Original article

Detection of early gastric cancer: misunderstanding the role of mass screening

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Abstract

Background. The proportion of early gastric cancer (EGC) increased from 15% during the 1960s to 50% recently, leading to a remarkable improvement of the 5-year survival rate of gastric cancer patients from 40% to 70%. This has been attributed to mass screening together with extended lymphadenectomy. However, more and more patients with EGC are diagnosed outside of mass screening. The aim of this study was to determine whether patients are symptomatic at the time of early detection and the method of tumor detection.

Methods. From 2001 to 2003, a total of 1226 patients (male/female 2.2:1.0, age 26–95 years) with EGC were treated at the National Cancer Center Hospital, Tokyo. We reviewed their medical records.

Results. Of these 1226 patients, 512 (41.8%) were symptomatic, and 714 (58.2%) reported no symptoms. Among the symptomatic patients, 468 (91.4%) were examined at outpatient clinics, 39 (7.6%) by private health assessment clinics, and 5 (1.0%) by mass screening. In total, 91.6% of the symptomatic patients directly underwent esophagogastroduodenoscopy (EGD). Of the asymptomatic patients, 320 (44.8%) were examined at outpatient clinics, 306 (42.9%) by private health assessment clinics, and 88 (12.3%) by mass screening. EGD was the initial assessment in 67.8% and radiography in 32.2% of asymptomatic patients.

Conclusion. Most patients with EGC were detected outside of mass screening. This suggests that the Japanese public and physicians are well aware of the risk of gastric cancer and the importance of early detection. The effect of mass screening is misunderstood.

Key words Early gastric cancer · Mass screening · Symptom · Esophagogastroduodenoscopy

Introduction

Gastric cancer remains one of the major causes of cancer death not only in Japan but also worldwide [1,2]. Early detection of the disease is vital. Whereas advanced gastric cancer has a poor prognosis, early gastric cancer (EGC) represents a potentially curable stage in the natural history of the disease. Gastrectomy with lymph node dissection in particular has provided an excellent therapeutic outcome for EGC, achieving 5-year survival rates higher than 90% [3,4]. In addition, early detection might increase the number of patients whose lesion can be treated endoscopically [5–7].

A nationwide mass screening program for gastric cancer has been active for about 50 years in Japan employing mostly photofluorography [8–15]. This involves double-contrast barium meal studies of the stomach, with seven principal views. More than 6 million people are screened per annum by this program. Although accurate data are unavailable, more and more patients are thought to undergo some form of screening outside the mass screening program, mostly with esophagogastroduodenoscopy (EGD), which is quite accurate in detecting EGC [16–20].

It has been estimated that EGC progresses to advanced gastric cancer after a median period of 37 months [21]. During this time span EGC proceeds from the asymptomatic and undetectable stage to the asymptomatic but detectable one, and finally to the symptomatic and detectable stage [22]. Patients with advanced cancer typically have severe anemia and malnutrition and sometimes stenotic symptoms at either the pylorus or the cardia. Although no symptoms are caused directly by the tumor itself in EGCs, patients with EGC may develop symptoms, mainly those related to peptic ulcers occurring inside the cancerous mucosa [22–35].

The aim of this study was to determine how often patients with EGC have symptoms on presentation and by what means these tumors are detected.

Patients and methods

From 2001 to 2003, a total of 1264 patients with EGC underwent cancer resection in the National Cancer Center Hospital (NCCCH), Tokyo. We excluded 38 patients who had EGC diagnosed during a pretreatment workup for another malignancy and reviewed the medical records of 1226 patients. We analyzed patients' reported symptoms and the procedures involved in EGC detection, including the motivation for investigation and the initial examinations leading to detection of the cancer. Screening examinations were classified as radiological or endoscopic.

Based on the existence of symptoms, we divided the patients with EGC into two groups — with or without symptoms — and we analyzed the age, sex, and clinical features of each group. We investigated 847 (69.1%) men and 379 (30.9%) women with a mean age of 62.8 years (range 26–95 years). All patients were treated with either surgical or endoscopic resection of the disease in the NCCCH. The resected specimens were histologically assessed in detail. In all cases, the adenocarcinoma of stomach was histologically confirmed to be limited to either the mucosa or submucosa irrespective of lymph node involvement [36].

