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Efficacy of Risk-Stratified Screening for Gastric Cancer: A Retrospective Repeated Cross-Sectional Study in Yokosuka, Japan

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Abstract

Introduction: Gastric cancer (GC) is mostly related to Helicobacter pylori (Hp) infection, and risk-stratified screening (RS) for GC has been adopted in some cities. We aimed to investigate the efficacy of RS as compared with barium X-ray screening (XR) recommended by Japan for GC.

Methods: Repeated cross-sectional study from the data of Yokosuka Public Health Center. The GC screening participants were >40 years old from 2002 to 2018. RS was classified by pepsinogen test screening (PG) and Helicobacter pylori (Hp) tests into low and high-risk groups. The primary endpoints were detection rates of all GC and early GC (TNM T1). Secondary endpoints were participation rate and GC detection cost. For GC detection, the odds ratios were calculated by logistic regression models adjusted for age, sex, and first visit or revisit.

Results: A total of 448,244 participants' data were included. In multivariable analyses, the odds ratios of PG and RS vs XR were 2.26 and 3.73 for GC detection, and 4.64 and 10.63 for early GC detection, respectively (p<.00001). The citizens' participation rate increased significantly from 3.9% in XR to 22.2% in RS, and 23.1% in RS. Hp eradication was successful in 83.9% of the high-risk groups. GC detection cost by RS was 29.99 and 1.60 times lower as compared with XR and PG, respectively (p<0.0001).

Conclusion: RS was more effective than XR for detecting GC and the detection cost was lower. RS might contribute to citizens' future survival by the improved early GC detection, participation, and Hp eradication system.

Keywords: Gastric cancer; Screening; Helicobacter pylori; Pepsinogen test; Detection cost

Introduction

Cancer is related to lifestyle, but 15% is caused by infection and gastric cancer (GC) is mostly related to Helicobacter pylori (Hp) infection. Hp causes chronic active gastritis, atrophic gastritis, and intestinal metaplasia, which lead to GC. Pepsinogen I and II are produced by the gastric mucosa, and serum pepsinogen test screening (PG) is used for screening to identify the atrophic gastritis. The incidence of GC varies widely in the world related to various pathogenic factors including Hp CagA gene and its polymorphisms. Although the prevalence of GC is extremely high in Asia and can be cured by early detection, population-based screening has not been organized other than in Japan and South Korea, with no global standard [1-5].

Japan has organized gastric barium X-ray screening (XR) for a long time since the 1960's. At the time of the screening introduction, there were more than 70% of Hp infections in Japanese people, and most of them were in the high-risk group for GC. By cohort studies, the XR contributed to the reduction of the mortality rate, and it has been recommended in the Japanese guideline since 2005. Besides, endoscopic screening was required among the advancement of electronic endoscopes; it had been postponed with no clear effectiveness for survival until 2016 as a second option. In recent years, the infection rate of Hp and high-risk people has decreased, and the past effectiveness of XR is unclear right now, and some cities have adopted a different type of screening [6-8].

Yokosuka is a core city of about 400,000 people, and the Public Health Center added PG to XR for GC screening in 2001. Initially, the participants could choose either XR or PG; then in 2012, the city discontinued XR and changed to risk-stratified screening (RS) combining PG and Hp antibody (HpAb). RS improves the sensitivity by adding the high-risk group that is not included in the PG method alone. No specialist would argue that endoscopy is the most accurate for early GC detection; however, there are several problems in adopting it as the primary screening as follows. GC has been decreasing along with the lowering Hp infection rate, and participation in endoscopy is poor due to its cost, burden, and inadequate stuffing. We aim to examine the efficacy of RS for GC using the large data including participants' characteristics in Yokosuka City [9].

It was reported that cost-effectiveness could be improved by conducting selective screening focusing on human papillomavirus and hepatitis virus for cervical and liver cancer, respectively. Also in Singapore, a significant cost reduction effect was observed when endoscopic surveillance was performed for patients combining the risks for GC. Until now, Japan has standardized relatively high-cost XR and endoscopy for GC screening

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without choosing high-risk groups. In this repeated cross-sectional study, we compared RS and XR for the efficacy of GC detection [10-13].

