Is Screening for and Surveillance of Atrophic Gastritis Advisable?

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Key Words

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Abstract

Gastric cancer remains a leading cause of cancer-related deaths in many parts of the world. At present, prevention seems to be the most effective means to reduce its the incidence and mortality rate. Gastric atrophy is considered the first relevant step in the histogenesis of gastric adenocarcinoma. However, whether screening for and surveillance of atrophic gastritis is advisable is debated. The prevalence and pattern of chronic atrophic gastritis varies greatly from country to country, being higher and mainly diffuse pangastritis or localized in those countries with a high gastric cancer incidence. The only method available to detect gastric atrophy is histopathological examination of endoscopic specimens, but there is no consensus about diagnosis. Serum gastric secretion may be a marker of gastric atrophy, although it has high specificity but low sensitivity. Gastric atrophy is mainly related to chronic *Helicobacter pylori* (*H. pylori*) infection. Thus, the only effective strategy for gastric cancer prevention is eradication of *H. pylori* infection to arrest atrophy progression in selected populations. In conclusion, there is insufficient evidence to suggest screening for and surveillance of atrophic gastritis in the general population; however, this strategy should be applied in countries with a high incidence of gastric cancer.

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Before entering into the timely issue of whether screening for and surveillance of atrophic gastritis is advisable, we should ask several questions, e.g.: What is screening? What is the purpose of screening? Who is eligible? Is it cost-effective?

Screening is a public health service that has the potential to save lives and to improve quality of life through the early diagnosis of serious conditions. Screening is the process of checking people who have no symptoms or signs of an unsuspected disease that can be treated more successfully than if the disease had been left until it became manifest. In 2003 the United Kingdom National Screening Committee established a series of criteria that should be met before screening for a disease (<http://www.nsc.nhs.uk/pdfs/criteria.pdf>). These criteria concern four aspects: (1) the condition should be an important health problem, the epidemiology and natural history should be well understood, and the risk factors and disease markers should be detectable; (2) the diagnostic test should be simple, safe, validated and acceptable to the population; (3) treatment should better the outcome, and (4) the protocol should be effective in reducing mortality and morbidity and be cost-effective.

Condition

Gastric atrophy is considered the first relevant step in the histogenesis of intestinal gastric adenocarcinoma according to Correa's multistep process [1]. In fact, the risk

Table 1. Epidemiology of chronic atrophic gastritis

Group (first author)	Ref.	Year	Country	n	Age range years	Prevalence of CAG, %	
						overall	range
Correa	8	1990	Columbia	1,670	15–55	45	23–59
Johnsen	9	1991	Norway	273	20–69	51	–
You	10	1993	China	3,400	35–64	98	93–100
Katellaris	11	1993	Australia	50	18–30	22	0–39
Asaka	12	1996	Japan	85	30–60	53	–
You	13	1998	China	214	35–64	82	76–87
Borch	14	2000	Sweden	501	35–85	28	8–56
Malekzadeh	15	2004	Iran	1,001	40–92	–	22–47

CAG = Chronic atrophic gastritis.

of gastric cancer is closely related to the grade and extension of gastric atrophy being up to 80- to 90-fold higher in patients with severe atrophy involving both the antrum and body than in the general population [2]. Recently, Dinis-Ribeiro et al. [3] reported that the progression to low-grade dysplasia was higher in patients with chronic atrophic gastritis than in those with type I intestinal metaplasia.

Gastric cancer still ranks as a leading cause of cancer-related deaths in many parts of the world [4]. According to the American Cancer Society, there were ~800,000 new cases of gastric cancer in the USA in 2000 and >600,000 people died of the disease in the same year, with an estimated 5-year relative survival rate <20% (American Cancer Society, www.cancer.org 2000) [5]. At present, primary or secondary prevention, which means management of precancerous lesions such as atrophy, are likely to be the most effective strategies with which to reduce the incidence of the disease and its mortality rate.

From an epidemiological point of view, a study reported in 1984 showed that the prevalence of chronic atrophic gastritis in adult Europeans was between 22 and 37% and that the incidence of gastric cancer was between 7 and 13% after a follow-up of 11 years (about 1% per year) [6]. These early findings have been confirmed in a very recent study from Germany in which the rate of chronic atrophic gastritis, affecting prevalently the antrum, was 24% (845 out of 3,548 patients) [7]. However, the prevalence and the pattern of chronic atrophic gastritis varies greatly from country to country, being higher and mainly diffuse pangastritis or localized in those countries with a high incidence of gastric cancer (table 1) [8–15]. Thus,

gastric cancer and the management of precancerous lesions still remain a major clinical challenge and a public health concern.

