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【 ORIGINAL ARTICLE 】

Usefulness and Limitations of a Serum Screening System to Predict the Risk of Gastric Cancer

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Abstract:

Objective The aim of the present study was to evaluate the effectiveness and limitations of a serum screening system for predicting the risk of gastric cancer.

Methods Serum pepsinogen I (PG I)/pepsinogen II (PG II) and *Helicobacter pylori* (HP) antibody levels were measured. Subjects were classified into four groups according to their serological status (the ABC classification system). The grade of atrophic gastritis was assessed endoscopically. We evaluated gastric cancer detection rates according to the ABC classification system and the endoscopic grade of atrophy.

Patients Individuals who underwent esophagogastroduodenoscopy (EGD) in a health check were prospectively enrolled in the present study.

Results According to the ABC classification system, the gastric cancer detection rates in groups A, B, C, and D were 0.07% (4/6,105), 0.5% (8/1,739), 0.8% (16/2,010), and 1.1% (3/281), respectively. The gastric cancer detection rates in subjects with no atrophy, closed type (C-type) atrophy, and open type (O-type) atrophy were 0% (0/4,567), 0.2% (4/2,581), and 0.9% (27/2,987), respectively. In group A (HP(-)/PG(-)), the proportions of subjects with no atrophy, C-type atrophy, and O-type atrophy were 71.2%, 22.8%, and 6.0%, respectively. In group A, the gastric cancer detection rates in subjects with no atrophy, C-type atrophy, and O-type atrophy were 0%, 0.07%, and 0.8%, respectively.

Conclusion The ABC classification system is useful for predicting the risk of gastric cancer. However, this system was limited in group A, which included individuals with a high risk of developing gastric cancer. An endoscopic diagnosis of atrophy may be more effective than the ABC classification system for predicting the risk of gastric cancer.

Key words: stomach neoplasms, *Helicobacter pylori*, pepsinogens, gastritis, atrophic, serological risk prediction system

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Introduction

Stomach cancer is the second leading cause of cancer death in both sexes worldwide (738,000 deaths, 9.7% of all deaths from cancer) (1). Thus, a simple and effective screening system needs to be developed for gastric cancer.

Correa et al. proposed that intestinal-type gastric cancer develops in association with intestinal metaplasia in patients with severe atrophic gastritis (2). A follow-up study by Uemura et al. showed that gastric cancer only developed in patients infected with *Helicobacter pylori* (HP) (3). The findings of these studies suggest that HP infection and HP-induced atrophic gastritis play important roles in the development of gastric cancer. The serum pepsinogen (PG) levels reflect the status of gastric mucosal inflammation and serve as a marker of atrophic gastritis (4-10). Miki et al. developed a serum screening system (the ABC classification sys-

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tem) that evaluates the serum anti-HP antibody titer and serum PG levels (11), which are known to reflect the status of gastric inflammation, including corpus atrophy. Ohata et al. reported that gastric cancer was not detected in their HP(-)/PG(-) group during a study period of 10 years (12). Previous studies have demonstrated that the ABC classification system was effective for evaluating the individual risk of gastric cancer (13, 14); thus, this stratification is expected to serve as a mass screening system for this disease.

However, Kudo et al. reported that 11% of consecutive patients with gastric cancer were classified into the HP(-)/PG(-) group (15), and Boda et al. showed that approximately 10% of patients with gastric tumors (cancer or adenoma) were classified as HP(-)/PG(-) (16). Moreover, a previous 4.7-year prospective study revealed that gastric cancer was detected in 7 of 3,324 subjects in the HP(-)/PG(-) group (13). These findings suggest that the HP(-)/PG(-) group includes patients with a high risk of developing gastric cancer. However, the evidence on the relationship between the ABC classification system and the grade of atrophic gastritis remains insufficient.

We therefore evaluated the gastric cancer detection rates and grades of endoscopic atrophy according to the ABC classification system, and interpreted its efficacy and limitations, with a focus on the HP(-)/ PG(-) group, which is expected to include individuals with a low risk of developing gastric cancer.