Statistical analysis

The chi-squared test was used for statistical analysis using a standard computer software statistical package

(SPSS for Windows, release 6.0; SPSS, Chicago, IL, USA). $P < 0.05$ was considered significant.

Results

Of 1226 patients with EGC, 512 patients (41.8%) were symptomatic and 714 (58.2%) had no symptoms. The demographic details of the patients are shown in Table 1. Univariate analysis showed that the percentage of men was higher in the asymptomatic group than the symptomatic group ($P < 0.0001$). No significant difference in age between symptomatic and asymptomatic patients was found.

The symptoms and signs of the patients with EGC are shown in detail in Table 2. Epigastric pain, gastric discomfort, or hunger pain were the most common chief complaints being reported by 376 patients (73.4%) at the detection of EGC.

The procedures for detecting EGC, the motivation for investigations, and the initial examinations are shown in Table 3 and Table 4, respectively. Of the patients, 788 (64.3%) were examined at outpatient clinics, 345 (28.1%) were investigated by private health assessment clinics, and 93 (7.6%) were participating in the mass screening program. Of the symptomatic patients, 468 (91.4%) were examined at outpatient clinics, 39 (7.6%) were investigated by private health assessment clinics, and 5 (1.0%) were participating in the mass screening program. In contrast, of the asymptomatic patients, 320 (44.8%) were examined at outpatient

Table 1. Patient details

Parameter	Asymptomatic patients (<i>n</i> = 714)	Symptomatic patients (<i>n</i> = 512)	<i>P</i>
Mean age (years)	62.9 (32–86)	62.8 (26–95)	NS
Sex			
Male	75.9% (<i>n</i> = 542)	59.6% (<i>n</i> = 305)	<0.0001
Female	24.1% (<i>n</i> = 172)	40.4% (<i>n</i> = 207)	

Table 2. The symptoms and signs of patients with EGC

Symptoms and signs	No.
Epigastric pain, gastric discomfort, or hunger pain	376 (73.4%)
Chest discomfort, nausea and vomiting, or frequent belching	65 (12.7%)
Gastrointestinal bleeding, manifesting with melena or anemia	33 (6.4%)
Appetite loss	22 (4.3%)
Weight loss	9 (1.8%)
Throat pain	5 (1.0%)
Diarrhea	2 (0.4%)
Total	512 (100)

Table 3. Motivation for investigations

Location	Asymptomatic patients 100% (<i>n</i> = 714)	Symptomatic patients 100% (<i>n</i> = 512)	Total 100% (<i>n</i> = 1226)
Outpatient clinics	44.8% (<i>n</i> = 320)	91.4% (<i>n</i> = 468)	64.3% (<i>n</i> = 788)
Private health assessment clinics	42.9% (<i>n</i> = 306)	7.6% (<i>n</i> = 39)	28.1% (<i>n</i> = 345)
Mass screening	12.3% (<i>n</i> = 88)	1.0% (<i>n</i> = 5)	7.6% (<i>n</i> = 93)

Table 4. Initial examinations

Examination	Asymptomatic patients 100% (<i>n</i> = 714)	Symptomatic patients 100% (<i>n</i> = 512)	Total 100% (<i>n</i> = 1226)
EGD	67.8% (<i>n</i> = 484)	91.6% (<i>n</i> = 469)	77.7% (<i>n</i> = 953)
Radiography	32.2% (<i>n</i> = 230)	8.4% (<i>n</i> = 43)	22.3% (<i>n</i> = 273)

clinics, 306 (42.9%) were investigated by private health assessment clinics, and 88 (12.3%) were participating in the mass screening program.

EGD was the initial assessment in 77.7% of the patients with EGC, and radiography was used in only 22.3%. In total, 91.6 % of the symptomatic patients directly underwent EGD, and radiography was the initial assessment in only 8.4% of them. In contrast, of the asymptomatic patients, EGD was the initial assessment in 67.8%, and radiography was the initial assessment in only 32.2%.

Discussion

Mass screening for gastric cancer with photofluorography has been widely conducted in Japan since 1960 [8–15]. With the establishment of the Japanese Society of Gastric Mass Survey in 1962 (later renamed Gastroenterological Mass Survey), the program has spread throughout the country. At present more than 6 million people are screened annually, and the number of gastric cancers detected by screening is increasing. Cohort and case-control studies generally show a decrease in the mortality risk from gastric cancer because of this program [10].

