoplasms. Exclusion criteria were as follows: age <20 or >80 years, anemia (serum hemoglobin level <10 g/dL), severe systemic disease or advanced chronic liver disease, a history of *H pylori* eradication or gastric surgery, and recent use

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of certain medications, including proton pump inhibitors, H_2-receptor blockers, or antibiotics. This study protocol was approved by the institutional review board of our hospital. Written informed consent was obtained from all subjects.

2.2. Evaluation of H pylori infection, gastric atrophy, and intestinal metaplasia

Two gastric biopsies for the rapid urease test (Pronto Dry; Gastrex Sarl, Gilly les Citeaux, France) were performed in the gastric antrum and body (1 sample each). In addition, 2 biopsy specimens were collected for histological examination from the lesser curvature of the gastric antrum and body (1 sample each). These specimens were fixed in 10% formalin and embedded in paraffin wax, and 5 μm sections were stained with hematoxylin and eosin and modified Giemsa. *H pylori* infection was confirmed by a positive result on either the rapid urease test or histological analysis. Using the Kimura–Takemoto classification,[12] gastric atrophy was classified endoscopically as closed (C-1, C-2, C-3) or open (O-1, O-2, O-3) type. The degree of gastric atrophy was categorized as mild (C-1, C-2), moderate (C-3, O-1), or severe (O-2, O-3). Intestinal metaplasia was diagnosed on the basis of the biopsy sample by a single expert pathologist.

2.3. Classification of gastric neoplasm risk using serum PG measurements

Before endoscopy, blood samples were collected during a 12-hour fasting period. Serum PG I and PG II levels were measured using a latex turbidimetric immunoassay (HiSens; HBI, Anyang, Korea), and the PG I/II ratios were calculated. According to the serum PG I/II ratio, the enrolled subjects were divided into 4 groups: group A, PG I/II ratio >4; group B, >3 and ≤4; group C, >2 and ≤3; and group D, ≤2.

2.4. Statistical analysis

Continuous variables were presented as means with standard deviation. Student *t* test or 1-way analysis of variance (ANOVA) was used to compare the continuous variables. When a significant difference was found by 1-way ANOVA, Bonferroni test was performed for post hoc analysis. Categorical variables were presented as sample numbers and proportions. The x^2 test or linear-by-linear association was used to analyze the categorical variables. The risk of gastric neoplasms based on the serum PG I/II ratio was expressed as the odds ratio (OR) with 95% confidence interval (CI). To determine the cutoff value, receiver operating characteristic (ROC) curves and the Youden index were used. *P* values <.05 were considered statistically significant. All statistical analyses were performed using SPSS (version 19.0; SPSS Inc, Chicago, IL).

3. Results

3.1. Characteristics of the study population

Table 1 summarizes the baseline characteristics of the study population. A total of 398 subjects (170 males, 228 females) were eligible for this study, and their mean age was 48.2 (±16.6) years. The mean serum PG I and PG II levels and PG I/II ratio were 55.5 (±29.9), 15.0 (±10.4), and 4.6 (±2.4) ng/mL, respectively. The proportion of subjects with *H pylori* infection was 52.5%. Atrophic mucosal changes were not observed in the stomach of 184 subjects (46.2%). The remaining 214 subjects had a mild (16.6%), moderate (19.3%), or severe (17.8%) degree of gastric atrophy. Intestinal metaplasia was present in 135 subjects (33.9%) and absent in 263 subjects (66.1%).

A total of 87 subjects with gastric neoplasms, comprising low-grade dysplasia (n=19), high-grade dysplasia (n=16), early gastric cancer (n=40), and advanced gastric cancer (n=12), were enrolled in this study. The characteristics of the subjects with gastric neoplasms and those without neoplasms (n=311) were compared; significant differences in age and proportion of males were found ($P<.001$). Among the serological markers evaluated, the PG I level was not significantly different between the 2 groups (57.0 ± 28.2 vs 50.2 ± 34.8 ng/mL, $P=.099$). However, significant differences were found in the serum PG II level (13.7 ± 10.1 vs 19.5 ± 10.2 ng/mL, $P<.001$) and PG I/II ratio (5.2 ± 2.4 vs 2.5 ± 1.2, $P<.001$). The rate of *H pylori* infection was higher in the subjects with neoplasms than in those without neoplasms (75.9% vs 46.0%, $P<.001$). There were significant differences in the

Table 1

Baseline characteristics of the study population according to the presence of gastric neoplasms.