Material and Methods

Patients

A total of 11,781 individuals (male, n=6,646; female, n=5,135) who underwent esophagogastroduodenoscopy (EGD) in a health check at Saku Central Hospital between June 2010 and May 2011 were prospectively enrolled in this study. We questioned all subjects about their history of HP eradication, previous medical history, medication, and comorbidities. Patients who underwent gastrectomy, had a history of peptic ulcer disease, gastric cancer, HP eradication or renal failure, or who used proton pump inhibitors (PPI), which influences PG levels, were excluded from the study. All eligible patients provided their written informed consent. The study protocol was approved by the Institutional Review Board. This trial was also registered with the UMIN Clinical Trials Registry (clinical trial registration number: UMIN 000003677).

Serological tests and the definition of the ABC classification system

Anti-HP antibody levels and serum PG I/PG II were measured. The serum anti-HP antibody levels were measured using a commercial enzyme-linked immunosorbent assay (ELISA) kit (E-plate EIKEN *H. pylori*, Eiken Chemica, Tokyo, Japan).

Serum PG was measured using a commercial chemiluminescent enzyme immunoassay (CLEIA) kit (Lumipulse Presto pepsinogen I/II kit; Fujirebio, Tokyo, Japan). HP infection positivity was defined based on an anti-HP antibody titer of ≥10 U/mL. The serum PG status was defined as positive when the serum PG I level was ≤70 ng/mL and the PG I/PG II ratio was ≤3.0.

We divided subjects into the following 4 groups according to their serological status: group A, HP(-)/PG(-); group B, HP(+)/PG(-); group C, HP(+)/PG(+); and group D, HP(-)/PG(+).

Endoscopy and the grade of atrophic gastritis

EGD was performed by endoscopists who had experienced ≥500 cases. They were not informed of the ABC classification. The grade of atrophic gastritis was assessed endoscopically according to the Kimura-Takemoto classification (17). This classification divides the extent of atrophy into closed-type (C-type) atrophy and open type (O-type) atrophy. C-type atrophy indicates that the atrophic border remains on the lesser curvature of the stomach, while O-type atrophy means that the atrophic border no longer exists on the lesser curvature, but extends along the anterior and posterior walls of the stomach.

EGD was performed using a zoom video endoscope (GIF-H260Z or GIF-Q240Z; Olympus Medical Systems, Tokyo, Japan) and an endoscopic video imaging system (EVIS LUCERA CV-260 SL; Olympus Medical Systems).

Statistical analysis

Age, PG I and PG II concentrations, and PG I/II ratios are shown as the mean±standard deviation. The gastric cancer detection rates were statistically analyzed with an adequate sample size using a chi-squared test. P values of <0.05 were considered to indicate statistical significance. All statistical analyses were performed using EZR (Saitama Medical Center, Jichi Medical University, Saitama, Japan), which is a graphical user interface for R (The R Foundation for Statistical Computing, Vienna, Austria). More precisely, it is a modified version of R commander designed to add statistical functions frequently used in biostatistics.

Sub-analysis

In 2016, the Japan Research Foundation Prediction, Diagnosis and Therapy for Gastric Cancer advocated the "new ABC classification" using two parameters: 1) HP serology (regarded as positive when the antibody titer is ≥3 U/mL); and 2) conventional criteria of a pepsinogen test (defined as positive when both PGI≤70 ng/mL and PG I/II ratio ≤3.0 are fulfilled). This classification is now widely used in Japan. Based on these new criteria, we evaluated the gastric cancer detection rates and the grades of atrophic gastritis in each group.

Table 1. Sex and Age Distribution of the Subjects.

All patients (n=10,135)	80 years of age or older n=209 (2.1%)	70 to 79 years old n=1,208 (11.9%)	60 to 69 years old n=2,981 (29.4%)	50 to 59 years old n=3,339 (33.0%)	40 to 49 years old n=1,802 (17.8%)	30 to 39 years old n=582 (5.7%)	20 to 29 years old n=14 (0.1%)
Male (n=5,536)	137	683	1,564	1,741	1,038	367	6
Female (n=4,599)	72	525	1,417	1,598	764	215	8

Table 2. Characteristics of Subgroups Classified according to the Serum Pepsinogen and *Helicobacter pylori* Antibody Status (The ABC Classification System).