Materials and Methods

Study design and enrollment

In this repeated cross-sectional study, we analyzed the screening data between April 2002 and March 2018 from the Yokosuka Public Health Center. Screening methods were XP or PG between 2002 and 2011, and RS between 2012 and 2018. The target citizens were aged >40 excluding the following criteria:

1. Obvious symptoms strongly suspected of gastric or duodenal disease
2. Undergoing treatment for diseases of the oesophagus, stomach, or duodenum
3. Have taken gastric acid secretion inhibitors within 2 months
4. After gastrectomy
5. After treatment to eradicate Hp
6. Renal failure (serum creatinine >3 mg/dl)
7. RS result was judged as A (Hp-PG-) and has not passed 5 years
8. Already judged other than A.

The data were yearly summarized by background factors: age, sex, first visit or revisit, and the short-term results of GC and/or other disease detection in all groups. The results of the RS work-up examination for high-risk groups and the cost for GC detection were collected from the medical association in the city. The database was used by the analysis team (MM, MT, and AT) excluding the personal information.

Risk-stratification procedure

Atrophic gastritis was stratified using a combination of PGI 70 ng/ml or less and I/II ratio 3.0 or less (PG+) or others (PG-). In the RS, groups were classified into A (Hp-PG-), B (Hp+ PG-), C (Hp+ PG+), and D (Hp-PG+). Groups B, C, and D were subjected to work-up endoscopic examination by public insurance and followed up. Group A was not re-examined for 5 years after diagnosis, but endoscopy was available for insurance medical treatment. The cutoff value of HpAb (E-plate, Eiken Chemical Co.) was changed from 10 to 3 U/mL in 2016, and 3 to 9.9 U/mL cases were reassessed by urea breath test or Hp stool antigen after endoscopy. Hp eradication results in the Hp+ group were confirmed annually. Long-term course and prognosis data were not included. The cost for GC detection was analyzed among 77,714 people who visited medical institutions: hospitals or clinics, other than the Public Health Center from 2006 to 2018.

Statistical analysis

For efficacy, we set the primary endpoints as detection rates of all GC and early GC (TNM T1: M or SM). Secondary endpoints were participation rate in target citizens and cost for GC detection. For these outcomes, the PG or RS group was compared to the XR group as a control. Characteristics of the groups and participation rate were compared by chi-square tests between the groups. For GC detection, the odds ratios were calculated by multivariable logistic regression models adjusted for age (40-49/50-59/60-69/70-74/75≤), sex (male/female), and the number of visits (first visit/revisit). The cost for GC detection was calculated by dividing the total cost by the number of detected GC for each group. The annual cost required for the screening was the sum of reward, travel, and consumables expenses (printing and transportation costs), maintenance and business management fees (system development, medical checkup, image interpretation, and medical checkup administration fees).

A two-sided $p<0.05$ were regarded as statistically significant. All analyses were conducted using Microsoft Excel and SAS Version 9.4 (SAS Institute, Inc., Cary, NC, USA). The study was conducted according to Declaration of Helsinki, and started after approval and waiver of informed consent by the Institutional Review Board of the Yokosuka City Medical Association (#143, 26 March 2019).

Results

Characteristics of study participants

This analysis included 448,244 citizens who participated in the GC screening from 2002 to 2018. Age and sex were almost similar among the groups, and the number of participants tended to be higher in 60-69 years old and female groups (Table 1). First visit was more common in RS group, followed by PG and then XR. Target citizens were 1,747,939 in total and the overall participation rate was 25.6%. The rate was higher in RS group (23.1%), followed by PG (22.8%) and then XR (3.9%) groups. Between 2002 and 2011, 85.3% of the participants chose PG method, and the higher participation was maintained after the change to RS.