From the 1980s it became evident that EGD was promising in the earlier detection of gastric cancer because of its ability to detect subtle mucosal abnormalities better than radiography. Its accuracy is higher, and it enables simultaneous biopsy for histological confirmation of malignancy [16–20]. Nowadays the so-called gastritis-like type of early gastric cancer is increasing in Japan [37,38]. This type of EGC cannot be identified by radiological investigation, so suspicions of its existence are generated during endoscopy and confirmed only

by pathology. Furthermore, earlier detection of gastric malignancies increases the possibility of a successful endoscopic treatment instead of surgery [39].

Although the positive predictive value of radiographic screening for gastric cancer organized by the government is only 1%–2%, its sensitivity is 70%–90% [10]. Unfortunately, only 20% of the eligible population aged >40 years accept this governmental screening program [40,41]. On the other hand, it is believed that each year more than 6 million people are examined by either radiography or EGD outside of the mass screening program. According to the Survey of Medical Care Activities in Public Health Insurance 2004 [42], more than 7.8 million people are examined annually by EGD in Japan. With a population of 85 million >20 years old, 9% of Japanese undergo EGD every year. The explanation for this trend is that endoscopic examination is widely considered to be more accurate for detecting EGC [16–20]. In our sample, EGD was the initial assessment in most (77.7%) of the patients.

According to the 4th and 5th National Cancer Surveys in Japan [40], gastric cancer (including the advanced cases) is most commonly detected in outpatient clinics, whereas only 6.0% is identified by the government-based mass screening program and 4.6% by private health assessment clinics. In our cohort of EGC, more patients were diagnosed by the private clinics (28.1%), and the contribution of the mass screening program was less than 10%. Of the asymptomatic patients, only 12.3% participated in the mass screening program; the rest were examined outside of mass screening. Thus, most of the patients with EGC were detected outside the mass screening program regardless of symptoms. In addition, univariate analysis showed that the proportion of men was higher in the asymptomatic group than the symptomatic group. The reason for

this discrepancy may be due to the fact that men have greater accessibility to health checkups (including mass screening or private health assessment clinics) at the workplace than women in Japan [17,24,26].

The proportion of EGC cases among those of gastric cancer is more than 50% in Japan [8], whereas in the West the proportion is much lower [43]. In the West, it is widely believed that this difference is due to the mass screening program [2,31]. However, our study suggests that the reason for the increased detection of EGC in Japan is not only the success of the mass screening program but also the cautious attitude of Japanese people and physicians toward gastric cancer. The awareness of the risk of gastric cancer and the importance of early detection has increased recently, and many individuals attend private health assessment clinics without symptoms [14]. Also, if individuals have symptoms, they generally seek medical consultation at outpatient clinics. Similarly, all physicians perform some kind of investigation to rule out gastric malignancy. This suggests that outpatient clinics or private clinics have a more important role in early detection than mass screening. In this way, in the West the role of mass screening is misunderstood.

This study was conducted in the National Cancer Center Hospital in Tokyo, which is a major referral center in Japan. The background of patients may not represent the rest of the country, as they are usually of higher socioeconomic status. They are more aware of the risk of gastric cancer and the importance of early detection. Therefore, they may attend outpatient clinics or private clinics for endoscopy more frequently. A nationwide project is required in the future to study the true effect of mass screening.

From the aspect of medical science, EGD was promising in the earlier detection of gastric cancer [16–20]. To detect gastric cancer at an earlier stage and to reduce the mortality due to gastric cancer, mass screening using EGD may be useful screening program. However, no studies have directly examined whether the screening using EGD reduced the mortality due to gastric cancer. Therefore, this endoscopic screening program should be evaluated in terms of the mortality due to gastric cancer. In addition, from the aspect of medical economics, despite its diagnostic advantages, its cost is much higher and it requires more staff and technical expertise compared to radiology [17,44]. In financial terms, perhaps its economic efficiency is low. Therefore, at this moment mass screening using EGD with governmental support would be beneficial only in a population at high risk for gastric cancer.

Measures similar to those of employed in Japan with an aim of earlier detection of gastric cancer should be considered in the areas with a high incidence of gastric cancer, such as Latin America and eastern Europe [41].

They may decrease the morbidity and mortality of this formidable disease and improve its dismal prognosis throughout the world.

Acknowledgments There was no grant for this study. We thank Dr. Bruce Mann and Dr. Ioannis Karavokyros for providing useful advice and language revision of the text.

