Gastric Cancer Screening

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Abstract

Gastric cancer is one of the most common cancers worldwide, and East Asian countries including Korea, Japan, and China have a higher incidence of gastric cancer. Although there was no randomized controlled study for effectiveness of gastric cancer screening, Korea and Japan have provided government-supported national screening programs for gastric cancer. Several case-control studies and recent cohort studies have reported the effectiveness of radiographic screening for gastric cancer in Japan. Japanese guidelines for gastric cancer screening recommend that radiographic screening was the only effective method because of a lack of studies using endoscopic screening. From analysis of Korean national cancer screening data, endoscopy was more effective than radiography for gastric cancer screening because the accuracy of endoscopy is much higher than that of radiography. The Korean National Cancer Screening Program has recommended either endoscopy or radiography screening for gastric cancer, but the 2015 updated Korean guideline recommends only endoscopy for national cancer screening program. In this chapter, the accuracy and effectiveness of gastric cancer screening by screening modalities and gastric cancer screening guidelines of Korea and Japan will be discussed.

Keywords

Gastric cancer • Screening • Mortality • Case-control study • Cohort study • Stage shift • Early gastric cancer

49.1 Introduction

Gastric cancer is one of the most common cancers and ranks as the third leading cause of cancer-related deaths worldwide [1]. East Asian countries including Korea, Japan, and China have a higher incidence of gastric cancer

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than other countries. Korea and Japan have provided government-supported national screening programs for gastric cancer. Since 1965, the Japanese government has provided annual radiographic screening. The South Korean government has provided biennial gastric cancer screening using endoscopy or radiography to people over 40 years, since 1999 [2]. There was no randomized controlled study for effectiveness of gastric cancer screening. However, several case-control studies and recent cohort studies have reported the effectiveness of radiographic screening for gastric cancer in Japan [2, 3]. In 2008, the Japanese guidelines for gastric cancer screening through evidence-based methods reported that radiographic screening was the only effective method because of a lack of studies using endoscopic screening [3]. From analysis of Korean national cancer screening data, endoscopy was reported to be more effective than radiography for gastric cancer screening because the accuracy of endoscopy was much higher than that of radiography [4]. Before the 2015 Korean National Cancer Screening Program (NCSP) has recommended either endoscopy or radiography screening for gastric cancer but the updated Korean gastric cancer screening guideline in 2015 recommends only EGD for national cancer screening program based on a meta-analysis for the effect of endoscopic screening on gastric cancer mortality [5].

The main modalities for gastric cancer screening are esophagogastroduodenoscopy (EGD) and contrast imaging study. EGD allows direct visualization of the entire gastric mucosa and biopsies to confirm the histologic type. Although EGD is more invasive and usually has a higher cost, it is more sensitive for diagnosing gastric lesions. Double-contrast barium radiographs with photofluorography or direct radiography can also identify gastric lesions. However, the rate of false-negative study was reported up to 50% of cases [6]. In early gastric cancer, the sensitivity of radiographic study may be as low as 14% [7]. In this chapter, the accuracy and effect of gastric cancer screening by screening modalities and gastric cancer screening guidelines of Korea and Japan will be discussed.

49.2 Accuracy of Gastric Cancer Screening Methods

49.2.1 Endoscopic Screening

Sensitivity and specificity of endoscopic screening was constantly high in both Korean and Japanese studies [4, 8]. In a large Korean cohort study using 2,250,392 gastric cancer screenees, sensitivity and specificity for 924,822 cases of endoscopic screening were 0.69 (95% confidence interval [CI], 0.67–0.71) and 0.96 (95% CI, 0.96–0.96) [4]. In a Japanese study using 56,676 screenees, sensitivity for 7,388 cases of endoscopic screening was 0.89 (95% CI, 0.70–0.98) in the prevalence method and 0.95 (95% CI, 0.84–0.99) in the incidence method. And specificity was 0.85 (95% CI, 0.84–0.86) in the prevalence method and 0.89 (95% CI, 0.88–0.89) in the incidence method [8].

49.2.2 Radiographic Screening

Sensitivity of radiographic screening for gastric cancer was far different between the Korean and the Japanese study (Fig. 49.1). A large Korean study showed very low sensitivity (0.37) and high specificity (0.96) [4]. Sensitivity from a Costa Rican study by Rosero-Bixby (58%) was better 58% than that of the Korean study [9]. A Japanese study showed higher sensitivity ranging from 0.69 to 0.93 and lower specificity ranging from 0.88 to 0.91 than that of the Korean study [8, 10–13]. Pooled sensitivity of radiographic screening except that of the Korean study was 0.84 [5].