Study subjects	Total (n=398)	Without neoplasms (n=311)	With neoplasms (n=87)	$P^{*,\dagger}$
Age, y, mean (SD)	48.2 (16.6)	43.4 (14.6)	65.5 (11.3)	<.001
Male (%)	170 (42.7)	115 (37.0)	55 (63.2)	<.001
Serum PG, mean (SD)				
PG I, ng/mL	55.5 (29.9)	57.0 (28.2)	50.2 (34.8)	.099
PG II, ng/mL	15.0 (10.4)	13.7 (10.1)	19.5 (10.2)	<.001
PG I/II ratio	4.6 (2.4)	5.2 (2.4)	2.5 (1.2)	<.001
H pylori infection (%)	209 (52.5)	143 (46.0)	66 (75.9)	<.001
Gastric atrophy (%)				<.001
None	184 (46.2)	184 (59.2)	0	
Mild	66 (16.6)	60 (19.3)	6 (6.9)	
Moderate	77 (19.3)	39 (12.5)	38 (43.7)	
Severe	71 (17.8)	28 (9.0)	43 (49.4)	
Intestinal metaplasia (%)				<.001
Present	135 (33.9)	59 (19.0)	76 (87.4)	
Absent	263 (66.1)	252 (81.0)	11 (12.6)	

H pylori=*Helicobacter pylori*, PG=pepsinogen, SD=standard deviation.

* The Student *t* test was performed for comparisons of age and serum PG levels between the groups with and without neoplasm.

† The x^2test or linear-by-linear association was performed for comparisons of sex, *H pylori* infection, gastric atrophy, and intestinal metaplasia between the groups with and without neoplasm.

Table 2

Characteristics of the subjects according to the serum pepsinogen I/II ratio.

Risk group	Group A (n = 198)	Group B (n = 79)	Group C (n = 76)	Group D (n = 45)	P*,†
Age, y, mean (SD)	38.8 (13.2)	52.5 (14.8)	57.1 (12.7)	67.3 (10.8)	<.001
Male (%)	69 (34.8)	38 (48.1)	36 (47.4)	27 (60.0)	.001
Serum PG, mean (SD)					<.001
PG I, ng/mL	54.5 (23.7)	70.8 (35.5)	62.3 (26.4)	21.3 (20.2)	
PG II, ng/mL	8.9 (5.3)	19.9 (9.9)	24.3 (10.1)	17.2 (11.7)	
PG I/II ratio	6.6 (1.7)	3.6 (0.3)	2.6 (0.3)	1.1 (0.5)	
H pylori infection (%)	40 (20.2)	70 (88.6)	71 (93.4)	28 (62.2)	<.001
Gastric atrophy (%)					<.001
None	167 (84.3)	15 (19.0)	2 (2.6)	0	
Mild	20 (10.1)	26 (32.9)	17 (22.4)	3 (6.7)	
Moderate	10 (5.1)	32 (40.5)	29 (38.2)	6 (13.3)	
Severe	1 (0.5)	6 (7.6)	28 (36.8)	36 (80.0)	
Intestinal metaplasia (%)					<.001
Present	12 (6.1)	41 (51.9)	46 (60.5)	36 (80.0)	
Absent	186 (93.9)	38 (48.1)	30 (39.5)	9 (20.0)	

H pylori = *Helicobacter pylori*, PG = pepsinogen, SD = standard deviation.

Group A, serum PGI/II ratio >4; Group B, serum PGI/II ratio >3 and ≤4; Group C, serum PGI/II ratio >2 and ≤3; Group D, serum PGI/II ratio ≤2.

* One-way analysis of variance was performed for comparisons of age and serum PG levels among the 4 groups.

† Linear-by-linear association was performed for comparisons of sex, *H pylori* infection, gastric atrophy, and intestinal metaplasia among the 4 groups.

degree of gastric atrophy and intestinal metaplasia between the 2 groups ($P < .001$).