Characteristics	XR (2002-2011)		PG (2002-2011)		p-value	RS (2012-2018)		p-value
	n=46,808		n=272,114			n=129,322		
	n	%	n	%		n	%	
Age								
40-44	2,188	4.70%	13,754	5.10%	<0.001	10,174	7.90%	<0.001
45-49	2,344	5.00%	12,688	4.70%		8,376	6.50%	
50-54	3,358	7.20%	17,102	6.30%		8,046	6.20%	
55-59	5,586	11.90%	27,984	10.30%		8,786	6.80%	
60-64	10,216	21.80%	46,206	17.00%		16,568	12.80%	
65-69	10,720	22.90%	54,346	20.00%		25,824	20.00%	
70-74	7,124	15.20%	46,346	17.00%		24,356	18.80%	
75-79	3,952	8.40%	31,924	11.70%		15,842	12.30%	
80<	1,320	2.80%	21,764	8.00%		11,350	8.80%	
Sex								

Male	18,644	39.80%	92,674	34.10%	<0.001	49,500	38.30%	<0.001
Female	28,164	60.20%	1,79,440	65.90%		79,822	61.70%	
Visit								
First	14,600	31.20%	1,24,528	45.80%	<0.001	1,12,996	87.40%	<0.001
Second ≤	32,208	68.80%	1,47,586	54.20%		16,326	12.60%	
Target citizens and participation rate								
	11,90,916	3.90%	11,90,916	22.80%		5,59,023	23.10%	<0.001
Abbreviations: XR barium X-ray screening, PG pepsinogen test screening, RS risk-stratified screening								

Table 1: Participants' characteristics and participation rate (n=448,244)

Detection rate of gastric cancer

Table 2 shows cases of detected GC and early GC by screening methods and background factors. In the same ten years (2002-2011), a total of 28 and 454 GC, 4 and 135 early GC were detected by XR and PG, respectively. Approximately 16 and 34 times more GC and early GC were detected by PG compared to XR, respectively. In the next seven years (2012-2018), total cases detected by RS were much higher including 554 GC and 237 early GC. In multivariable logistic regression analyses, GC detection rates were higher in older groups (>50 years old) with odds ratios between 10.1 and 42.7 as compared to <50 years old group, and odds ratios for early GC detection tended to be much higher between 19.0 and 77.0 (Table 3). In sex and visit categories, detection rates were lower in female and revisit groups with odds ratios between 0.25 and 0.30 for both GC and early GC. Comparing the screening types adjusted by other factors, the odds ratios of PG and RS vs XR were 2.26 and 3.73 for GC detection and 4.64 and 10.63 for early GC detection, respectively (p<.00001) (Table 2 and 3).

Characteristics	XR (n=46,808)				PG (n=272,114)				RS (n=129,322)			
	GC		Early GC		GC		Early GC		GC		Early GC	
	n	%	n	%	n	%	n	%	n	%	n	%
Age												
40-49	0	0.00%	0	0.00%	2	0.00%	0	0.00%	3	0.00%	1	0.00%
50-59	1	0.00%	0	0.00%	33	0.01%	11	0.00%	22	0.02%	9	0.01%
60-69	15	0.03%	3	0.01%	141	0.05%	45	0.02%	191	0.15%	85	0.07%
70-79	8	0.02%	1	0.00%	213	0.08%	60	0.02%	254	0.20%	109	0.08%
80 ≤	4	0.01%	0	0.00%	65	0.02%	19	0.01%	84	0.07%	33	0.03%
Sex												
Male	20	0.04%	3	0.01%	293	0.11%	93	0.03%	398	0.31%	171	0.13%
Female	8	0.02%	1	0.00%	161	0.06%	42	0.02%	156	0.12%	66	0.05%
Visit												
First	14	0.03%	2	0.00%	310	0.11%	95	0.04%	547	0.42%	235	0.18%
Second ≤	14	0.03%	2	0.00%	144	0.05%	40	0.02%	7	0.01%	2	0.00%
Total												
	28	0.06%	4	0.01%	454	0.17%	135	0.05%	554	0.43%	237	0.18%
Abbreviations: XR barium X-ray screening, PG pepsinogen test screening, RS risk-stratified screening, GC gastric cancer												

Table 2: Gastric cancer detection rate by participants' characteristics and screening methods

	Univariate analysis			Multivariate analysis		
		Odds ratio (95% CI)	p-value		Odds ratio (95% CI)	p-value
Method	**Gastric Cancer (all)**					
XR	ref			ref		
PG	2.79	(1.91-4.09)	<.0001	2.26	(1.54-3.31)	<0.001
RS	7.19	(4.92-1051)	<.0001	3.73	(2.53-5.49)	<0.001
Age (years)						
40-49	ref			ref		

