Table 3 Screening performance of the two esophagogastroduodenoscopies in subjects with or without chronic atrophic gastritis (mean ± SD) *n* (%)

	Total subjects	CAG	
		Positive	Negative
Screened by transnasal EGD			
Screened subjects	1382	560	822
Age (yr)	53.4 ± 15.4	60.3 ± 11.8[c]	47.0 ± 14.5
Males	684 (49.4)[a]	316 (56.4)[a]	368 (44.8)[a]
Smokers	267 (19.3)	121 (21.6)	146 (17.8)
Subjects with gastric neoplasia/DR	23/0.0166	22/0.0286[c]	1/0.00122[a]
Location of neoplasia (U/M/L)	8/7/8	8/6/8	0/1/0
Adenoma cases/DR	3/0.0022	3/0.00536	0/0
Size of adenoma (mm)	9.7 ± 4.0	9.7 ± 4.0	0
Cancer cases/DR	20/0.0145	19/0.0315[c]	1/0.00122
Size of cancer (mm)	32.6 ± 19.5[a]	34.1 ± 18.8[a]	5 ± 0
Morphological cancer type (Ⅰ-Ⅱa/Ⅱb/Ⅱc-Ⅲ/Ad)	6/1/5/8	6/1/4/8	0/0/1/0
With intestinal-type cancer	18 (90.0)	18 (94.7)	0 (0)
Depth of invasion (m/sm/pm-)	5/7/8	4/7/8	1/0/0
With early cancer	12 (60.0)	11 (57.9)[a]	1 (100)
Screened by transoral EGD			
Screened subjects	1942	800	1142
Age (yr)	53.5 ± 15.6	62.3 ± 11.4[c]	47.3 ± 14.2
Males	758 (39.0)	363 (45.3)	395 (34.6)
Smokers	411 (21.2)	165 (20.6)	246 (21.6)
Subjects with gastric neoplasia/DR	32/0.0164	24/0.0300[c]	8/0.0070
Location of neoplasia (U/M/L)	12/8/12	8/7/9	4/1/3
Adenoma cases/DR	9/0.0046	7/0.00875[c]	2/0.00175
Size of adenoma (mm)	10.8 ± 7.9	11.7 ± 8.8	7.5 ± 3.5
Cancer cases/DR	23/0.0118	17/0.0213[c]	6/0.00525
Size of cancer (mm)	22.3 ± 12.8	19.4 ± 11.7	31.4 ± 12.1
Morphological cancer type (Ⅰ-Ⅱa/Ⅱb/Ⅱc-Ⅲ/Ad)	6/0/12/5	6/0/9/2	0/0/3/3
With intestinal-type cancer	15 (65.2)	12 (70.6)[c]	2 (33.3)
Depth of invasion (m/sm/pm-)	15/3/5	13/2/2	2/1/3
With early cancer	8 (78.3)	15 (88.2)	3 (50.0)

[a]$P < 0.05$ *vs* transoral; [c]$P < 0.05$ *vs* CAG-negative. CAG: Chronic atrophic gastritis; DR: Detection rate; U: Upper third of the stomach; M: Middle third of the stomach; L: Lower third of the stomach; EGD: Esophagogastroduodenoscopy.

each of the two EGDs were significantly higher in the *H. pylori*-positive group than in the negative group (Table 2). No significant differences in the detection rate of neoplasia, as either adenoma or cancer, or in the size or percentage of early cancers were found between the two EGDs, irrespective of *H. pylori* infection. The percentage of morphologically depressed and histologically diffuse-type cancer tended to be higher among cancers detected by standard transoral EGD than by transnasal EGD, irrespective of *H. pylori* infection, but no significant differences were evident. Table 3 shows the results of screening by the two EGDs according to CAG status. The detection rate for gastric mucosal neoplasia was significantly higher among CAG-positive subjects than among negative subjects, regardless of the type of endoscope. In CAG-positive subjects, 65% (30/46) of detected neoplasias were located in the lower two-thirds of the stomach, 50% (23/46) showed an elevated-type morphology and 87% (40/46) displayed intestinal-type histology. No significant differences in the detection rate of neoplasia, morphological or histological types or location were noted between the two EGD groups. However, mean size of the cancer detected was significantly smaller and the percentage of early cancers was higher with standard transoral EGD than with transnasal EGD. Among CAG-negative subjects, 44.4% (4/9) of detected neoplasias were located in the upper third of the stomach and all cancers detected showed depressed- or ulcerated-type morphology. Seventy-one percent (5/7) displayed diffuse-type histology and 42.9% of cases (3/7) showed complications of nodular gastritis. Detection rates of neoplasia were significantly higher in the standard transoral EGD group (0.70%) than in the transnasal EGD group (0.12%, $P < 0.05$). This reflects the high rate of cancer detection for standard transoral EGD in the CAG-negative stomach.