Diagnostic Tests

The second criterion that should be met before screening concerns the tests available to diagnose the condition. Since the multistep process is triggered often, if not always, by *Helicobacter pylori* infection, one may look for *H. pylori* infection. This can be done by three means: a serological test, the ¹³C-urea breath test (¹³C-UBT) and the *H. pylori* stool antigen test (HpSA). All these tests are non-invasive, and ¹³C-UBT and HpSA are sensitive and specific. In addition to etiological tests, it is possible to test for the presence of the disease. There is increasing evidence that the serum profile of gastric secretion is a marker of gastric atrophy. In fact, pepsinogen I (PGI) is secreted by peptic cells, which are restricted to the gastric body, thus a decrease of PGI or of the ratio of PGI/PGII (secreted in different regions of the stomach) may indicate the presence and the grade of chronic atrophic gastritis. In a large European multicenter cohort study, the PGI/PGII ratio had good diagnostic accuracy in discriminating between patients with chronic atrophic gastritis and those with normal or mild inflammation of the gastric mucosa [16]. While the evaluation of serum pepsinogen has been proposed as a new screening test for gastric cancer in Japan [17], other studies have demonstrated that the gastric serum profile is not reliable for the diagnosis of atrophy [18, 19]. Most studies report high specificity but low sensitivity. Ley et

al. [20] reviewed a number of screening methods, and not surprisingly, they found that no screening method had both a high sensitivity and a high specificity for the diagnosis of chronic atrophic gastritis. Thus, the only method currently available to detect gastric atrophy is histopathological examination of endoscopic biopsy specimens performed according to the Sydney System (5 biopsies: 2 from the antrum, 2 from the body, and 1 from the angulus) [21]. Although endoscopy is an invasive method, it is safe, only moderately uncomfortable for patients, and in the appropriate setting, large numbers of procedures can be carried out at low cost. However, notwithstanding the progress made in recent years, there is still no general consensus about the diagnosis of atrophic gastritis. Atrophy is defined as the loss of appropriate glands in a given gastric compartment, but two questions remain unanswered, namely: What are the missing glands replaced by? Is the atrophy reversible?

When the gastric mucosa is damaged by such factors as *H. pylori* infection, the lamina propria is generally occupied by a dense inflammatory infiltrate that alters the architecture and function of the glands, and induces regenerative processes and recruitment of fibroblasts [22]. Disappearance of the inflammatory infiltrate, i.e. after eradication of *H. pylori* infection, is followed by reorganization of the mucosal architecture, reappearance of glands and normal acid secretion [23]. However, if the inflammatory infiltrate persists, the glands lose their ability to regenerate and the lamina propria can be occupied by interstitial fibrosis composed of collagen fibers that replace the glandular structure. There are two main routes to atrophy. Glands and/or stem cell compartments are completely destroyed by inflammatory cells, or specialized epithelial cells are destroyed and stem cells are preserved [24]. When the stem cell compartment is preserved, the removal of an injurious factor could lead to regeneration of glands and restoration of function.

Pathologists may have difficulty in recognizing definite gastric atrophy when the mucosa is densely infiltrated by inflammatory cells. To overcome this problem, Genta et al. [22] suggested that gastric atrophy be diagnosed not earlier than 6 months after *H. pylori* eradication therapy, thereby leading to the definition chronic gastritis 'indefinite for atrophy' [24]. However, the drawback of this approach is that patients must undergo repeat upper endoscopy and mucosal biopsies with consequent major discomfort and higher health costs.

Treatment

The third criterion for screening concerns treatment, which should improve the outcome of atrophy. Gastric atrophy is prevalently related to *H. pylori* infection. Indeed, in a large multicenter study (21 centers) involving 2,455 subjects, the prevalence of gastric atrophy was >80% in *H. pylori*-positive patients and <20% in *H. pylori*-negative subjects [25]. Thus, the only effective treatment is eradication of *H. pylori* infection. Many studies have focused on the issue of reversibility and the results have been controversial. Hojo et al. [26] evaluated indexed literature on the effects of *H. pylori* cure on the dynamics of gastric atrophy and/or intestinal metaplasia from 1992 to June 2001. Of 25 studies, 11 reported a significant regression of atrophy, 1 reported a significant worsening and the remaining 13 found no significant change. We examined the literature about the dynamics of gastric atrophy up to February 2004, and found no significant changes with respect to previous findings [27]. A review of data from Japan revealed more reports of regression of atrophy after eradication than progression [28]. The discrepancy between studies can be attributed to differences in various factors: the populations studied, study design, follow-up, age of patients, *H. pylori* strain, pattern of atrophy, etc.

Screening Program

The third criterion is that the screening program must be effective in reducing mortality and morbidity. Uemura et al. [29] showed that none of the 1,246 patients treated with eradication therapy developed gastric cancer during a 12-year follow-up compared with 36 of 280 *H. pylori*-positive patients [29]. However, a recent large randomized double-blind controlled study showed that during an 8-year follow-up, eradication therapy significantly reduced cancer risk only in patients without precancerous lesion at baseline [30]. In conclusion, there is insufficient evidence to suggest screening for and surveillance of atrophic gastritis in the general population. However, in geographical areas with a high incidence of gastric cancer, this strategy should be mandatory. The serological gastric profile corresponds with the histological diagnosis of atrophy. But given its low sensitivity, it would be useful only in screening for chronic atrophic gastritis.

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