50-59	7.83	(3.14-19.55)	<.0001	10.08	(4.04-25.16)	<0.001
60-69	21.01	(8.69-50.81)	<.0001	23.26	(9.62-56.25)	<0.001
70-74	34.48	(14.23-83.51)	<.0001	35.14	(14.51-85.14)	<0.001
75 <	41.33	(17.10-99.90)	<.0001	42.74	(17.68-103.3)	<0.001
Sex						
Sex		ref		ref		
Gastric	0.26	(0.22-0.29)	<0.001	0.30	(0.27-0.35)	<0.001
Visit						
First	ref			ref		
Second ≤	0.24	(0.21-0.29)	<.0001	0.29	(0.25-0.35)	<0.001
Method	**Early Gastric Cancer**					
XR	ref			ref		
PG	5.81	(2.15-15.71)	<.0001	4.64	(1.71-12.55)	0.002
RS	21.52	(8.01-57.81)	<.0001	10.63	(3.93-28.81)	<0.001
Age						
40-49	ref			ref		
50-59	13.96	(1.88-103.9)	0.01	19.02	(2.55-141.8)	0.004
60-69	40.2	(5.63-287.0)	<.0001	46.3	(6.47-331.2)	<0.001
70-74	60.51	(8.45-433.4)	<.0001	62.98	(8.78-451.9)	<0.001
75<	73.11	(10.23-522.3)	<.0001	77.04	(10.76-551.4)	<0.001
Sex						
Male	ref			ref		
Female	0.23	(0.18-0.29)	<.0001	0.27	(0.22-0.34)	<0.001
Visit						
First	ref			ref		
Second ≤	0.17	(0.12-0.23)	<.0001	0.25	(0.18-0.35)	<0.001
Abbreviations: XR barium X-ray screening, PG pepsinogen test screening, RS risk-stratified screening,						

Table 3: Odds ratios for gastric cancer detection rate

Outcome of RS group and cost for detecting gastric cancer

In the RS, Hp+ rate was 33.8%, and the high-risk groups (B, C, D) was 39.9%, in which 82.8% received the work-up examination, i.e., endoscopy (Table 4). A close examination revealed that 57% had no abnormality and 43% had some disease including early GC in 1.0% and advanced GC in 0.3%. Hp eradication had been successful in 83.9% of the target participants, which was equivalent to 11.0% of the whole examinees. Among the detected GC between 2016 and 2018 (n=57), five cases (8.8%) were PG and 3 to 9.9 U/mL HpAb titer, all of them were early GC.

Classification (n=64,661)		n	%
HP	Hp-	42,647	66.00%
	Hp+	21,831	33.80%
RS	A	38,838	60.10%
	B	15,183	23.50%
	C	8,720	13.50%
	D	1,737	2.70%
Workup	Early GC	214	1.00%
(n=21,230) examination	Advanced GC	74	0.30%
	Gastric polyp	2,321	10.90%
	Gastric/ duodenal ulcer	1,447	6.80%
	Gastritis	5,030	23.70%
	Other cancers	59	0.30%
Hp eradication (n=7093)			
	Success	5,948	83.90%
	Failure	1,064	15.00%
	Interruption	81	1.10%
All GC (n=2161a)			
	Detected by RS	288	13.30%
Abbreviations: Hp Helicobacter pylori, RS risk-stratified screening, GC gastric cancer			
a New GC cases in the same years in Yokosuka			

Table 4: RS and work-up examination results

The costs required to detect one GC case were compared among the groups (Table 5). Detection cost by RS was 30.0 and 1.60 times lower than by XR and PG, respectively (p<0.0001). Personal fees for the participant were also higher in XR than in PG or RS, 5.03 and 3.63 times, respectively. By year, the costs required for RS were almost the same (data not shown).