	Total	Group A	Group B	Group C	Group D
Pepsinogen status		negative	negative	positive	Positive
HP antibody status		negative	positive	positive	Negative
No. of subjects	10,135	6,105 (60.2%)	1,739 (17.2%)	2,010 (19.8%)	281 (2.8%)
Male	5,536	3,313	993	1,073	157
Female	4,599	2,792	746	937	124
Age (y) [mean (SD)]	57.0 (11.0)	55.0 (11.0)	59.0 (10.0)	62.0 (10.0)	65.0 (11.2)
Pepsinogen I [mean (SD)]	53.7 (37.8)	51.5 (38.6)	80.6 (40.4)	41.2 (17.7)	25.5 (17.7)
Pepsinogen II [mean (SD)]	15.4 (11.2)	9.8 (5.8)	27.0 (15.0)	22.5 (8.2)	14.0 (7.0)
Pepsinogen I/II [mean (SD)]	4.2 (1.8)	5.3 (1.1)	3.4 (1.2)	1.9 (0.7)	1.8 (0.9)
Grade of endoscopic atrophy					
None	4,567	4,347 (71.2%)	147 (8.5%)	35 (1.7%)	38 (13.5%)
Closed type	2,581	1,394 (22.8%)	760 (43.7%)	380 (18.9%)	47 (16.7%)
Open type	2,987	364 (6.0%)	832 (47.8%)	1,595 (79.4%)	196 (69.8%)

Values for age, PG I and PG II concentrations, and PG I/II ratios are shown as means±standard deviation (SD). *HP antibody status was defined as being positive when the anti-HP antibody titer was 10 U/mL or more. The serum PG status was defined as being positive when the criteria of serum PG I ≤70 ng/mL and PG I/PG II ratio ≤3.0 were simultaneously fulfilled. HP: *Helicobacter pylor*i

Results

Patient characteristics

A total of 10,135 individuals (male, n=5,536; female, n=4,599) were analyzed. The baseline clinical characteristics and the distribution of sex and age of the study population are summarized in Tables 1 and 2. According to the ABC classification system, the majority of patients were classified into group A (60.2%). A total of 28.8% [(1,394+364)/6,105] of the patients in group A had endoscopic atrophy. On the other hand, patients without endoscopic atrophy accounted for 5.5% [(147+35+38)/(1,739+2,010+281)] of the subjects other in groups B, C, and D.

The proportion of patients with endoscopic atrophy according to age in group A are shown in Table 3. For all ages, 6.0% of the subjects in group A had open-type atrophy, and the rate increased with age. The rates of HP antibody-positivity according to age are shown in Table 4. The rate was the highest (51.8%) among patients of 70-79 years of age.

Gastric cancer detection rates according to the ABC classification system and endoscopic grade of atrophy

The gastric cancer detection rates according to the ABC classification system are shown in Table 5A. Based on the ABC classification system, the gastric cancer detection rates in groups A, B, C, and D were 0.07% (4/6,105), 0.5% (8/1,739), 0.8% (16/2,010), and 1.1% (3/281), respectively. (p=0.001 for group A vs. B, p=0.28 for group B vs. C, p=0.397 for group B vs. D) The detection rates increased with the progression of the ABC classification from B to D.

The gastric cancer detection rates according to the endoscopic grade of atrophy are shown in Table 5B. The gastric cancer detection rates in those with no atrophy, C-type atrophy, and O-type atrophy were 0% (0/4,567), 0.2% (4/2,581), and 0.9% (27/2,987), respectively. (p=0.032 for no atrophy vs. C-type, p=0.0004 for C-type vs. O-type).

Characteristics of patients with gastric cancer according to the ABC classification system and the endoscopic grade of atrophy

Table 5A shows a summary of subjects with gastric cancer according to the ABC classification system. Gastric cancer was detected in 31 subjects. Four of 31 subjects (13%)

Table 3. The Proportions of Endoscopic Atrophy in Group A according to Age.