Possible explanations for the different sensitivities are the screening intervals (2 years in Korea vs. 1 year in Japan), the definition of positive findings (only gastric cancer-suspected lesions were regarded as positive findings in the Korean study but all abnormal findings were considered as positive findings in Japanese studies),

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)
Choi (2012)	1,196	68,853	2,067	1,693,793	0.37 [0.35, 0.38]	0.96 [0.96, 0.96]
Rosero-Rixby (2007)	38	163	27	6,600	0.58 [0.46, 0.71]	0.98 [0.97, 0.98]
Fukao (1992)	356	17,375	158	138,049	0.69 [0.65, 0.73]	0.89 [0.89, 0.89]
Abe (2000)	315	15,684	77	152,417	0.80 [0.76, 0.84]	0.91 [0.91, 0.91]
Ishida (1994)	53	6,703	10	29,055	0.84 [0.73, 0.92]	0.81 [0.81, 0.82]
Hamashima (2013)	48	2,001	6	14,772	0.89 [0.77, 0.96]	0.88 [0.88, 0.89]
Yamamoto (2010)	227	11,114	19	112,137	0.92 [0.88, 0.95]	0.91 [0.91, 0.91]
Higashiyama (2010)	782	39,953	57	391,107	0.93 [0.91, 0.95]	0.91 [0.91, 0.91]

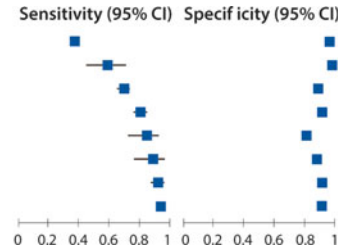

Fig. 49.1 Meta-analysis on the accuracy of radiographic screening. *TP* true-positive, *FP* false-positive, *FN* false-negative, *TN* true-negative, *CI* confidence interval (Adapted from Park et al. [5])

or the film-reading system (one reader in Korea vs. two well-trained readers in Japan).

49.2.3 Comparison of Sensitivity Between Endoscopic and Radiographic Screening

One Korean and one Japanese study showed the sensitivity of endoscopic and radiographic screening at the same time [4, 8]. A huge Korean cohort study showed higher sensitivity for endoscopic screening compared to radiographic screening (69.0 % vs. 36.7 %) and similar specificity (96.0 % vs. 96.1 %) [4]. A Japanese case-control study also showed similar pattern [8].

49.3 Effect of Gastric Cancer Screening on Gastric Cancer Mortality

49.3.1 Endoscopic Screening

Two case-control and two cohort studies evaluated the effect of endoscopic screening on gastric cancer mortality in the general population [14–17]. In a case-control study by Hamashima et al., odds ratio (OR) for endoscopic screening within 36 months of the date of diagnosis was 0.70 [14]. The Korean NCSP report by Cho enrolled a baseline cohort between 2002 and 2003 and investigated gastric cancer development up to 2008 and gastric cancer death up to 2011 [15]. Endoscopic screening decreased gastric cancer mortality (adjusted OR, 0.43). A Japanese cohort study by Matsumoto showed that the relative risk (RR) of gastric cancer mortality was 0.35 [16]. A Japanese cohort study by Hosokawa demonstrated that the RR for gastric cancer death in the screened group was 0.35 [17]. Three Japanese studies and a large Korean study constantly showed that endoscopic screening reduced gastric cancer mortality.

49.3.2 Radiographic Screening

The effect of radiographic screening on gastric cancer mortality was far different among nations. A case-control study by Oshima et al. reported that the OR of gastric cancer mortality in the radiographic-screened group was estimated at 0.52 (90 % CI, 0.30–0.91) in men and 0.49 (90 % CI, 0.24–0.99) in women [18]. A case-control study in Venezuela demonstrated that radiographic screening reduced gastric cancer mortality [19]. In a case-control study from Miyagi prefecture in Japan, radiographic screening reduced gastric cancer mortality in men but not in women [20]. Another case-control study by Tsubono et al. reported a reduction in mortality of 79 % in the radiographic-screened group [21]. However, radiographic screening did not reduce gastric cancer mortality in a study by Hamashima et al. [14]. Cho et al. conducted a large-scale case-control study from the Korean NCSP. Radiographic screening showed only a 7 % reduction in gastric cancer mortality [15].