References

1. Ministry of Health and Welfare of Japan. Vital statistics of Japan 1995. Tokyo: Ministry of Health and Welfare; 1997.
2. Everett SM, Axon ATR. Early gastric cancer: disease or pseudo-disease. *Lancet* 1998;351:1350–2.
3. Sasako M, Kinoshita T, Maruyama K. Prognosis of early gastric cancer. *Stomach Intest* 1993;28:139–46 (English abstract).
4. Nishi M, Ishihara S, Nakajima T, Ohta K, Ohya S, Ohta H. Chronological changes of characteristics of early gastric cancer and therapy: experience in the Cancer Institute Hospital of Tokyo, 1950–1994. *J Cancer Res Clin Oncol* 1995;121:535–41.
5. Gotoda T, Yanagisawa A, Sasako M, Ono H, Nakanishi Y, Shimoda T, et al. Incidence of lymph node metastasis from early gastric cancer: estimation with a large number of cases at two large centers. *Gastric Cancer* 2000;3:219–25.
6. Gotoda T, Sasako M, Ono H, Katai H, Sano T, Shimoda T. Evaluation of the necessity for gastrectomy with lymph node dissection for patients with submucosal invasive gastric cancer. *Br J Surg* 2001;88:444–9.
7. Soetikno R, Kaltenbach T, Yeh R, Gotoda T. Endoscopic mucosal resection for early cancers of the upper gastrointestinal tract. *J Clin Oncol* 2005;23:4490–8.
8. Hisamichi S. Screening for gastric cancer. *World J Surg* 1989;13:31–7.
9. Tsubono Y, Nishino Y, Hisamichi S. Screening for gastric cancer in Miyagi, Japan: evaluation with a population-based cancer registry. *Asian Pacific J Cancer Prev* 2000;1:57–60.
10. Tsubono Y, Nishino Y, Hisamichi S. Screening for gastric cancer in Japan. *Gastric Cancer* 2000;3:9–18.
11. Medical examinations for digestive cancer in 2002 groups, national report. *J Gastroenterol Mass Surv* 2005;43:195–8 (in Japanese).
12. Shiratori Y, Nakagawa S, Kikuchi A, Ishii M, Ueno M, Miyashita T, et al. Significance of a gastric mass screening survey. *Am J Gastroenterol* 1985;80:831–4.
13. Han JY, Son H, Lee WC, Choi BG. The correlation between gastric cancer screening method and the clinicopathologic features of gastric cancer. *Med Oncol* 2003;20:265–9.
14. Kampschoer GH, Fujii A, Masuda Y. Gastric cancer detected by mass survey: comparison between mass survey and outpatient detection. *Scand J Gastroenterol* 1989;24:813–7.
15. Akaza H, Tsuruo T, Saijo N, Sone S, Isonishi S, Ohashi Y, et al. Cancer screening. *Jpn J Cancer Chemother* 2005;32:125–34 (in Japanese).
16. Kaizaki Y, Hosokawa O, Yamazaki S, Tsuda S, Watanabe K, Takeda T, et al. An analysis of early gastric cancer cases to determine the effectiveness of a panendoscope. *Jpn J Cancer Clin* 1991;37:497–505 (in Japanese).
17. Takemoto C, Isechi T, Matsumoto J, Kusano K, Mishige K, Nuruki F. Current status and problems of screening for gastric cancer using endoscopy. *J Gastroenterol Mass Surv* 2004;42:322–30 (in Japanese).
18. Hosokawa O, Hattori M, Takeda T, Watanabe K, Fujita M. Accuracy of endoscopy in detecting gastric cancer. *J Gastroenterol Mass Surv* 2004;42:33–9 (in Japanese).