	All ages (n=6,105)	80 years of age or older (n=92)	70 to 79 years old (n=511)	60 to 69 years old (n=1,549)	50 to 59 years old (n=2,077)	40 to 49 years old (n=1,374)	30 to 39 years old (n=489)	20 to 29 years old (n=13)
None	4,347 (71.2%)	35 (38.1%)	257 (50.3%)	1,042 (67.3%)	1,532 (73.8%)	1,063 (77.4%)	409 (83.6%)	9 (69.2%)
Closed	1,394 (22.8%)	21 (22.8%)	150 (29.3%)	376 (24.3%)	473 (22.7%)	293 (21.3%)	77 (15.8%)	4 (30.8%)
Open	364 (6.0%)	36 (39.1%)	104 (20.4%)	131 (8.4%)	72 (3.5%)	18 (1.3%)	3 (0.6%)	0 (0%)

Table 4. The Rates of HP Antibody-positive Subjects according to Age.

	All patients (n=10,135)	80 years of age or older (n=209)	70 to 79 years old (n=1,208)	60 to 69 years old (n=2,981)	50 to 59 years old (n=3,339)	40 to 49 years old (n=1,802)	30 to 39 years old (n=582)	20 to 29 years old (n=14)
HP (+)	3,749 (37.0%)	90 (43.1%)	626 (51.8%)	1,321 (44.3%)	1,218 (36.5%)	410 (22.8%)	83 (14.3%)	1 (7.1%)

*HP antibody status was defined as being positive when the anti-HP antibody titer was 10 U/mL or more. HP: *Helicobacter pylori*

Table 5. Characteristics of Patients with Gastric Cancer according to the ABC Classification System and Grade of Endoscopic Atrophy.

A

The ABC classification system		All patients (10,135)	Group A (6,105)	Group B (1,739)	Group C (2,010)	Group D (281)
No. of patients with GC (detection rate: %)		31 (0.3)	4 (0.07)	8 (0.5)	16 (0.8)	3 (1.1)
Age (y)	Median (range)	69 (37-83)	75.5 (75-82)	62.5 (40-73)	69.5 (59-83)	66 (37-83)
Sex	Male/Female	23/8	2/2	6/2	12/4	3/0
Location	U/M/L	4/15/12	1/1/2	1/4/3	2/8/6	0/2/1
Differentiation	Well diff/poor diff	26/5	4/0	5/3	15/1	2/1
Grade of endoscopic atrophy	None/closed/Open	0/4/27	0/1/3	0/1/7	0/2/14	0/0/3

B

Grade of endoscopic atrophy		All patients (10,135)	None (4,567)	Closed type (2,581)	Open type (2,987)
No. of patients with GC (detection rate: %)		31 (0.3)	0 (0)	4 (0.2)	27 (0.9)
Age (y)	Median (range)	69 (37-83)	-	66.5 (59-75)	69 (37-83)
Sex	Male/Female	23/8	-	1/3	22/5
Location	U/M/L	4/15/12	-	0/1/3	4/14/9
Differentiation	Well diff/poor diff	26/5	-	3/1	23/4
ABC classification system	Group A/B/C/D	4/8/16/3	-	1/1/2/0	3/7/14/3

GC: gastric cancer, U, M, L: upper, middle or lower third of the stomach, Well diff: well or moderately differentiated adenocarcinoma, poor diff: poorly differentiated adenocarcinoma or signet ring cell carcinoma

with gastric cancer belonged to group A, while 3 of 4 (75%) of the patients in group A had O-type atrophy. Based on the results of histological examinations, differentiated-type cancer was the most frequently diagnosed type of cancer. Table 5B shows a summary of the subjects with gastric cancer according to the endoscopic grade of atrophy; the numbers of subjects with gastric cancer in the groups with no atrophy, C-type atrophy, and O-type atrophy were 0, 4, and 27, respectively.

