ABC screening for gastric cancer is not applicable in a Japanese population with high prevalence of atrophic gastritis

Tadashi Shimoyama · Masahiko Aoki ·
Yoshihiro Sasaki · Masashi Matsuzaka ·
Shigeyuki Nakaji · Shinsaku Fukuda

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Abstract A combination of the detection of serum anti-*Helicobacter pylori* antibody and measurement of the level of serum pepsinogens (PG)s, known as the ABC method, has been used in screening for gastric cancer. The ABC method has been shown to be useful in urban and/or younger populations. The aim of this study was to assess whether this method is applicable for an agricultural population with a high incidence of gastric cancer. In all, 1048 healthy adults (401 men and 647 women) who participated in a mass survey in April 2005 were examined. Their serum samples were tested to determine the prevalence of anti-*H. pylori* antibody, and the levels of PG I and PG II were also measured to assess the presence of atrophic gastritis. Of the elderly subjects born before 1940, 59.4% were classified into groups C and D, with a high risk for gastric cancer, and only 22.7% were classified into group A, with the lowest risk. Of the middle-aged subjects born in the 1940s and the 1950s, 66.5% were classified into groups B–D. If the ABC method is performed in the mass screening for gastric cancer in this population, a large number of subjects will be identified for further examinations. The applicability of the

ABC method should be evaluated before use in the screening for gastric cancer, particularly in an aging population with a high prevalence of *H. pylori* infection and atrophic gastritis.

Keywords Gastric cancer · ABC method · *Helicobacter pylori* · Atrophic gastritis · Pepsinogen

Introduction

The incidence rate of gastric cancer in Japan is the highest of that in developed countries [1]. To decrease the mortality caused by gastric cancer, mass screening for gastric cancer has been performed in Japan. Gastric cancer screening using barium radiography reduces the mortality from gastric cancer and is the most common screening method in Japan [2]. However, barium radiography is not convenient and it is associated with radiation exposure and adverse effects from barium ingestion. Recent studies have focused on designing easier tests to enable a large number of subjects to undergo gastric cancer screening. Such screening tests would also be useful in many countries with a high incidence of gastric cancer where barium radiography screening is not available.

Atrophic gastritis is a condition well known to be associated with gastric cancer [3]. Human pepsinogens (PGs) are proenzymes that act on pepsin; these proenzymes are secreted by the gastric mucosa and are classified as PG I or PG II. The levels of serum PGs reflect the status of the gastric mucosa and thus serve as markers of atrophic gastritis. In Japan, the measurement of serum PG I and PG II levels has been introduced in the screening for gastric cancer [4], and it was found to be useful in a population-based cohort study [5]. Infection with *Helicobacter pylori*

T. Shimoyama (✉) · Y. Sasaki · S. Fukuda
Department of Gastroenterology, Hirosaki University Graduate
School of Medicine, 5 Zaifu-cho, Hirosaki 036-8562, Japan
e-mail: tsimo-hki@umin.ac.jp

M. Aoki
Department of Radiology, Hirosaki University Graduate School
of Medicine, Hirosaki, Japan

M. Matsuzaka · S. Nakaji
Department of Social Medicine, Hirosaki University Graduate
School of Medicine, Hirosaki, Japan

has also been associated with the development of gastric cancer [6]. A combination of the measurement of serum PG levels and detection of the anti-*H. pylori* antibody—known as the ABC method—was initially proposed to assess the degree of health of the stomach [7]. Several studies have shown the usefulness of this method for the assessment of the risk of gastric cancer in urban and younger Japanese populations [8, 9]. The incidence of gastric cancer is higher in the agricultural areas of north Japan. However, to date, the ABC method has not been used for gastric cancer screening in such areas. It is necessary to examine whether the ABC method can adequately identify the subjects who should receive further examinations.

In this study, to evaluate the results of classification by the ABC method, we measured the levels of serum anti-*H. pylori* antibody and PG I and II in a public health survey in an agricultural population of north Japan with a high incidence of gastric cancer.

Subjects, materials, and methods

Among healthy adults who participated in a mass survey in the Iwaki area of Hirosaki City in April 2005, 1048 subjects (401 men and 647 women) who were born before 1980 participated in the study. Serum samples were obtained and stored at -20°C and were tested for the prevalence of the IgG antibody to *H. pylori* by enzyme immunoassay with an E-plate (Eiken, Tokyo, Japan), which uses antigens from the Japanese *H. pylori* strain [10]. The levels of PG I and PG II were also measured, by radioimmunoassay. The result was considered indicative of atrophic gastritis when both a PG I level of $<70\text{ }\mu\text{g/L}$ and a PG I/II ratio of <3.0 were obtained [4]. The subjects were divided into the following 4 groups according to the presence of atrophic gastritis identified by serum PGs and *H. pylori* seropositivity. Group A comprised the subjects whose results were negative for both anti-*H. pylori* antibody and atrophic gastritis. Group B comprised subjects whose results were seropositive for *H. pylori* but negative for atrophic gastritis. Group C comprised subjects whose results were positive for both anti-*H. pylori* antibody and atrophic gastritis. Group D comprised subjects with atrophic gastritis and anti-*H. pylori* antibody levels lower than the cut-off value. All the subjects provided their written informed consent, and this study was approved by the ethics committee of Hirosaki University.

