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Detection and treatment of early cancer in high-risk populations

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In this paper we describe how to more efficiently detect and treat early gastric cancer (EGC) in high-risk populations. For detection, we first assess the value of known risk factors from the viewpoint of availability for cancer screening. Serum pepsinogen appears to be the most useful and realistic of the factors examined, although its adequacy needs to be assessed in high-risk populations other than those in Japan. *Helicobacter pylori* infection is known to be a universal risk factor (or gastric carcinogen), and several interventional studies have recently shown positive results. However, *H. pylori* infection can be eradicated from at-risk populations, thereby decreasing its availability for cancer screening. Smokers are thought to be at risk epidemiologically, but the efficacy of screening in this population has yet to be elucidated, and further studies are warranted. Gender and aging can be risk factors in Japanese populations; male gender and old age are predominant in the intestinal type of carcinoma which is dominant in Japan, although this is not the case in the West. As for early diagnosis of cancer, only endoscopy can be

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commonly used for the detection of gastritis-like EGC, seen as a faint mucosal irregularity or discoloration. To make early diagnosis more accurate, it is indispensable to carry out detailed endoscopy together with careful scrutiny of the mucosa using dye-spraying techniques. The remarkable progress of early diagnosis in Japan prompted the endoscopic treatment for less invasive EGCs. The first success was with endoscopic mucosal resection (EMR). Although convenient, its therapeutic efficacy is inadequate, particularly for larger lesions. Endoscopic submucosal dissection (ESD) has no limitation on resection size and is expected to replace surgery, although it needs a high level of skill and there are several technical problems to be solved.

Key words: cancer screening; high-risk population; smoking; histological type; *Helicobacter pylori*; pepsinogen; gastrin; early gastric cancer; endoscopic/barium surveillance; detailed endoscopy; endoscopic treatment; EMR; ESD.

Recently, early gastric cancer (EGC) has been increasing, not only in Japan but also in other countries, and it is now recognized that it is not a Japanese monopoly. At present, the detection of EGC is thought to be beneficial only for individual welfare, because no definitive comparative studies have been carried out for clarifying the effectiveness of early diagnosis. In recent decades, however, the age-adjusted annual death rate for major cancers in Japanese populations reveals a striking decrease in that for gastric cancer in both men and women, as shown in Figure 1. On the other hand, according to the regional cancer registry reports on the actual incidence of major cancers, gastric cancer is still the most frequent in males and the second most frequent (after breast cancer) in females.[1,2] In short, there is a considerable discrepancy between incidence and mortality.[3] This may indicate that the diagnosis and therapeutics for gastric cancer have reached a very high standard in Japan, and that early diagnosis can actually decrease cancer mortality.

Early detection of gastric cancer, therefore, is undoubtedly important, and it should be done more efficiently by screening high-risk populations. Another advantage of early diagnosis is that considerable numbers of EGC cases detected can be treated with non-invasive therapy such as endoscopic treatment.

This chapter attempts to assess the value of known risk factors available for cancer screening, and then introduces the latest trends in the detection and treatment of EGC in Japan, where the results have been considerably better than in other countries.

DETECTING PATIENTS AT HIGH RISK OF EGC

Value of smoking, gender and age

Smoking

Unlike pulmonary cancer, the effect of cigarette smoking on the risk of gastric cancer was not well elucidated until 2002, when the Japan Public Health Centre Study Group showed definitive results in a cohort study which prospectively examined a total of 19,957 Japanese men. According to this study, smoking was associated with an increased risk of the intestinal (differentiated) type of distal gastric cancer compared to the group who never smoked; the adjusted rate ratios (RRs) for past and current smokers were 2.0 (95%CI 1.1−3.7) and 2.1 (95%CI 1.2−3.6) respectively.[4] Thereafter, several papers have demonstrated the significant risks of gastric cancer in current smokers or in those who have ever smoked,[5−7] but there are some fine distinctions