Relationship between the ABC classification system and the endoscopic grade of atrophy in the detection of gastric cancer

The relationship between the ABC classification system and endoscopic grade of atrophy in the detection of gastric cancer is shown in Figure. The gastric cancer detection rates among subjects with O-type atrophy in groups A, B, C, and D were 0.8% (3/364), 0.8% (7/832), 0.9% (14/1,595), and 1.5% (3/196), respectively (p=0.731 for group A with O-type atrophy vs. group D with O-type atrophy).

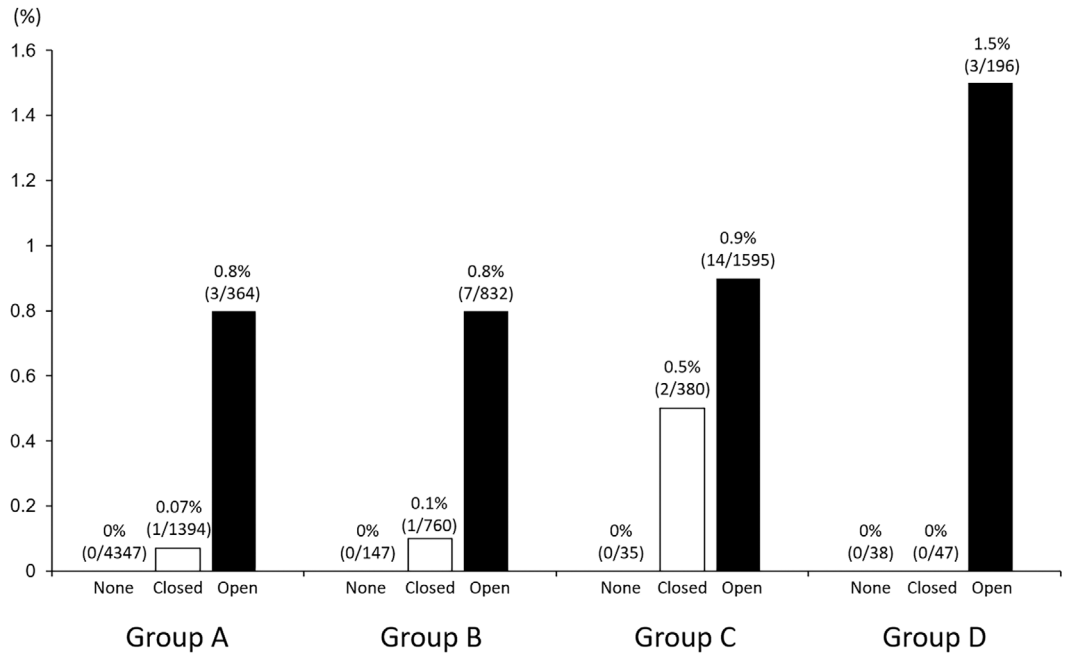

Figure. **Relationship between the ABC classification and the endoscopic grade of atrophy in relation to the detection rate of gastric cancer. None: no atrophy, Closed: closed-type atrophy, Open: open-type atrophy**

Table 6. **Summary of 4 Patients with Gastric Cancer in Group A.**

	Case 1	Case 2	Case 3	Case 4
Age (y)	75	75	82	76
Sex	Female	Female	Male	Male
Previous EGD	3 years ago	1 year ago	1 year ago	1 year ago
Macroscopic type	Depressed	Protruding	Depressed	Depressed
Size (mm)	11×8	11×10	26×13	16×13
Location	L	M	L	U
Invasion depth	M	SM2	SM2	SM2
Histological type	Well diff	Well diff	Well diff	Well diff
Anti-HP antibody titer	3.9	4.7	0.7	2.1
PG I level (ng/mL)	32.1	88.6	67	26.2
PG II level (ng/mL)	6.8	15.8	14.7	8.3
PG I/II ratio	4.7	5.6	4.6	3.2
Grade of AG	Closed	Open	Open	Open
Treatment	ESD	Surgical operation	ESD and surgical operation	ESD and surgical operation

EGD: esophagogastroduodenoscopy, HP: *Helicobacter pylori*, PG: pepsinogen, AG: atrophic gastritis, U, M, L: upper, middle or lower third of the stomach, Well diff: well or moderately differentiated adenocarcinoma, ESD: endoscopic submucosal dissection.

