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Efficacy of Screening for Gastric Cancer in a Korean Adult Population : A Case-Control Study

While gastric cancer is the most common malignancy in the Korean adult population, little is known of the efficacy of gastric cancer screening among Koreans. To study the efficacy of gastric cancer screening, this case-control study was conducted. From November 1996 to July 1998, 441 newly diagnosed gastric cancer (321 advanced, 120 early) patients were enrolled at the Department of General Surgery and 107 controls were enrolled at the inpatient Department of Family Medicine and Otolaryngology. History of gastric examinations and possible risk factors were collected through interview with a structured questionnaire. Patients with advanced gastric cancer were 61% less likely to have had a gastric examination than those with early gastric cancer (OR 0.39; 95%CI 0.23-0.65). Patients with advanced gastric cancer were 53% less likely to have had a gastric examination within two years of diagnosis (OR 0.47; 95%CI 0.23-0.98) and 69% less likely to have had a gastric examination within three years of diagnosis (OR 0.31; 95%CI 0.11-0.86). The data, showing a significant relationship between the history of gastric examinations and severity of gastric cancer, suggests that gastric cancer screening is effective in catching gastric cancer at early stages. It also suggests less than three years for screening interval.

Key Words: *Stomach Neoplasms; Mass Screening*

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INTRODUCTION

Gastric cancer is the most common malignant tumor in Korea. Its annual incidence is approximately 58 per 100,000 population in men and 25 in women (1). The prevalence of this malignant disease is 74 per 100,000 population in men and 45 in women (2). Gastric cancer is the most prevalent cancer for men (25.3%) and the second most prevalent one for women (15.0%), after cervical cancer (3). As the leading cause of cancer-related deaths for both genders in Korea, its mortality was 23.9 per 100,000 population in 1998, the third highest gastric cancer mortality rate for men in the world after Japan and Portugal (4). However, the rate has been gradually decreased since 1989 (4).

Prognosis of gastric cancer strongly depends on the tumor-stage. The five-year survival rate is more than 90% for early gastric cancer group but only 20-40% for the advanced cancer group (5, 6). Various cancer screening methods have been initiated and evaluated in Japan in order to reduce gastric cancer mortality.

Population-based gastric cancer screening had been carried out between 1960 and 1985 in Japan (7). The result showed that there was no significant difference in gastric cancer detection rate, but the proportion of the early gastric cancer to all gastric cancers has been increased from 13% in 1960 to 62% in 1985. The mortality rate was reduced by 50% in the screened group compared to the control group.

Other studies also reported that gastric cancer screening reduced gastric cancer-related death rate by 48-60% (8, 9) and 2-5 years interval of participation might reduce gastric cancer mortality significantly (8-11).

From the perspective of Korean public health care, reducing the gastric cancer-related mortality rate appears to have the utmost importance. Although there have been some studies done on the risk factors for gastric cancer (12, 13), there is neither a study evaluating the efficacy of gastric cancer screening nor an established screening protocol. This problem is more complicated by the absence of community-based mass screening programs like in Japan.

We have conducted a case-control study to evaluate the efficacy of stomach cancer screening and establish the

optimal screening interval.

MATERIALS AND METHODS

Study population

From November 1996 to July 1998, 441 newly diagnosed gastric cancer (321 advanced, 120 early) patients were enrolled at the inpatient Department of General Surgery in Asan Medical Center, Seoul, Korea and 107 controls were enrolled at the inpatient Department of Family Medicine and Otolaryngology in the same hospital. A total of 548 individuals was studied. The control group was matched to the advanced gastric cancer group by age.

Information on the history of gastric examinations and possible risk factors were collected through interview with a structured questionnaire. Gastric examinations conducted within six months of diagnosis were ignored on the presumption that they were symptom-related.