Results

The prevalence of serum anti-*H. pylori* antibody is shown in Table 1. The prevalence of the antibody increased with

age, and nearly 70% of the subjects born before 1950 were seropositive. However, seropositivity was observed in only 21.3% of the subjects born in the 1970s. The proportion of the subjects who were defined to have atrophic gastritis also increased along with age (Table 1). Approximately 60% of the 374 subjects born before 1940 and more than 40% of the 472 subjects born in the 1940s and the 1950s had atrophic gastritis. In contrast, atrophic gastritis was rarely observed in the subjects born in the 1970s.

The results of the classification by the ABC method are shown in Fig. 1. The proportion of the subjects classified into group C or D (higher risk for gastric cancer) increased with age. Of the elderly subjects born before 1940, 59.4% were classified into group C or D and only 22.7% were classified into group A (the lowest risk for gastric cancer). Of the middle-aged subjects born in the 1940s and the 1950s, 66.5% were classified into groups B–D. Overall, regarding the subjects who were more than 40 years old who were covered by public gastric cancer screening, the proportions of subjects in groups B, C, and D were 31.9,

Table 1 Prevalence of serum antibody to *Helicobacter pylori* and atrophic gastritis

Birth year	N (male/female)	<i>H. pylori</i> antibody (%)	Atrophic gastritis (%)
1920s	81 (37/44)	69.1	71.6
1930s	293 (103/190)	70.6	56.0
1940s	268 (93/175)	66.8	44.0
1950s	204 (82/122)	59.8	39.7
1960s	127 (57/70)	46.5	22.8
1970s	75 (29/46)	21.3	4.0
Total	1048	60.9	43.2

Fig. 1 Classification of the subjects by a combination of the detection of serum anti-*Helicobacter pylori* antibody and measurement of the level of serum pepsinogens (PG)s: ABC method

42.1, and 4.1%, respectively. Therefore, if the ABC method is performed in the mass screening for gastric cancer in this population, a large number of subjects will be identified as needing to undergo upper gastrointestinal endoscopy.

Discussion

In Japan, persons older than 40 years are able to receive public gastric cancer screening. Generally, 55–60% of subjects 50s and 45–50% of those 60s were found to be in the lowest risk group for gastric cancer by the ABC method. In the present study, however, in a population with a high incidence of gastric cancer, 70% of the subjects born before 1960 and 45% of the subjects born in the 1960s were classified into groups B–D, who may require further examinations. Therefore, at present, the ABC method is not applicable in the screening for gastric cancer in similar populations, because a large number of subjects would be identified for further examinations.

A factor contributing to the results of the present study was the high *H. pylori* seropositivity in the population studied. In a previous study that examined the risk of gastric cancer by the ABC method in an urban population with a lower incidence of gastric cancer, only 30.6, 15.4, and 0.7% of the subjects were classified into groups B, C, and D, respectively [8]. *H. pylori* seropositivity in the population in that study was similar to that in our younger subjects born in the 1960s. Because the prevalence of *H. pylori* infection was higher in our elderly subjects, the proportion of the subjects who were deemed to require further examination was higher in our study.

The prevalence of atrophic gastritis was also remarkably high in the present study. Previous studies have also examined the risk of gastric cancer by the ABC method in populations with high *H. pylori* seropositivity. Ohata et al. [9] examined 4655 male subjects born between 1935 and 1955 and classified 0.7 and 28.3% of them into groups D and C, respectively. In the present study, of the subjects born during the same period, 3.5% were classified into group D and 43.9% were classified into group C. Mizuno et al. [11] examined 2895 subjects who were born before 1952 in a population in western Japan. In that population, there was an *H. pylori* seropositivity of 77%, and 2.4 and 36.8% of the subjects were classified into groups D and C, respectively. In the present study, among subjects who were born before 1952, 4.6 and 45.3% were classified into groups D and C, respectively. These results suggest that, compared to the results reported by Mizuno et al. [11], atrophic gastritis was more frequent in our population, although the rate of *H. pylori* seropositivity was similar. The most probable cause of the difference in the frequency

of atrophic gastritis was the difference in subjects' ages at the time of assessment. In the study by Mizuno et al. [11], the subjects were assessed in 1987, while we assessed our subjects in 2005. Therefore our subjects were assessed at a higher age. Atrophic gastritis usually develops after a long period of *H. pylori* infection. Therefore, if subjects infected with *H. pylori* are examined at an older age, the prevalence of atrophic gastritis could be higher, resulting in higher proportions in groups C and D. The age of the subjects should be considered before the ABC method is used in the screening for gastric cancer, particularly in populations with a high prevalence of *H. pylori* infection.

The ABC method was originally proposed to assess the degree of health of the stomach [7]. Although the present results suggest that the ABC method would not be useful for gastric cancer screening in some populations, they indicate that the subjects classified into group A were at a low risk of gastric cancer. Indeed, in the present study, 21.9% of the subjects born before 1970 were classified into group A and considered to have healthy stomachs. Thus, the ABC method would be applicable in determining which subjects do not require gastric cancer screening in populations with a high incidence of gastric cancer.

In conclusion, the applicability of the ABC method should be evaluated before its use as a screening method for gastric cancer in populations with a high incidence of *H. pylori* infection and atrophic gastritis, such as the population in the agricultural area of north Japan. Although the ABC method could be a possible screening method for gastric cancer in other countries, this limitation should be recognized.

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