Finally, screening for gastric mucosal neoplasias using the two different EGDs was analyzed according to the stages of *H. pylori*-related chronic gastritis. Mean age in each stage group increased in a stepwise manner with the progression of *H. pylori*-related chronic gastritis from Group A to Group D, and no significant differences were found between the two EGD groups in any stage. The transnasal EGD group showed a higher proportion of men than the transoral group throughout all stages, with significant differences in Groups A and C. In Group A, the standard transoral EGD group included significantly more smokers than the transnasal EGD group,

Table 4 Screening performance of the two esophagogastroduodenoscopies according to the stages of *Helicobacter pylori*-related chronic gastritis (mean ± SD) *n* (%)

	Group A	Group B	Group C	Group D	Total subjects (*H. pylori* analyzed)
Screened by transnasal EGD					
Screened subjects	572	189	321	198	1280
Age (yr)	45.3 ± 13.8	49.2 ± 14.6[c]	59.8 ± 12.1[c]	63.4 ± 12.8[c]	53.4 ± 15.4
Males	257 (44.9)[a]	74 (39.3)	194 (60.2)[a]	98 (49.4)	623 (48.7)[a]
Smokers	89 (15.6)[a]	43 (22.8)[a]	75 (23.3)	40 (20.2)	247 (19.2)
Subjects with gastric neoplasia/DR	0/0	1/0.0053[a,c]	15/0.0466[c]	5/0.0253	21/0.0164
Location of neoplasia (U/M/L)	0	0/1/0	4/5/6	3/0/2	7/6/8
Adenoma cases/DR	0/0	0/0	3/0.0093	0/0	3/0.0023
Size of adenoma (mm)	0	0	9.7 ± 4.0	0	9.7 ± 4.0
Cancer cases/DR	0/0	1/0.00532	12/0.0373	5/0.0253	18/0.0141
Size of cancer (mm)	0	5 ± 0	27.3 ± 12.3	46.0 ± 28.2	31.2 ± 19.5
Morphological cancer type (Ⅰ-Ⅱa/Ⅱb/Ⅱc-Ⅲ/Ad)	0	0/0/1/0	5/0/3/4	1/1/0/3	6/1/4/7
With intestinal-type cancer	0 (0)	0/1 (0)	12/12 (100)	4/5 (80)	16/18 (88.9)
Depth of invasion (m/sm/pm-)	0	1/0/0	3/5/4	1/1/3	5/6/7
With early cancer	-	1 (100)	8 (66.7)	2 (40)	12 (66.7)
Screened by transoral EGD					
Screened subjects	751	257	435	264	1707
Age (yr)	46.0 ± 12.6	46.6 ± 15.4	60.9 ± 11.8[c]	64.0 ± 11.4[c]	53.5 ± 15.4
Males	247 (32.9)	95 (37.0)	203 (46.7)	110 (41.7)	655 (38.4)
Smokers	167 (22.2)	39 (15.2)	102 (23.4)	46 (17.4)	354 (20.7)
Subjects with gastric neoplasia/DR	0/0	8/0.0311[c]	18/0.0414[c]	6/0.0227	32/0.0187
Location of neoplasia (U/M/L)	0	4/1/3	6/7/5	2/0/4	12/8/12
Adenoma cases/DR	0/0	2/0.00778	3/0.00689	4/0.0152	9/0.0052
Size of adenoma (mm)	0	7.5 ± 3.53	8.0 ± 13.9	10 ± 4.08	10.8 ± 7.9
Cancer cases/DR	0/0	6/0.0233	15/0.0345	2/0.00758	23/0.0134
Size of cancer (mm)	0	31.4 ± 12.1	19.4 ± 12.5	20 ± 0	22.3 ± 12.8
Morphological cancer type (Ⅰ-Ⅱa/Ⅱb/Ⅱc-Ⅲ/Ad)	0	0/0/3/3	6/0/7/2	0/0/2/0	6/0/12/5
With intestinal-type cancer	0 (0)	2/6 (33.3)	12/15 (80)	1/2 (50)	16/24 (66.7)
Depth of invasion (m/sm/pm-)	0	2/1/3	11/2/2	2/0/0	15/3/5
With early cancer	-	3 (50)	13 (86.7)	2 (100)	18 (78.3)

