The Impact of High-Density Barium Use in Double Contrast Radiographic Methods for Gastric Cancer Screening in Niigata, Japan

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WAKAI, S., TANABE, N. and SUZUKI, H. The Impact of High-Density Barium Use in Double Contrast Radiographic Methods for Gastric Cancer Screening in Niigata, Japan. Tohoku J. Exp. Med., 2005, 205 (4), 343-349 —— Use of high-density barium (= or > 180 w/v%) has been widely spread in community-based mass screening for gastric cancer in Japan. However, the impact on outcomes of the screening has not been fully evaluated. Then, we investigated the advantage of high-density barium use by comparing the outcomes between a period with high-density barium and that with low-density barium (< 180 w/v%) each for 3 consecutive years between 1991 and 2002 at 5 medical examination organizations in Niigata Prefecture, Japan. Multivariate logistic regression analysis adjusted for age, sex and medical organization revealed that the introduction of high-density barium decreases the positive finding rate in initial mass screening x-ray examinations by 12% (odds ratio, 0.88; 95% confidence interval, 0.86 - 0.90) and increase the gastric cancer detection rate by diagnostic examination by 15% (odds ratio, 1.15; 95% confidence interval, 1.01-1.31). We conclude that introduction of high-density barium has improved the efficiency of mass screening for gastric cancer by decreasing unnecessary diagnostic examinations and reducing the total personal and public health costs. Thus, nationwide use of high-density barium is recommended for mass gastric cancer screening in Japan. ——— gastric cancer; mass screening; double contrast indirect radiography; high-density barium; cost effectiveness

Gastric cancer remained very common in Japan (World Cancer Research Fund and American Institute for Cancer Research 1997; Levi et al. 1999; Lambert et al. 2002), and the disease is still the second largest cause of cancer-related death (Statistics and Information Department, Minister’s Secretariat, Ministry of Health Labour and Welfare 2004). Community-based mass screening for gastric cancer by indirect x-ray examination with double contrast barium (x-ray examination) was initiated around 1960 in Japan (Hisamichi 1989; Tsubono and Hisamichi

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Low-density barium (< 180 w/v%) was employed initially for x-ray examination but recently, high density and low viscous barium (high-density barium, = or > 180 w/v%) has been introduced in order to increase the accuracy (Abe et al. 2000; Aoyagi et al. 2000; Tsuchigame et al. 2000; Noguchi et al. 2001; Tanno et al. 2003; Yamamoto et al. 2004). Because of the good mucosal adhesive strength, decrease of false positive cases have been achieved at many medical examination organizations (Tsuchigame et al. 2000; Tanno et al. 2003; Yamamoto et al. 2004). However, the impact of high-density barium use has not been fully evaluated by large-scale multi-center studies.

x-ray examinations for mass screening are now carried out at 17 medical examination organizations in Niigata, Japan (Wakai et al. 2003). During 1995 to 2001, the number of organizations using high-density barium increased from 3 to 9, and the percentage of participants undergoing testing with the high-density barium system increased from 12.2% to 23.7% (unpublished data). During the same period, the rate of positive findings decreased from 10.8% to 7.6%, and the gastric cancer detection rate from diagnostic examination by endoscopy for suspected cases increased from 2.4% to 3.4%. Thus, required number of diagnostic examination decreased to find a subject with gastric cancer, and the mass screening for gastric cancer has become more efficient in Niigata prefecture. These simultaneous changes suggest that introduction of high-density barium could improve the efficiency of mass screening for gastric cancer.

From these backgrounds, the present study was conducted to evaluate the impact of high-density barium use on mass screening for gastric cancer in a large-scale multi-center investigation in Niigata Prefecture.

**Materials and Methods**

The study was conducted in Niigata Prefecture in Japan, which is located in the middle of Honshu Island with a total population of approximately 2.5 million (in the 2,000 census). Mass screening using x-rays in accordance with the Health and Medical Services Law for the Aged is being carried out at 17 medical examination or-

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**Fig. 1. Flow chart of the mass screening survey for gastric cancer in Niigata.**