	XR	PG	RS
Year	2006-2011	2011	2012-2018
Factors and calculations			
Total cost	$1,651,120	$378,093	$1,958,666
Detected GC (n)/Total (n)	7 / 12,118	30 / 14,021	249 / 51,575
Median cost/year	$330,224	$378,093	$279,809
Personal fee	$136	$27	$38
Cost/detected case	$235,874	$12,603	$7,866
Discovery cost ratio	30.0	1.60	1.00 ref
***P<0.001**			
Abbreviations: XR barium X-ray screening, PG pepsinogen test screening, RS risk-stratified screening, GC gastric cancer			

Table 5: Gastric cancer detection cost by screening methods (n=77,714)

Discussion

Our results showed that detection odds ratios of RS vs XR were 3.7 and 10.6 for GC and early GC, respectively, by multivariable logistic regression analysis. Combining the Hp test with PG, RS further improved the detection rates. The participation rate also increased from 3.9% in XR to about 23% in PG and RS, resulting in annual detection from 2.8 cases in XR to 79.1 cases in RS (28 times higher). In Japan, 2,206 new GC were found by XR in 2015 with a detection rate of 0.09% (http://gdb.ganjoho.jp); accordingly about 1.7% of 128,881 new GC cases were found by XR screening in the year across the country. In our study, 13.3% of the new GC in the city was found by RS, and 74.3% of them were early GC. Since in many cases curative endoscopic treatment was possible for early GC, RS could contribute to the improvement of survival. In a meta-analysis of screening effects in Asia, the early cancer detection rate in the screened group was 3.90 times higher than in the non-screened group; also the 5 year survival rate was significantly better (HR0.56, p<0.0001) [14,15].

PG test focuses on chronic atrophic gastritis, while RS aims to identify the high-risk group for cancer by examining the current/pre-existing infection of oncogenic Hp. The advantage of the Hp test is not only to detect GC but also to prevent it by removing Hp. Choi IJ et al. reported that preventive Hp eradication reduced the incidence of GC by about half in a randomized trial. In our study, Hp eradication was successful in 84% of the target group (9.2% of the total participants). Vaccines have become the global standard for the prevention of cervical and liver cancer, while there is no vaccine for Hp. Hp eradication is not recommended in Japan, also it is estimated that the Japanese vaccine crisis has caused about 5,000 deaths so far in cervical cancer alone. The healthcare system focusing on preventive and effective medicine should be promoted [16,17].

In XR between 1994 and 2000 before the introduction of PG in 2001, the participation rate was 4.9% (the data were not in the results). The participation increased to 23% after introducing PG, and 85% of them chose PG other than XR. PG and RS are performed only by blood sampling for a short time at a low cost, which may have led to the participants' choice. Screening burden, time and cost; and risks such as radiation exposure and constipation by barium should be considered for the citizens. The cost required to detect GC was the lowest by RS at 1/30 of XR. Although the survival was not analyzed, considering the odds ratio of early GC detection (10.6), the cost-effectiveness of the RS might reach up to 150 times compared to XR. The RS is not approved by the national government, and many local governments are reluctant to introduce RS. On the other hand, the Yokosuka Public Health Center has built a good relationship with the city's medical associations, and they agreed to organize the public screening system. Although there are some barriers for cities to adopt such systems, local governments and doctors need fair and scientific cooperation for the well-being of their citizens in countries like Japan. Further to increase the participation, insufficient health literacy should be improved in Japan [18].

Our study has some limitations. This is a repeated cross-sectional study and detailed individual background data were not included, and the detection cost was analyzed only in the medical associations' data. The objectives of cancer screening are early detection and improvement of the prognosis of citizens, but it is difficult to complete large randomized trials and consequently, guidelines are limited. Also in Japan, the digitization of public health information has not developed over the years; we needed to confirm the efficacy of ongoing screening methods using large data as in this study. Digitalized healthcare systems should contribute to the future health and quality of life of citizens.

Conclusion

RS was more effective than XR for detecting GC with odds ratios of 3.73 and 10.63 for GC and early GC, respectively. In the RS group, the participation was about four times higher and the cost for GC detection was 30 times lower as compared to XR. Hp eradication had been successful in 83.9% of the target participants in RS. These results suggest that RS may improve the future survival of the citizens by increasing early GC detection and HP eradication with the low-cost and low-burden screening system.

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Authors' Contributions

AT designed the study and contributed to writing the manuscript. MM performed data collection, and MT and AT analyzed the data. All authors contributed to the research agenda and development process. All authors read and approved the final version of the manuscript.