3.2. Characteristics of the subjects according to serum PG I/II ratio

According to the serum PG I/II ratio, 198 (49.7%) subjects were categorized as group A, 79 (19.8%) as group B, 76 (19.1%) as group C, and 45 (11.3%) as group D. In Table 2, the baseline characteristics of the 4 groups were compared. The mean age of the subjects was 38.8 (±13.2) years in group A, 52.5 (±14.8) years in group B, 57.1 (±12.7) years in group C, and 67.3 (±10.8) years in group D ($P < .001$). The proportion of males was significantly different among all groups ($P = .001$). The rate of *H pylori* infection was significantly higher ($P < .001$) in groups B, C, and D (88.6%, 93.4%, and 62.2%, respectively) than in group A (20.2%). The degree of gastric atrophy was significantly different among all groups ($P < .001$). Groups C and D had a higher proportion of subjects with moderate to severe gastric atrophy than groups A and B. Significant differences in the presence of intestinal metaplasia were also found among the groups ($P < .001$).

3.3. Serum PG I and II levels according to serum PG I/II ratio

Serum PG I levels were 54.5 (±23.7) ng/mL in group A, 70.8 (±35.5) ng/mL in group B, and 62.3 (±26.4) ng/mL in group C (Fig. 1). Group B had a significantly higher serum PG I level versus group A ($P < .001$). In group D, the serum PG I level was 21.3 ± 20.2 ng/mL, which was significantly lower than those of groups A, B, and C ($P < .001$). The serum PG II level was 8.9 ± 5.3 ng/mL in group A, 19.9 (±9.9) ng/mL in group B, 24.3 (±10.1) ng/mL in group C, and 17.2 (±11.7) ng/mL in group D (Fig. 2). The serum PG II level was significantly higher in groups B, C, and D than in group A ($P < .001$) and in group C

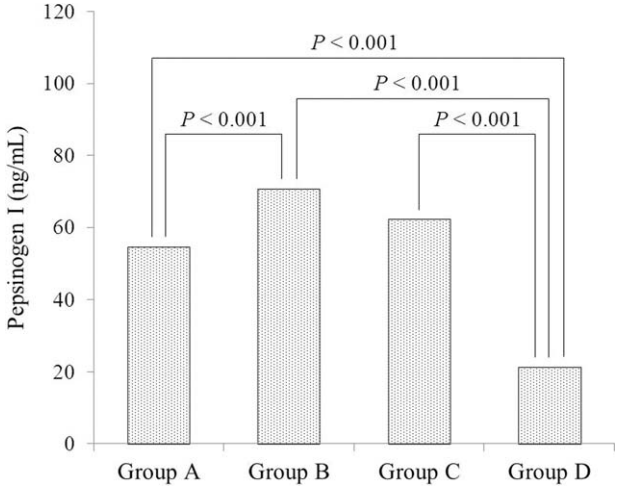

Figure 1. Relationship between the serum PG I level and serum PG I/II ratio. Bonferroni test was performed for comparisons of the PG I levels among the 4 groups. PG = pepsinogen.

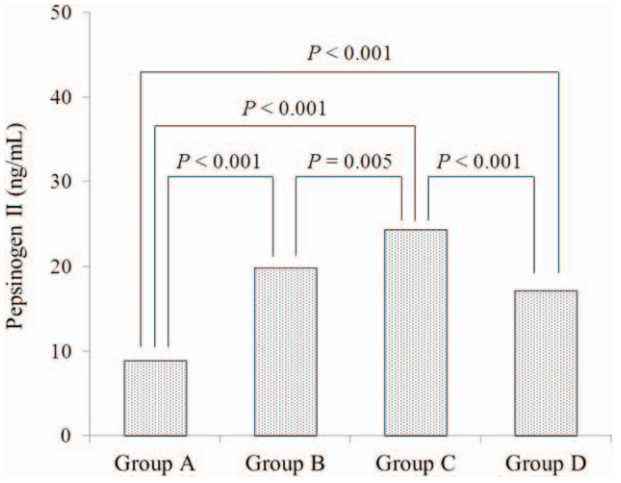

Figure 2. Relationship between the serum PG II level and serum PG I/II ratio. Bonferroni test was performed for comparisons of the PG II levels among the 4 groups. PG = pepsinogen.

Table 3

Risk assessment of gastric neoplasms according to the serum pepsinogen I/II ratio.