A population-based cohort study by Inaba et al. reported that radiographic screening did not reduce gastric cancer mortality signifi-

cantly in both men and women [22]. In a prospective cohort study by Mizoue et al., radiographic screening reduced gastric cancer mortality in men but not in women [23]. In a population-based prospective cohort study by Lee et al., 40 % reduction in gastric cancer death was noted in the screened group [24]. Another Japanese cohort study reported that radiographic screening reduced gastric cancer mortality [25]. A cohort study from Costa Rica suggested that gastric cancer mortality was about twofold higher in unscreened groups than screened groups [9]. A cohort study by Matusmoto demonstrated that gastric cancer mortality was 0.13 % in the unscreened group and 0.07 % in the radiographic-screened group [16].

Cohort studies from Japan and Costa Rica showed constant reduction of gastric cancer mortality in the radiographic-screened group. However, the effect from case-control studies has discrepancy by nations. Japan and Venezuela studies suggested significant reduction of gastric cancer mortality, but a huge Korean case-control study showed just 7 % reduction in radiographic-screened group. The main cause of this discrepancy seems to originate from the sensitivity difference of radiographic screening. The sensitivity was 69–83 % in the Japanese studies but 37 % in the Korean study.

49.4 Guidelines

49.4.1 Updated Korean Guideline 2015

The Korean government has provided gastric cancer screening program for the general population since 1999 even if the effectiveness or harms of gastric cancer screening using EGD and radiographic screening had not been fully evaluated. Recently the Korean multidisciplinary expert committee for developing a gastric cancer screening guideline systematically reviewed the evidence regarding the benefits and harms of gastric cancer screening and developed an evidence-based clinical guideline [5] (Table 49.1). They found a "low"-level evidence that gastric cancer screening using EGD or upper gastrointestinal (UGI) series could reduce gastric cancer mortality in the general population between 40 and 74 years. The benefits of gastric cancer screening using EGD were substantially higher than its harms, while the benefits of radiographic screening were moderately higher. Therefore, this guideline recommended biannual EGD for asymptomatic adults from 40 to 75 years (recommendation B). Radiographic screening in asymptomatic adults between 40 and 74 years could be recommended based on clinicians' judgment regarding the patient's risk and the patient's preference (recommendation

Table 49.1 Updated Korean gastric cancer screening guideline

		Substantial	Benefit size		
			Moderate	Small	Zero/negative
Evidence level	High	A	B	C	D
	Moderate	A	B	C	D
	Low	B (EGD from 40 to 74 years)	C (radiographic screening from 40 to 74 years)	C	D (asymptomatic adults older than 85 years)
	Very low	I	I	I (adults aged between 75 and 84 years)	I

Recommendation grade A means strong recommendations for screening; B means moderate recommendations for screening; C means selective recommendation considering clinical decision and screenee's favorites; D means no recommendation for screening; I means insufficient evidence to estimate the size of benefit and harm
EGD esophagogastroduodenoscopy

C). Gastric cancer screening had insufficient evidence (recommendation I) for adults aged between 75 and 84 years and was not recommended for asymptomatic adults older than 85 years (recommendation D).

49.4.2 Japanese Guideline

The Japanese committee evaluated four methods for gastric cancer screening (photofluorography, endoscopy, serum pepsinogen testing, and *H. pylori* antibody testing) and reported the screening guideline 2008. The studies that evaluated mortality reduction from gastric cancer included five case-control and two cohort studies for radiographic screening. Gastric cancer screening using photofluorography was recommended. The other methods were not recommended for population-based screening due to insufficient evidence. However, the recent Japanese committee suggested the effectiveness of endoscopic screening, and some provinces have used both endoscopic and radiographic study for gastric cancer screening.

Conclusion

Korea and Japan, high-prevalence areas of gastric cancer, have provided national screening programs for gastric cancer. Whereas the Japanese government has provided annual radiographic screening, the South Korean government has provided biennial gastric cancer screening using endoscopy or radiography to people over 40 years. Even if there was no randomized controlled study for the effectiveness of gastric cancer screening, several case-control studies and recent cohort studies have reported the effectiveness of radiographic screening for gastric cancer in Japan. However, recent population-based screening studies demonstrated reduced gastric cancer death in the endoscopic screening group. Furthermore, endoscopic screening was more sensitive than radiographic screening and constantly reduced gastric cancer mortality, whereas the sensitivity of radiographic screening was variable and mortality reduction was also variable by study area. Therefore, the 2015 updated Korean guideline recommends only EGD for gastric cancer screening because of the low sensitivity and minimal reduction of gastric cancer death of radiographic screening in Korea.

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