Study hypothesis

The most appropriate case-control method to evaluate the efficacy of cancer screening in a short time would be to compare the odds of having had a screening test between a group of patients dying of gastric cancer and a group of healthy living population. There is no national mass screening program for gastric cancer in Korea. Cancer screening is conducted voluntarily on an individual basis. It is difficult to accumulate accurate data on gastric cancer screening experience of patients dying with gastric cancer. Therefore, we divided the gastric cancer patients into early and advanced gastric cancer groups according to the surgical (post-op) stage. In our hypothesis, we considered the advanced gastric cancer group as a surrogate outcome for the group of patients dying of gastric cancer, and the early gastric cancer group as a surrogate outcome for the live control group. We also defined the history of gastric examination (radiological and endoscopic) before the diagnosis of gastric cancer as the exposure variable. Odds ratio for advanced gastric cancer group vs. early gastric cancer group of gastric examination was calculated to evaluate the efficacy of gastric cancer screening. In addition, odds ratio for advanced gastric cancer group vs. non-cancer control group of gastric examination was calculated and compared with the result of advanced and early gastric cancer patients.

Gastric examinations, which were performed more than six months prior to the diagnosis, were included irrespective of symptom. Any examination conducted within six months of diagnosis was ignored on the presumption that it was symptom related in the gastric cancer group as well as in the control group.

Data collection

Every patient was interviewed by trained examiners using a structured questionnaire. The questions included risk factors such as history of gastritis/gastric ulcer, experience of gastric examination, family history of gastric cancer, alcohol drinking, smoking history and socioeconomic factors including sex, age, place of residence, economic status, and level of education, etc. Serum IgG ELISA test was carried out to detect *Helicobacter pylori* infection.

Statistical analysis

Comparing advanced cancer group vs. early gastric cancer group and advanced cancer group vs. non-cancer patients (control), gastric cancer screening and other variables were analysed by linear logistic regression for gastric examinations to obtain odds ratios and 95% confidence intervals. Statistical analysis was conducted using SAS-PC 6.12 statistics program.

RESULTS

General characteristics of study population

The general characteristics of the advanced and early gastric cancer patients are summarized as follows: Advanced gastric cancer patients was older and had lower body mass index ($p<0.05$) than early gastric cancer patients, but were not significantly different statistically in sex distribution, place of residence, economic status and education ($p>0.05$) (Table 1).

Risk factors for gastric cancer patients

The advanced gastric cancer patients had significantly less history of gastric examinations than the early cancer group ($p<0.05$), but did not differ significantly with respect to history of gastritis, family history of gastric cancer, smoking, alcohol drinking and *H. pylori* infection ($p>0.05$) (Table 2).

The advanced gastric cancer patients also had significantly less history of gastric examinations than the control group, but had more history of gastritis/gastric ulcer and family history of gastric cancer than the control group ($p<0.05$). No significant differences could be observed in smoking, alcohol drinking and *H. pylori* infection ($p>0.05$).

Table 1. Distribution of advanced and early gastric cancer patients and controls according to sex, age and selected variables

Variables	AGC	EGC	p^*	Controls	$p^\dagger$
	No. (%)	No. (%)		No. (%)	
Sex					
Male	222 (69.2)	79 (65.8)	0.504	70 (65.4)	0.472
Female	99 (30.8)	41 (34.2)		37 (34.6)	
Age (years)					
< 40	38 (11.8)	22 (18.3)		12 (11.2)	
40-49	63 (19.6)	21 (17.5)		20 (18.7)	
50-59	103 (32.1)	49 (40.8)	0.038‡	35 (32.7)	0.873‡
60-69	94 (29.3)	20 (16.7)		29 (27.1)	
> 70	23 (7.2)	8 (6.7)		11 (10.3)	
Place of residence					
Large city	141 (44.3)	55 (46.2)		64 (68.8)	
Small city	118 (37.1)	51 (42.9)	0.145‡	22 (23.7)	0.001‡
Rural	59 (18.6)	13 (10.9)		7 (7.5)	
Economic status					
Low	68 (45.0)	21 (32.8)		30 (37.0)	
Middle	43 (28.5)	29 (45.3)	0.055‡	27 (33.3)	0.497‡
High	40 (26.5)	14 (21.9)		24 (29.6)	
Education (years)					
< 12	182 (56.7)	59 (49.2)		41 (38.3)	
12	81 (25.2)	35 (29.2)	0.365‡	26 (24.3)	0.001‡
> 12	58 (18.1)	26 (21.7)		40 (37.4)	
Body mass index (kg/m^2)					
< 20	76 (23.9)	9 (8.0)		9 (8.7)	
20-27	222 (69.8)	94 (83.2)	0.001‡	72 (69.9)	0.001‡
> 27	20 (6.3)	10 (8.8)		22 (21.4)	