19. Hosokawa O, Watanabe K, Hattori M, Douden K, Hayashi H, Kaizaki Y. Detection of gastric cancer by repeat endoscopy within a short time after negative examination. *Endoscopy* 2001;33:301–5.
20. Triantafyllidis JK, Cheracakis P. Diagnostic evaluation of patients with early gastric cancer — a literature review. *Hepatogastroenterology* 2004;51:618–24.
21. Tsukuma H, Mishima T, Oshima A. Prospective study of “early” gastric cancer. *Int J Cancer* 1983;31:421–6.
22. Look M, Tan YY, Vijayan A, Teh CH, Low CH. Management delays for early gastric cancer in a country without mass screening. *Hepatogastroenterology* 2003;50:873–6.
23. Sano T, Katai H, Sasako M, Maruyama K. The management of early gastric cancer. *Surg Oncol* 2000;9:17–22.
24. Kong SH, Park do J, Lee HJ, Jung HC, Lee KU, Choe KJ, et al. Clinicopathologic features of asymptomatic gastric adenocarcinoma patients in Korea. *Jpn J Clin Oncol* 2004;34:1–7.
25. Oliveira FJ, Ferrao H, Furtado E, Batista H, Conceicao L. Early gastric cancer: report of 58 cases. *Gastric Cancer* 1998;1:51–6.
26. Matsukuma A, Furusawa M, Tomoda H, Seo Y. A clinicopathological study of asymptomatic gastric cancer. *Br J Cancer* 1996;74:1647–50.
27. Pinto E, Roviello F, de Stefano A, Vindigni C. Early gastric cancer: report on 142 patients observed over 13 years. *Jpn J Clin Oncol* 1994;24:12–9.
28. Boldys H, Marek TA, Wanczura P, Matusik P, Nowak A. Even young patients with no alarm symptoms should undergo endoscopy for earlier diagnosis of gastric cancer. *Endoscopy* 2003;35:61–7.
29. Fernandez E, Porta M, Malats N, Belloc J, Gallen M. Symptom-to-diagnosis interval and survival in cancers of the digestive tract. *Dig Dis Sci* 2002;47:2434–40.
30. Everett SM, Axon ATR. Early gastric cancer in Europe. *Gut* 1997;41:142–50.
31. Maruyama M, Barreto-Zuniga R, Kimura K. Misconceptions on early gastric cancer in Japan. *Hepatogastroenterology* 2001;48:1560–4.
32. Eckardt VF, Giessler W, Kanzler G, Remmele W, Bernhard G. Clinical and morphological characteristics of early gastric cancer: a case-control study. *Gastroenterology* 1990;98:708–14.
33. Biasco G, Paganelli GM, Azzaroni D, Grigioni WF, Merighi SM, Stoja R, et al. Early gastric cancer in Italy: clinical and pathological observations on 80 cases. *Dig Dis Sci* 1987;32:113–20.
34. Malcolm R. Dyspepsia: Challenges in diagnosis and selection of treatment. *Clin Therapeutics* 2001;23:1130–44.
35. Agreus L, Talley N. Dyspepsia: current understanding and management. *Annu Rev Med* 1997;49:475–93.
36. Japanese Gastric Cancer Association, Japanese Classification of Gastric Carcinoma, 2nd English edition. *Gastric Cancer* 1998;1:10–24.
37. Yoshida S, Yamaguchi H, Tajiri H, Saito D, Hijikata A, Yoshimori M, et al. Diagnosis of early gastric cancer seen as less malignant endoscopically. *Jpn J Clin Oncol* 1984;14:225–41.
38. Yoshida S, Yoshimori M, Hirashima T, Yamaguchi H, Tajiri H, Nakamura K, et al. Nonulcerative lesion detected by endoscopy as an early expression of gastric malignancy: retrospective observation of 72 cases of gastric carcinoma. *Jpn J Clin Oncol* 1981;11:495–506.
39. Ono H, Kondo H, Gotoda T, Shirao K, Yamaguchi H, Saito D, et al. Endoscopic mucosal resection for treatment of early gastric cancer. *Gut* 2001;48:225–9.
40. Cancer statistics in Japan — 1997. Foundation for Promotion of Cancer Research, National Cancer Center, 1997.
41. Cancer statistics in Japan — 2005. Foundation for Promotion of Cancer Research, National Cancer Center, 2005.
42. Survey of Medical Care Activities in Public Health Insurance 2004, Vol. 2 (in Japanese). Statistics and Information Department, Minister’s Secretariat, Ministry of Health, Labour and Welfare.
43. Sue-Ling HM, Martin I, Griffith J, Ward DC, Quirke P, Dixon MF, et al. Early gastric cancer: 46 cases treated in one surgical department. *Gut* 1992;33:1318–22.
44. Waye JD, Aabakken L, Armengol-Miro JR, Llorens P, Williams CB, Zhang QL. Screening for GI cancer and payment mechanisms. *Gastrointest Endosc* 2002;55:453–4.