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Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due to organizational confidential but are available from corresponding author upon reasonable request.

Ethics Approval and Consent to Participate

The study was approved by the institutional review board of the Yokosuka Medical Association.

Consent for Publication

Not applicable.

Competing Interests

The authors declare that they have no competing interests.

References

1. Plummer M, Franceschi S, Vignat J, Forman D, de Martel C (2015) Global burden of gastric cancer attributable to Helicobacter pylori. Int J Cancer 136(2):487-490.
2. Correa P (1992) Human gastric carcinogenesis: A multistep and multifactorial process first american cancer society award lecture on cancer epidemiology and prevention. Cancer Res 52(24):6735-6740.
3. Dinis-Ribeiro M, Yamaki G, Miki K, Costa-Pereira A, Matsukawa M, et al. (2004) Meta-analysis on the validity of pepsinogen test for gastric carcinoma, dysplasia or chronic atrophic gastritis screening. J Med Screen 11(3):141-147.
4. Huang JQ, Zheng GF, Sumanac K, Irvine EJ, Hunt RH (2003) Meta-analysis of the relationship between cagA seropositivity and gastric cancer. Gastroenterology 125(6):1636-1644.
5. Sugano K (2015) Screening of gastric cancer in Asia. Best Pract Res Clin Gastroenterol 29(6):895-905.
6. Hamashima C (2018) Update version of the japanese guidelines for gastric cancer screening. Jpn J Clin Oncol 48(7):673-683.
7. Hamashima C, Ogoshi K, Narisawa R, Kishi T, Kato T, et al. (2015) Impact of endoscopic screening on mortality reduction from gastric cancer. World J Gastroenterol 21(8):2460-2466.
8. Gotoda T, Ishikawa H, Ohnishi H, Sugano K, Kusano C, et al. (2015) Randomized controlled trial comparing gastric cancer screening by gastrointestinal X-ray with serology for Helicobacter pylori and pepsinogens followed by gastrointestinal endoscopy. Gastric Cancer 18(3):605-611.
9. Chen XZ, Huang CZ, Hu WX, Liu Y, Yao XQ (2018) gastric cancer screening by combined determination of serum. Chin Med J (Engl) 131(10):1232-1239.
10. Chuck A (2010) Cost-effectiveness of 21 alternative cervical cancer screening strategies. Value Health 13(2):169-179.
11. Hutton DW, Tan D, So SK, Brandeau ML (2007) Cost-effectiveness of screening and vaccinating Asian and Pacific Islander adults for hepatitis B. Ann Intern Med 147(7):460-469.
12. Han Y, Yan T, Ma H, Yao X, Lu C, et al. (2020) Cost-effectiveness analysis of Helicobacter pylori eradication therapy for prevention of gastric cancer: A markov model. Dig Dis Sci 65(6):1679-1688.
13. Zhou HJ, Dan YY, Naidoo N, Li SC, Yeoh KG (2013) A cost-effectiveness analysis evaluating endoscopic surveillance for gastric cancer for populations with low to intermediate risk. Plos One 8(12):e83959.
14. An L, Gaowa S, Cheng H, Hou M (2019) Long-term outcomes comparison of endoscopic resection with gastrectomy for treatment of early gastric cancer: A systematic review and meta-analysis. Front Oncol 9:725.
15. Khanderia E, Markar SR, Acharya A, Kim Y, Kim YW, et al. (2016) The influence of gastric cancer screening on the stage at diagnosis and survival: A meta-analysis of comparative studies in the far east. J Clin Gastroenterol 50(3):190-197.
16. Choi IJ, Kook MC, Kim YI, Cho SJ, Lee JY, et al. (2018) Helicobacter pylori therapy for the prevention of metachronous gastric cancer. N Engl J Med 378(12):1085-1095.
17. Simms KT, Hanley SJB, Smith MA, Keane A, Canfell K (2020) Impact of HPV vaccine hesitancy on cervical cancer in Japan: A modelling study. Lancet Public Health 5(4):e223-e234.
18. Nakayama K, Osaka W, Togari T, Ishikawa H, Yonekura Y, et al. (2015) Comprehensive health literacy in Japan is lower than in Europe: A validated Japanese-language assessment of health literacy. BMC Public Health 15:505