AGC, advanced gastric cancer; EGC, early gastric cancer
*p value between AGC and EGC, †p value between AGC and controls, ‡Pearson chi-square test

Factors concerning the gastric examination

Factors associated with gastric examination were age and history of gastritis among gastric cancer patients in this study (data not shown). No significant differences were found according to sex, place of residence, family history of gastric cancer, smoking, alcohol drinking, education and economic status with respect to history of gastric examinations.

Multivariate analysis of gastric examination among patients with advanced and early gastric cancer

Multivariate analysis was performed to control for confounding variables such as sex, age and history of gastritis which was significant variable for the gastric examination among gastric cancer patients. Odds ratio of having been examined (at least one time) vs. unexamined for those who were diagnosed as advanced gastric cancer compared to those who were diagnosed early gastric cancer was calculated as 0.388 (95% CI 0.230-0.645) (Table 3).

Odds ratios for previous examination of less than two years of diagnosis and within 2-3 years of diagnosis compared with never examined in the same interval were 0.468 (95% CI 0.225-0.976) and 0.310 (95% CI 0.079-0.856), respectively ($p<0.05$). Odds ratios for previous examination within 3-4 years of diagnosis (OR=0.516, 95% CI 0.122-2.178), within 4-5 years of diagnosis (OR=0.314, 95% CI 0.079-1.250) and more than 5 years (OR=0.366, 95% CI 0.131-1.022) were not statistically significant.

Multivariate analysis of gastric examination among patients with advanced gastric cancer and controls

Odds ratio of having been examined vs. unexamined for those who were diagnosed as advanced gastric cancers compared to the control group was calculated as 0.401 (95% CI 0.228-0.705) (Table 4).

Odds ratios for previous examination of less than two years of diagnosis and within 2-3 years of diagnosis compared with never examined in the same interval were

Tabel 2. Distribution of advanced and early gastric cancer patients and controls according to the risk factors and selected variables

Risk factors	AGC	EGC	p^*	Controls	$p^\dagger$
	No. (%)	No. (%)		No. (%)	
History of gastritis / gastric ulcer					
No	231 (72.0)	95 (79.2)	0.125	95 (88.8)	0.001
Yes	90 (28.0)	25 (20.8)		12 (11.2)	
Experience of gastric examination					
No	262 (82.1)	81 (68.1)	0.001	78 (72.9)	0.039
Yes	57 (17.9)	38 (31.9)		29 (27.1)	
Family history of gastric cancer					
No	265 (82.8)	101 (84.2)	0.735	105 (98.1)	0.001
Yes	55 (17.2)	19 (15.8)		2 (1.9)	
Smoking history					
Non-smoker	145 (45.2)	55 (45.8)	0.901	59 (55.1)	0.074
Smoker	176 (54.8)	65 (54.2)		48 (44.9)	
Alcohol drinking					
No	158 (49.4)	63 (52.5)	0.559	63 (58.9)	0.089
Yes	162 (50.6)	57 (47.5)		44 (41.1)	
H. pylori infection					
No	114 (54.8)	47 (59.5)	0.475	17 (51.5)	0.724
Yes	94 (45.2)	32 (40.5)		16 (48.5)	

AGC, advanced gastric cancer; EGC, early gastric cancer
*p value between AGC and EGC, $^\dagger p$ value between AGC and controls

Table 3. Multivariate analysis of gastric examination among patients with advanced and early gastric cancer according to interval since last examination

Gastric examination	AGC	EGC	Adjusted OR	95% CI	Adjusted p^*
Not examined	262	81	1		
Examined	57	38	0.388	0.230-0.654	< 0.001
Months since last test					
Never	262	81	1		
< 24	23	14	0.468	0.225-0.976	0.043
24-35	9	8	0.310	0.112-0.856	0.024
36-47	6	3	0.516	0.122-2.178	0.368
48-59	5	4	0.314	0.079-1.250	0.100
> 60	12	7	0.366	0.131-1.022	0.055

