

[EDITORIAL]

The Clinical Benefits, Limitations, and Perspectives of the ABC Method

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Key words: gastric cancer, *Helicobacter pylori*, pepsinogens, cancer screening, ABC method, atrophic gastritis

(Intern Med 59: 1471-1472, 2020)

(DOI: 10.2169/internalmedicine.4450-20)

In Japan, over 99% of gastric cancer cases are associated with *Helicobacter pylori* infection (1). Because the grade of *H. pylori*-induced gastric atrophy correlates with gastric cancer development (2) and the serum pepsinogen (PG) levels reflect gastric mucosal atrophy, the combination of the PG test and the evaluation of the *H. pylori* antibody titer, a serological screening approach called the “ABC method” or “ABC classification,” efficiently and inexpensively stratifies the risk of gastric cancer in patients without a history of eradication (3).

The ABC method classifies patients into group A [*H. pylori*(-), PG(-)], *H. pylori*-negative; group B [*H. pylori*(+), PG (-)], *H. pylori* infection without extensive chronic atrophic gastritis (CAG); group C [*H. pylori*(+), PG(+)], *H. pylori*-induced extensive CAG; and group D [*H. pylori*(-), PG(+)], spontaneous disappearance of *H. pylori* due to severe CAG. This method can detect serologically negative but *H. pylori*-infected patients (group D) and thus is more accurate than *H. pylori* serology alone. Group B, C and D include candidates for endoscopy (3), and the cancer detection rate of the ABC method is 0.22%-0.42%, which is higher than historical data obtained by conventional X-ray mass screening (0.15%) (4). In the present report, the clinical benefits, limitations, and perspectives of the ABC method are discussed.

Few high-risk cases with gastric atrophy and gastric cancer are misclassified into group A, which is the “false group A problem” and regarded as the greatest weakness of the ABC method (5). Most of these patients have “past infection-induced atrophic gastritis” after normalization of PG and *H. pylori* serology caused by unintentional eradication through the incidental use of antibiotics (6). To avoid this misclassification, the cut-off value of the *H. pylori* antibody titer is set at a low value. In 2015, the Ministry of Health, Labor, and Welfare recommended population-based radiographic and endoscopic screenings for gastric cancer;

however, the ABC method was not recommended because of the lack of direct evidence of mortality reduction. The high rate of patients for whom endoscopy is indicated (more than that in group B) is the other weakness of the ABC method, which requires improvement in the future.

In this issue of *Internal Medicine*, Kishino et al. reported that about 6.0% (364/6,105) of group A patients showed open-type gastric atrophy. The detection rates of gastric cancer 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. No gastric cancer was recognized among endoscopically normal cases (0/4,567); they therefore suggested that an evaluation by endoscopy is superior to the serological screening method (7).

Is the ABC method a relic of gastric cancer screening? No, it has clinical significance, and whether or not the mortality rate decreases when using this screening method should be determined. The benefits of the ABC method are its cost effectiveness and high sensitivity rate. As Kishino et al. reported, its sensitivity for detecting gastric cancer was 87% (27/31) (7), which is better than the rate of the immunological fecal occult blood test (65.8%) (8). Henceforth, the rate of gastric cancer is expected to significantly decrease because the infection rate of *H. pylori* has decreased (9). Intensive detection and monitoring of *H. pylori*-positive cases is effective, and the ABC method will become more useful, especially in populations with low *H. pylori* infection rates.

In addition, the ABC method can be used in various clinical settings, especially in east Asian countries in the following instances: 1) to detect high-risk cases if its limitations are recognized, and 2) to determine the *H. pylori* infection status and risk of future gastric cancer development for patients who refuse endoscopy or have undergone endoscopy. Furthermore, it motivates patients to undergo endoscopy, en-

ables the potential eradication of *H. pylori* in positive cases, and provides information on the appropriate frequency of endoscopy in each case. Considering the decreasing infection rate of *H. pylori* and consequent decreasing incidence of gastric cancer in Japan, the clinical significance of the ABC method may become more important in the future.

The author states that he has no Conflict of Interest (COI).

References

1. Matsuo T, Ito M, Takata S, Tanaka S, Yoshihara M, Chayama K. Low prevalence of *Helicobacter pylori*-negative gastric cancer among Japanese. *Helicobacter* **16**: 415-419, 2011.
2. Correa P. Human gastric carcinogenesis: a multistep and multifactorial process-First American Cancer Society Award Lecture on Cancer Epidemiology and Prevention. *Cancer Res* **52**: 6735-6740, 1992.
3. Miki K. Gastric cancer screening by combined assay for serum anti-*Helicobacter pylori* IgG antibody and serum pepsinogen levels - "ABC method". *Proc Jpn Acad Ser B Phys Biol Sci* **87**: 405-414, 2011.
4. Yamaguchi Y, Nagata Y, Hiratsuka R, et al. Gastric cancer screening by combined assay for serum anti-*Helicobacter pylori* IgG antibody and serum pepsinogen levels-the ABC method. *Digestion* **93**: 13-18, 2016.
5. Kishikawa H, Kimura K, Ito A, et al. Cutoff pepsinogen level for predicting unintentionally eradicated cases of *Helicobacter pylori* infection in subjects with seemingly normal pepsinogen levels. *Digestion* **95**: 229-236, 2017.
6. Kishikawa H, Ojima K, Nakamura K, et al. Previous *Helicobacter pylori* infection-induced atrophic gastritis: a distinct disease entity in an understudied population without a history of eradication. *Helicobacter* **25**: e12669, 2020.
7. Kishino T, Oyama T, Tomori A, et al. Usefulness and limitations of a serum screening system to predict the risk of gastric cancer. *Intern Med* **59**: 1473-1480, 2020.
8. Morikawa T, Kato J, Yamaji Y, et al. A comparison of the immunochemical fecal occult blood test and total colonoscopy in the asymptomatic population. *Gastroenterology* **129**: 422-428, 2005.
9. Mizota Y, Yamamoto S. How long should we continue gastric cancer screening? From an epidemiological point of view. *Gastric Cancer* **22**: 456-462, 2019.

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