Risk group	Neoplasms (%)	Odds ratio*	95% CI	P
Group A (n=198)	7 (3.5)	Reference		
Group B (n=79)	21 (26.6)	9.879	3.999–24.408	<.001
Group C (n=76)	33 (43.4)	20.940	8.684–50.491	<.001
Group D (n=45)	26 (57.8)	37.338	14.317–97.375	<.001

Group A, serum PGI/II ratio >4; Group B, serum PGI/II ratio >3 and ≤4; Group C, serum PGI/II ratio >2 and ≤3; Group D, serum PGI/II ratio ≤2.
CI=confidence interval.
* Odds ratios were analyzed by logistic regression models.

compared with groups B and D ($P=.005$ and $P<.001$, respectively).

3.4. Risk assessment of gastric neoplasms according to serum PG I/II ratio

Table 3 summarizes the risk of gastric neoplasms in subjects grouped by serum PG I/II ratio. Gastric neoplasms were detected in 3.5% (n=7/198) of those in group A, 26.6% (n=21/79) in group B, 43.4% (n=33/76) in group C, and 57.8% (n=26/45) in group D. Compared with group A, significantly higher risks of gastric neoplasm were seen in group B (OR)=9.879; 95% CI=3.999–24.408, $P<.001$) and group C (OR=20.940; 95% CI=8.684–50.491, $P<.001$), with the highest risk observed in group D (OR=37.338; 95% CI=14.317–97.375, $P<.001$).

3.5. Optimal cutoff value of the serum PG I/II ratio for predicting gastric neoplasms

A ROC curve for the serum PG I/II ratio, used to predict gastric neoplasms, is shown in Fig. 3. The area under the curve was 0.840 (CI=0.800–0.881). The optimal cutoff value for the serum PG I/II ratio was 4.5. The sensitivity, specificity, and positive and negative predictive values were 97.7% (CI=91.5–99.6), 57.6% (CI=55.8–58.1), 39.2% (CI=36.7–39.9), and 98.9% (CI=95.9–99.8), respectively.

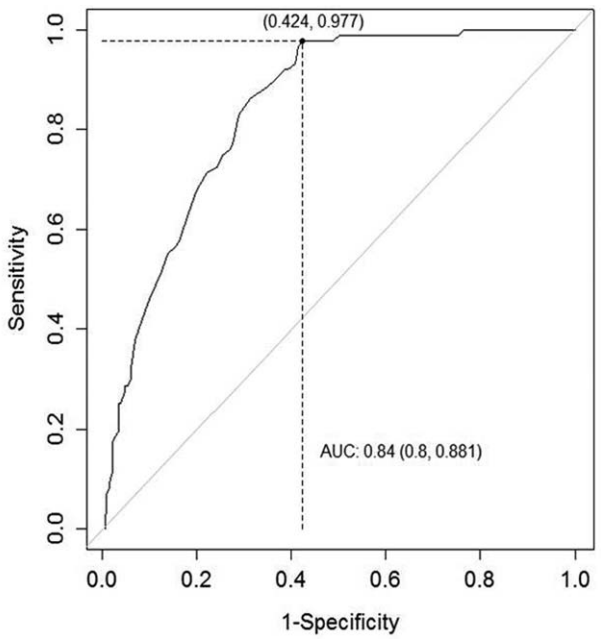

Figure 3. Receiver operating characteristic curve of the serum PG I/II ratio for the prediction of gastric neoplasms. The optimal cutoff value was 4.5, derived from the Youden index. The area under the curve was 0.840 (CI=0.800–0.881). CI=confidence interval.

4. Discussion

Serum PG levels differed according to the gastric mucosal histology, providing a so-called serological biopsy.[7] In mild to moderate gastritis, both the PG I and II levels are increased by *H pylori* induced stimulation of the gastric glands.[13] With a prominent increase in the PG II level, the PG I/II ratio decreases. When gastric atrophy progresses to a severe stage, chief cells in the corpus are replaced by pyloric gland cells, leading to a decreased level of PG I. Consequently, a further decrease in the PG I/II ratio is observed.

