MINI-REVIEW

Screening for Gastric Cancer in Miyagi, Japan: Evaluation with a Population-Based Cancer Registry

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Abstract

Mass screening for gastric cancer originated in Miyagi Prefecture, Japan, in 1960. This review summarizes studies assessing the efficacy of screening using data from a population-based cancer registry in the prefecture that was started in 1959. Sensitivity and specificity of screening photofluorography (indirect radiography) is 81.1% and 88.8%, respectively. Ten-year survival rates are 30-40% better in screen-detected cases than in symptom-diagnosed cases. No randomized controlled trials have reported the efficacy of the screening in the country. In a 18-year follow-up study of 7,008 residents in the prefecture, incidence from gastric cancer did not differ between screened and unscreened subjects, but mortality decreased significantly in screened subjects compared with unscreened subjects for men (61.9 vs. 137.2 per 100,000 person-years, P<0.005) and women (28.1 vs. 53.8 per 100,00 person-years, P<0.01). In a population-based case-control study with 198 cases and 577 controls, odds ratio (95% confidence interval) of gastric cancer mortality was 0.41 (0.28-0.61) for ever vs. never screened within 5 years. Studies conducted in other regions have provided similar findings. Substantial evidence indicates that the Japanese screening program is effective in reducing the mortality from gastric cancer. Population-based cancer registries play a crucial role in assessing the efficacy of cancer screening programs.

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Introduction

A screening program for gastric cancer using photofluorography (indirect radiography) originated in Miyagi Prefecture, Japan, in 1960 (Hisamichi et al., 1995). In 1995, 214,271 persons were screened in the prefecture (19.0% of the eligible population), of whom 20,805 were referred for further diagnostic examinations and 348 cases of gastric cancer were detected (Miyagi Cancer Society, 1996). The program is currently widespread throughout the country.

In order to assess the utility of cancer screening, we need to examine 1) the accuracy of the screening test, 2) the improved prognosis of screen-detected cancers relative to symptom-diagnosed cases, and 3) the reduced mortality rate from gastric cancer among screened population. We have conducted various studies on these issues using data from Miyagi Prefectural Cancer Registry, one of the earliest population-based cancer registrations in Japan that has been in full operation since 1959 (Takano and Okuno, 1997). We present here a summary of these investigations.

Accuracy of Screening Photofluorography

According to the standardized procedure proposed by the Japanese Society of Gastroenterological Mass Survey, seven consecutive photofluorograms covering the whole area of the stomach are taken for each screenee using roll films 70 or 100 mm in width (Committee of Photofluorography, 1984). Trained radiographic technicians take the photofluorogram, using effervescent granules without hypotonic agents. Two radiologists examine the films. The screenee with suspected abnormality is referred for further diagnostic examinations that include full-size radiography, endoscopy, and biopsy. We assessed the accuracy of photofluorography in 155,938 people who attended the screening program in 1985 (Table 1) (Fukao et al., 1992). For 17,731 subjects who were screened positive, we performed diagnostic examinations and detected 356 cases of gastric cancer. For 138,207

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Table 1. Accuracy of Screening Photofluorography

	Gastric cancer		
	Present	Absent	Total
Screening			
Positive	356	17,3575	17,731
Negative	83	138,124	138,207
Total	439	155,499	155,938

Sensitivity=81.1% (356/439)
Specificity=88.8% (138,124/155,499)
Positive predictive value= 2.0% (356/17,731)

subjects screened negative, we followed them up for one year using our cancer registry to find false-negative cases. We identified 83 such cases. In total, 439 cases were considered present at the time of the screening. Based on these results, the sensitivity of the test was estimated as 81.1% and the specificity 88.8%. Studies conducted in other regions of the country found the similar degree of accuracy .

Improved Prognosis in Screen-Detected Gastric Cancer

Table 2 compares the 10-year crude survival rates between screen-detected and symptom-diagnosed gastric cancers according to the 10-year age groups. The subjects were 12,182 gastric cancer cases (7,863 men and 4,319 women) registered to our cancer registry during 1978-1985. The survival of screen-detected cases was 30-40% better than symptom-diagnosed cases up to the age 70s. The prognosis in the 80s did not differ, but the result was based on only a small number of screen-detected cancers (16 men and 7 women). Our result is in agreement with other investigations (Miyagi Cancer Society, 1996), indicating that the screening leads to early detection and improved prognosis of gastric cancer patients.

However, this should be regarded only as a preliminary indicator for the potential benefit of screening, because the comparison of survival rates in screen-detected and symptom-diagnosed cancers tend to overestimate the true benefit of screening due to lead-time bias and length bias. Therefore the efficacy of screening should be evaluated in terms of whether the mortality in the screened population is reduced.

Cohort Study of Gastric Cancer Screening

Although randomized controlled trial is the most reliable method of the evaluation of cancer screening programs, no mortality results have been available for gastric cancer screening. Various observational studies have been conducted in Japan, and they generally showed the efficacy

Table 2. Comparison of 10-year Crude Survival Rates between Screen-detected and Symptom-diagnosed Gastric Cancer

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	Men		Women	
	N	Survival rate(%)	N	Survival rate (%)
<40 yrs				
Screen	50	85	22	81
Symptom	267	51	284	38
40-49 yrs				
Screen	217	79	112	80
Symptom	653	45	365	40
50-59 yrs				
Screen	537	72	215	73
Symptom	1,350	43	605	36
60-69 yrs				
Screen	552	70	229	73
Symptom	1,729	30	901	35
70-79 yrs				
Screen	224	57	61	65
Symptom	1,740	17	1,056	24
80- yrs				
Screen	16	17	7	0
Symptom	528	7	462	4

of the program (Miyagi Cancer Society, 1996).

