EDITORIAL

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Is your endoscopist qualified enough to detect *Helicobacter pylori*-naive status?

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See "Clinicopathological and endoscopic features of *Helicobacter pylori* infection-negative gastric cancer in Japan: a retrospective study" by Kentaro Imamura, Kenshi Yao, Satoshi Nimura, et al. Clin Endosc 2024;57:486–494.

National cancer screening programs enable detecting gastric cancers in asymptomatic people.[1] Nonetheless, diagnosing *Helicobacter pylori*-negative gastric cancers (HPNGCs) is still a challenge in endemic areas of *H. pylori* infection because most of noninfected gastric cancer patients have past infection.[2] In other words, unintended eradication is not rare in endemic areas. Therefore, to diagnose HPNGCs, endoscopists should know how to discriminate *H. pylori*-naive individuals among noninfected gastric cancer patients, even in the absence of a definite eradication history.

In this issue of *Clinical Endoscopy*, Imamura et al.[3] published clinicopathological and endoscopic features of HPNGCs. *H. pylori*-negative status was defined when the following three criteria were satisfied. First, there is no history of eradication. Second, there is no endoscopic finding that suggests *H. pylori* infection. Third, at least two *H. pylori* tests among the *H. pylori* serology test, stool antigen test, urea breath test, culture, rapid urease test, and microscopic findings are negative. In this way, 54 HPNGCs (2.6%) were detected among the 2,112 gastric cancers resected between 2013 and 2021.

Main strength of this study is that HPNGCs are well described according to their location and endoscopic findings. In the distal stomach, signet-ring cell carcinomas and well-differentiated adenocarcinomas were dominant, whereas fundic-gland type and foveolar-type adenocarcinomas were dominant in the proximal stomach. Furthermore, HPNGCs arising from autoimmune gastritis and gastrointestinal polyposis syndrome were mainly located in the proximal stomach. With regard to macroscopic appearance of HPNGCs, the elevated type was most common (61.5%) because most HPNGCs originated from the fundic gland area. Conversely, flat and depressed types were mainly located in the distal part, which lacks the fundic gland. Unfortunately, the authors could not show statistically significant evidence owing to the lack of controls.

In the study by Imamura et al.,[3] three (5.6%) HPNGC patients showed intestinal metaplasia in the background mucosa. Although the authors described that bile reflux might have led to development of intestinal metaplasia, there is still a possibility of unintended eradication because all three cases were well-differentiated adenocarcinomas located in the antrum. Another drawback of the study is the low prediction rate (53%) of magnifying narrow band imaging (M-NBI) for diagnosing HPNGCs. M-NBI findings were not useful for fundic-gland type adenocarcinomas because the cancers were located in the subepithelium. The role of M-NBI was also limited for undif-

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ferentiated-type HPNGCs because some were covered with noncancerous epithelium. Despite these limitations, the authors precisely analyzed 54 cases of HPNGCs, which is comparable to the number of 63 HPNGCs in a recent multicenter study.[4] In that multicenter study, HPNGCs were less invasive (98.4% detected in early stage), smaller (median size of 4.0 mm), and more frequently located in the proximal stomach than *H. pylori*-related gastric cancers.

H. pylori-naive status is rapidly increasing in young Koreans born since 1970[5]; nevertheless, there is no consensus or training program for the diagnosis of *H. pylori*-naive status and HPNGCs. Thus, prior to gastric cancer screening, training is expected to discriminate *H. pylori*-naive individuals from those with current or past infection.[6] To achieve this, a learning program on diagnosing types of gastritis is required alongside the program on the interpretation of serum pepsinogen (PG) assay findings.[7] In Koreans, gastric corpus atrophy determined by the GastroPanel test (PG I <30 μg/L or PG I <50 μg/L and PG I/II <3) is more consistent with advanced corpus atrophy (PG I ≤30 ng/mL and PG I/II ≤2) determined by the ABC method than is corpus atrophy (PG I ≤70 ng/mL and PG I/II ≤3).[8] Altogether, *H. pylori*-naive status can be diagnosed only when gastric atrophy or intestinal metaplasia are absent in serological, endoscopic, and histological findings.[9]

In summary, endoscopists should enhance their ability to identify *H. pylori*-naive status and HPNGCs. Ultimately, international consensus is needed to distinguish true *H. pylori*-naive status among the *H. pylori*-negative individuals. Such efforts will benefit participants with regard to gastric cancer screening in endemic areas of *H. pylori* infection.

Conflicts of Interest

The author has no potential conflicts of interest.

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