Miki et al[14] reported that the serum PG I level and PG I/II ratio were significantly lower in patients with gastric cancer than in cancer-free subjects. The serum PG level was considered low when the PG I level was ≤70 ng/mL and the PG I/II ratio was ≤3. When these cutoff values were used for the detection of gastric cancer, the sensitivity and specificity were 84.6% and 73.5%, respectively.[15] In a cohort study, mass screening for gastric cancer was performed using both serum PG measurements and X-ray methods; 23.6% of those screened by serum PG measurements, and 11.7% screened by X-ray, required further endoscopic screening.[16] In total, 10 gastric cancers were detected. The measurement of serum PG showed a higher rate of gastric cancer detection (0.18%) than the X-ray method (0.05%).

In addition to the serum PG level, the serum level of anti-*H pylori* IgG antibody was considered a predictive marker for the development of gastric cancer.[17] Gastric cancer screening has been performed using a combination of serum PG levels and the *H pylori* antibody status. In 1 study, the risk of gastric cancer was divided into the following 4 groups: normal PG level and negative *H pylori* antibody status, normal PG level and positive *H pylori* antibody status, low PG level and positive *H pylori* antibody status, and low PG level and negative *H pylori* antibody status. The group with a low PG level and negative *H pylori* antibody status showed the highest hazard ratio for gastric cancer (8.2, 95% CI=3.2–21.5).[18]

In Korea, the participation rate in gastric cancer screening programs has increased, and the proportion of screeners preferring endoscopy has increased gradually from 2002 to 2011.[19] Biennial endoscopic screening can lead to earlier detection of gastric cancer.[20] A shorter endoscopic surveillance interval is recommended for high-risk populations with atrophic gastritis or intestinal metaplasia.[21] However, a precise method to stratify gastric cancer risk has not been determined.[22] For the diagnosis of atrophic gastritis and intestinal metaplasia, a histological analysis of gastric mucosa is considered the gold standard. The operative links for gastritis and gastric intestinal metaplasia assessment

staging systems were proposed recently.[23,24] However, the use of multiple biopsy specimens can be time-consuming. With regard to atrophic gastritis, low interobserver agreement among pathologists remains.[25] Recently, image-enhanced endoscopy systems showed high accuracy for the diagnosis of premalignant gastric conditions.[26–28] However, these systems are not available in all endoscopy units, and their diagnostic accuracy may be operator-dependent. In contrast, the measurement of serum PG levels is a simple and noninvasive test for detecting gastric diseases.[29] Thus, the serum PG level can be considered a surrogate marker for the mass screening of gastric cancer.

Few studies have used serum PG measurements and/or the *H pylori* antibody status to predict gastric neoplasms in Korea. Kang et al[30] reported that the sensitivity and specificity of a low PG I/II ratio (≤3) for detecting gastric cancer were 59.2% and 61%, respectively. A low PG I level (≤70 ng/mL) had an adequate sensitivity (72.4%) but a low specificity (20.2%). In a study by Choi et al,[31] the risk of gastric neoplasms was evaluated by combination of the serum PG level and anti-*H pylori* IgG antibody status. Patients with a low PG level and negative *H pylori* antibody status had the highest OR (25.8, 95% CI= 2.26–294.77) for gastric neoplasms. However, the number of subjects in this group was quite small (0.7%, n=24/3328), including only 1 subject with low-grade dysplasia. For gastric neoplasm screening, Park et al[32] proposed using a cutoff serum PG I/II ratio ≤3.1 with negative *H pylori* antibody status, and ≤4.1 with positive *H pylori* antibody status. However, 27.5% (n=50/182) of the patients with gastric neoplasms were not categorized in the high-risk group.

In our study, the serum PG I level and *H pylori* antibody status were not used for the assessment of gastric neoplasm risk. Haj-Sheykholeslami et al[33] reported that the serum PG I level was not a suitable marker for atrophic gastritis screening among first-degree relatives of patients with gastric cancer. In a study by Kim et al,[34] a serum PG I level ≤70 ng/mL in combination with a low PG I/II ratio had a low sensitivity for predicting histologically confirmed atrophic gastritis (22.7% in the antrum and 42.1% in the corpus). Previously, those with a low PG level and negative *H pylori* antibody status were considered to be at the highest risk of gastric cancer. However, the proportion of such subjects in previous studies was small (2.4–4.1%).[35–37] Recently, no significant difference in the cumulative incidence of gastric cancer was found among subjects with low PG levels, regardless of the *H pylori* antibody status.[38–40] Subjects with low PG levels are often categorized into the same group.[41] Therefore, we divided the risk of gastric neoplasms into 4 groups according to the serum PG I/II ratio alone.