Summary of 4 patients with gastric cancer in group A

Four subjects were diagnosed with gastric cancer in group A; all were older ≥75 years of age. Although they had undergone EGD 1 or 3 years previously, neoplastic lesions had not been detected (Table 6). All lesions were treated with endoscopic submucosal dissection (ESD) or surgery. In all cases, the histological type was differentiated adenocarcinoma. The invasion depth was SM2 in three of the four patients.

Sub-analysis

Based on the new criteria, there were 2 patients with gastric cancer in group A (0.04%: 2/5,553). A total of 24.6% [(1,182+186)/5,553)] of the patients in group A had endoscopic atrophy. On the other hand, patients without endoscopic atrophy accounted for 8.3% [(310+39+33)/(2,291+2,187+104)] of the subjects in groups B, C, and D (Table 7).

Discussion

The present study identified two important clinical issues:

Table 7. Characteristics of Subgroups Classified according to the Serum Pepsinogen and *Helicobacter pylori* Antibody Status (The New Criteria of the ABC Classification System*).

	Total	Group A	Group B	Group C	Group D
Pepsinogen status		negative	negative	positive	Positive
HP antibody status		negative	positive	positive	Negative
No. of subjects	10,135	5,553 (54.8%)	2,291 (22.6%)	2,187 (21.6%)	104 (1.0%)
Male	5,536	3,014	1,293	1,179	50
Female	4,599	2,539	998	1,008	54
Age (y) [mean (SD)]	57.0 (11.0)	54.6 (10.7)	59.3 (10.4)	62.4 (9.8)	64.4 (11.6)
Pepsinogen I [mean (SD)]	53.7 (37.8)	51.5 (39.4)	73.7 (40.1)	40.1 (18.1)	23.0 (17.7)
Pepsinogen II [mean (SD)]	15.4 (11.2)	9.6 (5.4)	23.4 (15.2)	21.9 (8.4)	11.9 (6.2)
Pepsinogen I/II [mean (SD)]	4.2 (1.8)	5.4 (1.1)	3.7 (1.3)	1.9 (0.7)	1.8 (1.1)
Grade of endoscopic atrophy					
None	4,567	4,185 (75.4%)	310 (13.5%)	39 (1.8%)	33 (31.7%)
Closed type	2,581	1,182 (21.3%)	972 (42.4%)	416 (19.0%)	11 (10.6%)
Open type	2,987	186 (3.3%)	1,009 (44.1%)	1,732 (79.2%)	60 (57.7%)
No. of patients with GC (Detection rate: %)	31 (0.3)	2 (0.04)	10 (0.4)	18 (0.8)	1 (1.0)

Values for age, PG I and PG II concentrations, and PG I/II ratios are shown as means±standard deviation (SD). *HP antibody status was defined as being positive when the anti-HP antibody titer was 3 U/mL or more. The serum PG status was defined as being positive when the criteria of serum PG I ≤70 ng/mL and PG I/PG II ratio ≤3.0 were simultaneously fulfilled. HP: *Helicobacter pylori*

group A (HP(-)/PG(-)) included patients with a high risk of developing gastric cancer (open-type atrophy), and gastric cancer was not detected in subjects without endoscopic atrophy.

The gastric cancer detection rate in group A was very low (0.07%: 4/6,105) and increased with the progression of the ABC classification from B to D (p=0.001 for group A vs. B). These results suggest that the ABC classification system is useful for predicting the risk of gastric cancer.

On the other hand, the present study identified some limitations of the ABC classification system, with the most important being that the proportion of gastric cancer patients in group A was not low (13%: 4/31), even though it was predicted to be negligible in this group. In addition, 60.2% of all subjects belonged to this group. While group A was regarded as being HP-negative, 28.8% of the patients in this group had endoscopic gastric atrophy in the present study. Moreover, all 4 patients with gastric cancer in group A had endoscopic atrophy. These results suggest that group A included patients with a high risk of developing gastric cancer in spite of careful medical interviews, and also that group A cannot be regarded as being truly HP-negative. This is a crucial issue associated with applying the ABC system to a cancer mass screening program. Previous studies have also highlighted this issue (18-20).