AGC, advanced gastric cancer; EGC, early gastric cancer
*Based on unconditional logistic regression including terms for sex, age, and history of gastritis

0.444 (95% CI 0.208-0.948) and 0.287 (95% CI 0.097-0.847), respectively ($p<0.05$). Odds ratios for previous examination within 3-4 years of diagnosis (OR=0.339, 95% CI 0.074-1.561) and within 4-5 years of diagnosis (OR=1.097, 95% CI 0.100-8.336) were not statistically significant.

DISCUSSION

This study shows the effectiveness of gastric cancer screening for detecting gastric cancer at earlier stages. The effective interval of screening is also shown to be three years or less. Even though gastric cancer is a large problem in Korea, this study was the first to evaluate the effectiveness of gastric cancer screening in Korea. Elucidation of the effective interval for gastric cancer screening also significantly contributes to the efficient utilization of health care resources for management of this serious disease.

Limitations of this study stem from the study design and setting of the study in a tertiary medical center.

Table 4. Multivariate analysis of gastric examination among patients with advanced gastric cancer and controls according to interval since last examination

Gastric examination	AGC	Controls	Adjusted OR	95% CI	Adjusted *p**
Not examined	262	78	1		
Examined	57	29	0.401	0.228-0.705	0.002
Months since last test					
Never	262	78	1		
< 24	23	13	0.444	0.208-0.948	0.036
24-35	9	7	0.287	0.097-0.847	0.024
36-47	6	3	0.339	0.074-1.561	0.165
48-59	5	1	1.097	0.100-8.336	0.935
> 60	12	0	-	-	0.983

AGC, advanced gastric cancer
*Based on unconditional logistic regression including terms for sex, age, and history of gastritis

Randomized clinical trial to define cancer mortality difference between intervention and control groups would be ideal to assess this question (14-16). However, such studies are too costly and difficult. Also, as screening for gastric cancer is conducted on a voluntary basis in Korea, without a national mass screening program, such a study would be plagued with volunteer bias. As this study was a case-control design, we were not able to directly measure the effectiveness of the screening test. Though the odds of having been examined for those with early and advanced gastric cancer are different, they can only approximate the effectiveness of the gastric cancer screening test. However, to achieve as firm a comparison as possible, we utilized both the early gastric cancer group and hospitalized non-gastric cancer patients as comparison groups and found similar results. We excluded gastric cancer screening examinations within six months prior to diagnosis to ensure the screening nature of the examination. We included only new gastric cancer patients as cases to preserve the screening nature of the examinations by comparing only the expected outcomes of this screening test. The hospital setting of this study limits the generalization of this study, yet the findings of this study should prompt a larger study with general population level comparisons. Differences in age and body weight between early gastric cancer group and advanced gastric cancer group should not influence the comparison of history of gastric examinations.

The findings of this study are also consistent with studies in other countries. The odds ratio of 0.39 (0.23-0.65), comparing the patients with advanced and early gastric cancer who were never screened prior to their diagnosis with those who were screened once, is compatible with the result of Fukao et al. (0.41, 0.28-0.61) (9) and Pisani et al. (0.47, 0.24-0.98) (10). It is also concordant with Abe et al. (0.417 for men, 0.480 for women) (11) and Oshima et al. (0.590 for men, 0.382 for women), who calculated separate odds ratios for men and women (8).

Due to insufficient sample size, we failed to find a linear trend of odds ratios by years prior to screening. However, the result shows that screening interval of three years or less is statistically optimal to reduce the gastric cancer mortality. This is also concordant with the result of Pisani et al. (10) and Abe et al. (11). Others suggest 2 years (8) and 5 years (9) as optimal screening interval. For practical reasons, as well as based on our study results, we feel a screening interval of three years or less would be optimal.

In summary, patients with advanced gastric cancer were 61% less likely to have had a gastric examination than those with early gastric cancer. The optimal screening interval should be three years or less. Mass clinical trials would be able to analyse the cost-effectiveness of gastric cancer screening.

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