This study demonstrated that a decrease in the serum PG I/II ratio was significantly associated with a high risk of gastric neoplasms. The risk of gastric neoplasm increased in a stepwise manner from groups A to D. A serum PG I/II ratio ≤4.5 showed an excellent negative predictive value (98.9%), but a low positive predictive value (39.2%), for predicting gastric neoplasms in our study. However, measurement of serum PG levels is not a diagnostic method for gastric neoplasm itself, but rather a screening tool for those at a high risk of gastric neoplasms. In subjects with low PG I/II ratios, endoscopic examination is needed to confirm the presence of gastric neoplasms. Of the gastric neoplasm-free subjects with a PG I/II ratio ≤4.5, 87.1% (n=115/132) had a current *H pylori* infection. In another study, the diagnostic accuracy of the PG I/II ratio for *H pylori* induced gastritis, using the same cutoff value, was >80%.[42] This suggests that a serum PG I/II ratio ≤4.5 may be adequate for identifying candidates for primary prevention of gastric cancer. According to the Asia-Pacific guidelines for the management of *H pylori* infection,[43] eradication therapy for gastric cancer prevention is strongly recommended in countries with a high incidence of gastric cancer. In 2013, the Japanese government approved the coverage by national health insurance of eradication therapy for all *H pylori* infected populations.[44] Although the "test and treat" strategy for *H pylori* infection has not been introduced in Korea, *H pylori* eradication for gastric cancer prevention may be permitted in the near future.

In addition, we examined the relationship between serum PG I and II levels and the serum PG I/II ratio. Notably, the serum PG I level was lowest in group D, compared with the other 3 groups, suggesting that a prominent decrease occurred when gastric atrophy was severe. With regard to the serum PG II level, a significant increase was consistently seen in groups B, C, and D compared with group A. There was no linear correlation between serum PG I, II levels and gastric atrophy. In contrast, the serum PG I/II ratio was inversely associated with the severity of gastric atrophy and intestinal metaplasia, in a stepwise manner. These results were consistent with those of other studies. Kiyohira et al[45] reported that a decrease in the serum PG I level was affected by marked atrophy and intestinal metaplasia. In *H pylori* induced active and chronic inflammation, the serum PG II level was increased significantly. When serum PG measurements and the *H pylori* antibody status were both assessed for gastric cancer screening, the changes in serum PG I and II levels according to risk group were similar to our results.[17,18,46]

Herein, gastric dysplasia was included when the risk assessment and cutoff value for gastric neoplasm were calculated. Previous studies reported that gastric dysplasia might involve foci of malignant adenocarcinoma. In a study by Kato et al,[47] 44% of biopsy-proven gastric dysplasia cases were upgraded to adenocarcinoma by the postresection pathology. Moreover, a synchronous cancer in another part of the stomach was found in up to 30% of patients with gastric dysplasia.[48] For the management of gastric dysplasia, endoscopic resection has been accepted as a good therapeutic option.[49] Therefore, in surveillance programs for gastric cancer, gastric dysplasia must be treated in high-risk groups.

This study had several limitations. First, gastric atrophy was not assessed histologically. However, histological examination of gastric atrophy is well-correlated with endoscopic findings according to the Kimura–Takemoto classification.[50] Second, this study was conducted at a single center. The number of enrolled subjects may be insufficient for determining an accurate serum PG level to predict gastric neoplasms. Third, the serum *H pylori* antibody status was not evaluated. Fourth, the risks of gastric neoplasms were not presented as hazard ratios in this case–control study. A large-scale cohort study is needed to determine the incidence rate of gastric neoplasms.

In conclusion, a decrease in the serum PG I/II ratio was strongly associated with an increased risk of gastric neoplasms, in a stepwise manner. The serum PG I/II ratio can be used to identify those at a high risk of gastric neoplasms in mass screenings. A serum PG I/II ratio ≤4.5 was found to be a reliable marker for predicting gastric neoplasms among the Korean population.

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