In the present study, as shown in Tables 3 and 4, the rate of HP antibody-positive subjects and open-type atrophy was high in the elderly. Moreover, all 4 patients with gastric cancer in group A were older than 75 years of age. These results suggest that elderly people should undergo EGD rather than serum screening.

Although all 4 patients with gastric cancer in group A had undergone EGD 1 or 3 years previously, the depth of invasion in three out of four patients was SM2. This result suggests that the detection of early gastric cancers is sometimes difficult, and that patients at high risk of developing gastric cancer (open-type atrophy) should undergo EGD once every year.

In group A, there were two groups other than the HP true-negative group: an anti-HP antibody false-negative group (current infection) and a natural or accidental eradication group (previous infection).

Kiso et al. reported that 93.6% of group A patients with gastric cancer showed positive results on another HP test (histological examination, urea breath test, rapid urease test, anti-HP antibody in urine, stool antigen test, or microbial culture test) or had atrophic gastritis (18). Furthermore, up to 20% of subjects with an anti-HP IgG antibody titer that was lower than but close to the cut-off level of the E-plate kit had a previous or current infection (19). When the anti-HP IgG antibody level was measured using an E-plate kit with a cut-off value of 10 U/mL, sensitivity and specificity were 91.2 and 97.4%, respectively (21). We need to consider the limitations of the E-plate kit. A previous study suggested that subjects with anti-HP antibody titers of 3-9.9 should be considered to be a high-risk group (22). In a sub-analysis (Table 7), the number of patients with gastric cancer in group A decreased from 4 to 2. However, the number of patients in group A decreased from 6,105 (60.2%) to 5,553 (54.8%), suggesting that 45.2% (4,582/10,135) of all of the subjects in our study population required endoscopy. Moreover, 24.6% of the patients in group A still had endoscopic gastric atrophy (closed-type, 21.3%; open-type, 3.3%).

Patients with previous HP infection may not be detected

using a standard interview. Thus, there may have been some patients with previous HP infection in group A. An endoscopic or radiological evaluation of atrophic gastritis is currently considered to be an effective approach for identifying these subjects.

Gastric cancer was not detected in subjects without endoscopic atrophy and detection rates increased with the progression of the grade of atrophy. These results suggest that the endoscopic grade of atrophy is an accurate predictive marker for gastric cancer. The combination of serum anti-HP antibody levels and EGD is regarded as an ideal method for evaluating the risk of gastric cancer. However, it is inefficient to perform EGD for all patients from the viewpoint of the associated cost and manpower of endoscopists. Itoh et al. reported a strong correlation between the ABC classification and radiological findings in relation to the risk of gastric cancer (22). We consider the use of the ABC classification system in combination with a radiological evaluation of atrophic gastritis to represent an effective solution to the limitation of the ABC classification system.

The ABC classification system is ineffective for identifying gastric cancer among individuals without HP infection. Kiso et al. reported that all cases of gastric cancer in the HP uninfected group were classified as the undifferentiated type (18). Fundic gland-type cancer was recently reported to be a representative feature of gastric cancer in patients without HP infection (23). Although the development of gastric cancer in patients without HP infection is extremely rare in Japan (24), we need to inform patients of the limitation of the ABC classification system. Furthermore, since EGD is needed to detect these cancers, the establishment of the optimal timing for the performance of EGD is a future challenge.

The present study was associated with some limitations. This was a cross-sectional study. A prospective cohort study should be performed to evaluate the actual risk of gastric cancer according to the ABC classification system. Furthermore, the diagnosis of endoscopic atrophy may differ to some extent among endoscopists.

In conclusion, the ABC classification system was useful for predicting the risk of gastric cancer. However, one of its limitations is that group A may include some individuals who have a high risk of developing gastric cancer. Gastric cancer was not detected in subjects without endoscopic atrophy and the detection rates increased with the progression of the grade of atrophy. An endoscopic diagnosis of atrophy may be more effective than the ABC classification system for predicting the risk of gastric cancer.

The authors state that they have no Conflict of Interest (COI).

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