Number in parentheses shows number of subjects in each step for the present study.
<table>
<thead>
<tr>
<th>Medical examination organization</th>
<th>A</th>
<th>B</th>
<th>C</th>
<th>D</th>
<th>E</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barium density</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
<td>High</td>
<td>Low</td>
</tr>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Age</td>
<td>40-44</td>
<td>574</td>
<td>1,961</td>
<td>310</td>
<td>1,127</td>
</tr>
<tr>
<td>45-49</td>
<td>793</td>
<td>2,431</td>
<td>549</td>
<td>1,983</td>
<td>141</td>
</tr>
<tr>
<td>50-54</td>
<td>773</td>
<td>2,522</td>
<td>518</td>
<td>1,928</td>
<td>160</td>
</tr>
<tr>
<td>55-59</td>
<td>891</td>
<td>3,518</td>
<td>611</td>
<td>2,692</td>
<td>168</td>
</tr>
<tr>
<td>60-64</td>
<td>1,731</td>
<td>4,242</td>
<td>1,244</td>
<td>3,602</td>
<td>358</td>
</tr>
<tr>
<td>65-69</td>
<td>2,506</td>
<td>3,756</td>
<td>1,956</td>
<td>3,397</td>
<td>569</td>
</tr>
<tr>
<td>70-119</td>
<td>2,199</td>
<td>2,662</td>
<td>2,412</td>
<td>2,808</td>
<td>769</td>
</tr>
<tr>
<td>Total</td>
<td>9,467</td>
<td>21,092</td>
<td>7,600</td>
<td>17,537</td>
<td>2,236</td>
</tr>
</tbody>
</table>

Low, low-density barium, < 180 w/v%; High, high-density barium, = or > 180 w/v%.
ganizations in Niigata Prefecture, Japan. For our analysis, we selected 5 of them with the following criteria: more than 1,000 x-ray examinations/year, and possible comparison of outcomes with low-density and high-density barium for 3 consecutive years between 1991 and 2002.

Data for total of 356,962 participants aged over 40 years (130,795 males and 226,167 females) at the 5 medical examination organizations were analyzed for the present study (Table 1). Procedures of the mass screening were as follows (Fig. 1). As a first step, x-rays were taken using low or high density barium. As a next step in cases of suspected cancer, endoscopy and histological examination of stomach biopsies in case of need were carried out for final diagnosis. The final results were reported to the Niigata Association for Comprehensive Health Promotion and Research (the screening office) through the municipality office. A total of 981 of the 356,962 participants were diagnosed as having gastric cancers by these processes, and were analyzed in the present study. Information on invasion depth was mailed from clinics or hospitals to the screening office.

An intra-organizational comparative study was made of the following 4 items descriptively in the periods using low-density barium and high-density barium systems at the 5 medical examination organizations: the positive screening rate (rate for positive findings of mass x-ray examination, number of suspected gastric cancer cases / total numbers of the mass survey participants × 100), the positive diagnostic examination rate (gastric cancer detection rate from the diagnostic examinations, number of diagnosed gastric cancer cases / number of diagnostic examinations × 100), the gastric cancer detection rate (gastric cancer detection rate overall, the number of diagnosed gastric cancer cases / total number of mass screening participants × 100), and the early gastric cancer detection rate (early gastric cancer detection rate overall, number of diagnosed early gastric cancer cases / total number of mass screening participants × 100). The positive diagnostic examination rate was equivalent to the positive predictive value of the x-ray examination in the present study.

For the present study, there is no ethical problem because we used officially published statistics of mass screening and did not access the individual information of the study subjects.

Statistical analysis

Relative change in three markers from low- to high-density barium use, the positive screening rate, the positive diagnostic examination rate, and the gastric cancer detection rate, was estimated as an odds ratio by logistic regression analysis. In each model, each outcome from mass screening or diagnostic examination was entered as a dependent variable. Density of barium (high / low), age (dummy variables in 5-year interval as shown in Table 1), sex (male / female) and medical examination organization (A, B, C, D or E; dummy variables) were entered as independent variables in order to assess the overall intra-organizational effect of high-density barium use adjusting for sex, age and medical examination organization. The early gastric cancer detection rate, however, was excluded for this analysis, because sex- and age-specific information regarding the invasion depth was not reported officially by the screening office.

All statistical analyses were performed with SPSS11.0J for Windows (SPSS, Japan, Inc., Tokyo). A p value of less than 5% was defined as statistically significant.