We conducted a cohort study using 7,008 residents aged 40-69 years in 4 towns of Miyagi Prefecture (Hosamichi and Sugawara, 1984). A total of 4,325 subjects were screened at least once, while 2,683 subjects were not screened. During the 18 years of follow-up, 165 incident cases of gastric cancer and 81 deaths due to the disease had been ascertained. For men and women, the incidence rate did not differ significantly between the screened and unscreened group (Table 3). In contrast, the mortality rate in the screened group was significantly decreased by 50% compared with the rate in the unscreened group.

A cohort study conducted in Osaka Prefecture also suggested a decreased mortality among the screened population (Oshima, 1979), while a study in Gifu Prefecture with a small number of gastric cancer death (8 men and 4 women in the screened group) failed to find a reduced risk of death from the disease (Inaba et al., 1999).

Case-Control Study of Gastric Cancer Screening

We also conducted a population-based case-control study (Fukao et al., 1995). Cases were 198 persons who died of gastric cancer in 1990 in 57 municipalities of the prefecture. We selected 3 controls per case, 577 in total, from the general population who were matched on age, sex, and residential area on the corresponding case. We investigated the date of case diagnosis using our cancer

Table 3. A Cohort Study of Gastric Cancer Screening by Photofluorography

	N		No. of cases Inc	Mort	Gastric cancer Inc	Mort
Men						
Screened	2,098		74	25	187.7	61.9
Unscreened	1,287		44	30	201.8	137.2
					ns	P<0.005
Women						
Screened	2,227	29	14	58.1	28.1	
Unscreened	1,396	18	12	79.1	53.8	
					ns	P<0.01

Inc, Incidence, Mort, Mortality

registry and examined the history of screening for 5 years prior to that date using the record of the Miyagi Cancer Society Cancer Detection Center. We then compared the rates of screening between cases and controls and estimated odds ratios using conditional logistic regression. For gastric cancer cases, 20.2% of the subjects had attended the screening at least once within 5 years before their diagnosis. For control subjects, 37.8% participated in the screening during the corresponding period. The estimated odds ratio (OR) and 95% confidence interval (CI) was 0.41 (0.28-0.61).

Table 4 shows a summary of 3 case-control studies conducted in Japan, presenting sex-specific odds ratios of mortality from gastric cancer for subjects who had ever been screened during the study period, as compared with those who had never been screened. The studies were conducted in Miyagi (Fukao et al., 1995), Osaka (Oshima et al., 1986), and Chiba Prefecture (Abe et al., 1995). They generally showed a decreased risk among the screened subjects both for men and women. The OR for men in the Oshima's report (1986) and that for women in Fukao's study (1995) fail to attain statistical significance, partly due to a small number of cases. We calculated the weighed average of the ORs using the inverted variance of each OR as the weight. This pooled OR (95%CI) was 0.39(0.29-0.52) for men and 0.50(0.34-0.72) for women, suggesting that the screening can reduce about 60% of deaths from gastric cancer in men and 50% in women and that there is no marked sex difference in the efficacy.

Discussion

Summarizing the studies conducted in Miyagi and other parts of the country, gastric photofluorography is accurate and leads to early detection and better prognosis of gastric cancer cases; although no randomized controlled trials have been reported, observational studies generally showed a reduced mortality from gastric cancer in the screened population (ref).

As a limitation for most of the cohort and case-control studies, they did not address the potential for self-selection bias that might over- or underestimate the true benefit of screening. We are currently undertaking a case-control study nested within a population-based prospective cohort study conducted in Miyagi (Fukao et al., 1995), in which information for factors associated with incidence and mortality of gastric cancer are available and their differences between cases and controls can be controlled for.

In conclusion, there is substantial evidence suggesting the efficacy of photofluorographic screening for gastric

Table 4. Summary for Case-control Studies of Gastric Cancer Screening by Photofluorography: Sex-specific Odds Ratios (ORs) and 95% Confidence Intervals (CIs) of Mortality from Gastric Cancer for Ever vs Never Screened

	No. of Subjects		Screened (%)				
Authors	Cases	Controls	Cases	Controls	OR	(95%CI)	P-value
Men							
Fukao et al.,. 1995	126	364	16.7	38.5	0.32	(0.19-0.53)	0.001
Oshima et al., 1986	53	156	62.3	73.1	0.60	(0.34-1.05)*	0.065
Abe et al., 1995	527	1552	11.2	23.3	0.37	(0.24-0.57)	<0.01
Pooled OR					0.39	(0.29-0.52)	
Women							
Fukao et al.,. 1995	72	213	26.4	36.2	0.63	(0.34-1.16)	0.14
Oshima et al., 1986	37	105	40.5	59.0	0.38	(0.19-0.79)*	0.014
Abe et al., 1995	293	861	11.3	20.6	0.46	(0.26-0.80)	<0.01
Pooled OR					0.50	(0.34-0.72)	

* 90%CI

cancer in reducing the mortality. Further studies are required to better address the potential for self-selection bias. Our experiences indicate that population-based cancer registries play a crucial role in assessing the efficacy of cancer screening programs.

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