RESULTS

The findings of the intra-organizational comparative study are summarized in Tables 2. The positive screening rate decreased at 4 (A, B, D, E) of the organizations, and the positive diagnostic examination rate increased at all 5 after introduction of the high-density barium system. However, the gastric cancer detection rate increased at only 2 (C, D), while the early gastric cancer detection rate increased at 3 (C, D, E). Rate of diagnostic examinee generally increased in a period with high-density barium. Change in rate of early gastric cancer varied among 5 medical examination organizations.

On multiple logistic regression analysis adjusted for sex, age and medical examination organization, use of high-density barium was associated with a 12% decrease in the positive screening rate (odds ratio, 0.88; 95% confidence interval, 0.86-0.90, p < 0.001) and a 15% increase in the positive diagnostic examination rate (odds ratio, 1.15; 95% confidence interval, 1.01-1.31, p < 0.05), but not with the gastric cancer detection rate (odds ratio, 1.00; 95% confidence interval, 0.88-1.13) (Table 3).
**Table 2. Comparison of outcomes from the mass screening for gastric cancers by 5 medical examination organizations**

<table>
<thead>
<tr>
<th>Medical examination organization</th>
<th>A Low</th>
<th>A High</th>
<th>B Low</th>
<th>B High</th>
<th>C Low</th>
<th>C High</th>
<th>D Low</th>
<th>D High</th>
<th>E Low</th>
<th>E High</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barium density</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of participants</td>
<td>30,559</td>
<td>25,137</td>
<td>5,577</td>
<td>5,785</td>
<td>50,080</td>
<td>51,661</td>
<td>83,450</td>
<td>76,056</td>
<td>14,040</td>
<td>14,617</td>
</tr>
<tr>
<td>Positive screening rate (%)</td>
<td>5.7</td>
<td>3.2</td>
<td>2.0</td>
<td>1.6</td>
<td>13.1</td>
<td>13.8</td>
<td>11.8</td>
<td>10.6</td>
<td>12.3</td>
<td>10.5</td>
</tr>
<tr>
<td>Rate of diagnostic examine (%)</td>
<td>96.0</td>
<td>95.9</td>
<td>95.6</td>
<td>91.6</td>
<td>97.8</td>
<td>97.2</td>
<td>96.0</td>
<td>94.6</td>
<td>99.7</td>
<td>98.5</td>
</tr>
<tr>
<td>Positive diagnostic examination rate (%)</td>
<td>3.3</td>
<td>5.5</td>
<td>11.9</td>
<td>12.6</td>
<td>2.3</td>
<td>2.6</td>
<td>2.4</td>
<td>3.0</td>
<td>2.5</td>
<td>2.7</td>
</tr>
<tr>
<td>Gastric cancer detection rate (%)</td>
<td>0.183</td>
<td>0.171</td>
<td>0.233</td>
<td>0.190</td>
<td>0.290</td>
<td>0.350</td>
<td>0.267</td>
<td>0.297</td>
<td>0.306</td>
<td>0.274</td>
</tr>
<tr>
<td>Early gastric cancer detection rate (%)</td>
<td>0.115</td>
<td>0.107</td>
<td>0.161</td>
<td>0.121</td>
<td>0.194</td>
<td>0.256</td>
<td>0.218</td>
<td>0.235</td>
<td>0.192</td>
<td>0.198</td>
</tr>
<tr>
<td>Rate of early gastric cancer (%)</td>
<td>62.8</td>
<td>62.6</td>
<td>69.1</td>
<td>63.7</td>
<td>66.9</td>
<td>73.1</td>
<td>81.6</td>
<td>79.1</td>
<td>62.7</td>
<td>72.3</td>
</tr>
</tbody>
</table>

Low, low-density barium, < 180 w/v%; High, high-density barium, = or > 180 w/v%.

a Rate for positive findings of mass x-ray examination.
b Proportion of diagnostic examinee in subjects with positive screening.
c Gastric cancer detection rate from diagnostic examination.
d Gastric cancer detection rate overall.
e Early gastric cancer detection rate overall.
f Proportion of early gastric cancer in total gastric cancer.

**Table 3. Relative change in 3 outcomes of mass screening for gastric cancers by introduction of high-density barium at 5 medical examination organizations**

<table>
<thead>
<tr>
<th></th>
<th>Odds ratio</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive screening rate a</td>
<td>0.88</td>
<td>(0.86 - 0.90)</td>
</tr>
<tr>
<td>Positive diagnostic examination rate b</td>
<td>1.15</td>
<td>(1.01 - 1.31)</td>
</tr>
<tr>
<td>Gastric cancer detection rate c</td>
<td>1.00</td>
<td>(0.88 - 1.13)</td>
</tr>
</tbody>
</table>

Logistic regression analyses adjusted for sex, age and medical examination organization.
a Rate for positive findings of mass x-ray examination.
b Gastric cancer detection rate from diagnostic examination.
c Gastric cancer detection rate overall.
DISCUSSION

In the present study of gastric cancer, the positive screening rate was found to be decreased and the positive diagnostic examination rate increased after introduction of x-ray examinations with high-density barium. Thus, multiple logistic regression showed a 12% decrease and a 15% increase respectively, compared with use of low-density barium. Although rate of diagnostic examinee in subjects with positive screening decreased, the cancer detection rate was not changed (0% decrease) by the introduction of high-density barium, suggesting that introduction of high-density barium improves the efficiency of mass screening without impairment of cancer detection power. These effects could not be influenced by characteristics of medical examination organizations because decrease in positive screening rate was observed at 4 of 5 medical examination organizations and increase in positive diagnostic examination rate was in every organization.

Good depiction of the gastric mucosa by barium x-ray examination is essential for mass screening for gastric cancer and the performance of barium is one important factor influencing the quality of depiction. Thus, efforts have been made for improvement and high-density barium was developed for this purpose. Furthermore, 150 - 200 ml of low-density barium is a heavy physical load for persons to receive. High-density barium features several advantages, such as good adhesion to the stomach mucosa for effective delineation of pathological changes (Abe et al. 2000; Tsuchigame et al. 2000; Noguchi et al. 2001; Yamamoto et al. 2004), relatively low volume (120 - 150 ml) (Abe et al. 2000; Aoyagi et al. 2000; Noguchi et al. 2001; Imamura et al. 2002; Tanno et al. 2003), and thus low physical load. Thus, the Japanese Society of Gastroenterological Mass Survey has recommended a new stomach radiography method using high-density barium since 2002 (Imamura et al. 2002). Mass screening organizations in Niigata Prefecture have also encouraged the introduction of high-density barium (Department of Welfare and Health of Niigata Prefecture et al. 2003). Our findings support the view that the high-density barium system is effective.

Japan is the only country where mass screening for gastric cancer is carried out as a national policy, and it is believed that the early detection of gastric cancer dose have an impact on mortality rate (Oshshima et al. 1986; Hisamichi 1989; Fukao et al. 1995, 1998; Tsubono and Hisamichi 2000). The gastric cancer detection rate in the mass survey was 0.146% in the data base of the national gastroenterological mass screening organization for 2001 (The Japanese Society of Gastroenterological Mass Survey 2003), but our results are slightly higher (0.171 - 0.350%). Under these conditions, we estimated that screening of 286 to 588 participants is required to find one gastric cancer case. From the economic burden, reduction of the total operational cost is required, and this can be achieved largely by avoiding false positive cases in the first step mass x-rays. Presently, the cost for a diagnostic examination is approximately ¥18,600 (equivalent to approximately $179) per person (Wakai et al. 2003). The present study indicated the positive diagnostic examination rate to be increased from 2.3 - 11.9 to 2.6 - 12.6% with high in place of low density barium: in other words the number of diagnostic examinations decreased from 8.4-43.5 to 7.9-38.5 to find a gastric cancer. Therefore, we can estimate savings of approximately ¥9,000 to ¥90,000 (equivalent to $87 to $865) per cancer, a considerable sum when extrapolated to the national health expenditure covered by the national medical insurance system.

We can not deny the possibility that some factors other than barium concentration influenced the outcomes of mass screening. For example, new instruments or technique could have been introduced in accordance with high-density barium in some medical examination organizations. Such confounders should be analyzed in future studies in order to confirm the advantage of the use of high-density barium.

CONCLUSION

The present large-scale multi-center study indicated that introduction of high-density barium
for mass screening decreases the positive screening rate and increases the positive diagnostic examination rate, without impairment of the cancer detection power. Improvement in efficiency would contribute to decrease in unnecessary diagnostic examinations and reduce the total personal and public health costs of this activity. Thus, the introduction of high-density barium should be promoted for nationwide mass screening for gastric cancer in Japan.

References