[a]$P < 0.05$ *vs* transoral; [c]$P < 0.05$ *vs* previous stage. *H. pylori*: *Helicobacter pylori*; DR: Detection rate; U: Upper third of the stomach; M: Middle third of the stomach; L: Lower third of the stomach; EGD: Esophagogastroduodenoscopy. Group A: *H. pylori* (-), chronic atrophic gastritis (CAG) (-); Group B: *H. pylori* (+), CAG (-); Group C: *H. pylori* (+), CAG (+); Group D: *H. pylori* (-), CAG (+).

while Group B included significantly more smokers in the transnasal EGD group than in the standard transoral EGD group. No neoplasias were detected in Group A (*H. pylori*- and CAG-negative), which comprised of subjects with an infection-free healthy stomach (Table 4). In Group B (*H. pylori*-positive, CAG-negative), representing subjects with an *H. pylori*-infected non-atrophic stomach, the detection rate of gastric mucosal neoplasia was significantly higher in the standard transoral EGD group (3.11%) than in the transnasal EGD group (0.53%, $P < 0.05$). In Group C (*H. pylori*- and CAG-positive) and Group D (*H. pylori*-negative, CAG-positive), no significant differences in detection rates were found between endoscopy groups. Mean size of the detected cancer was smaller and the proportion of early cancers was higher in the standard transoral EGD group, although the difference was not significant. Furthermore, no significant differences in location, morphological type or histopathological type of detected cancers were seen, irrespective of differences in the endoscope used.

DISCUSSION

Previous studies have reported that the diagnostic accuracy of transnasal EGD is equivalent to that of standard transoral EGD for the detection of esophagogastric lesions, including gastric cancer[23-30]. However, despite recent advances in endoscopic technologies, small-diameter endoscopes used for transnasal EGD still show disadvantages when compared to standard endoscopes, due to lower luminous intensity, lower resolution of endoscopic images, a narrow field of view, low maneuverability and low biopsy performance, all of which are attributable to the small diameter of the endoscope[31]. Yoshida *et al*[30] found no significant differences in detection rates of early gastric cancer and adenoma between transnasal and standard transoral EGD, but also noted that gastric cancers may be overlooked by transnasal EGD when performed by less-experienced endoscopists. Furthermore, Hayashi *et al*[32] investigated the detection of early gastric cancer ≤ 2 cm in diameter using the two different EGDs and indicated that transnasal EGD offers inadequate diagnostic yield compared with standard transoral EGD. Supporting those findings, the present results strongly suggest that, although detection rates of gastric mucosal neoplasia might not differ significantly between transnasal and standard transoral EGDs, mean sizes of the detected cancers were significantly larger with transnasal EGD. In addi-

tion, percentages of early or diffuse-type cancers, which require higher resolution for detection, were lower among cancers detected by transnasal EGD. Of note, the difference in detection rates of diffuse-type cancer between the two EGDs was significant. Hayashi *et al*[32] also reported that ultra thin endoscopes were less efficient in screening for lesions located in the upper third of the stomach, due to the narrower field of view and low luminous intensity. Diffuse-type cancer tends to develop from fundic gland mucosa located mainly in the gastric body[14,15,17], providing a possible explanation for the low diagnostic performance of transnasal EGD in detecting diffuse-type cancer. However, the present study found no significant differences in the locations of detected neoplasias between the two EGDs. Screening performance of transnasal EGD thus seems to remain suboptimal compared with standard transoral EGD, at least in the detection of subtle mucosal changes presented by small-sized cancers or by diffuse-type cancers with biologically infiltrating characteristics.

The proliferation and growth of neoplastic cells derived from the stomach mucosa is widely accepted to be regulated by the acidic environment in the gastric lumen. The morphological and biological characteristics of gastric mucosal neoplasia are under the influence of the stage of *H. pylori*-related chronic gastritis[14-16]. With the development of gastric atrophy together with intestinal metaplasia, intra-luminal pH in the stomach becomes less acidic and mucosal neoplasia with an elevated or protruding morphological type and intestinal histological type tends to become more prevalent[14-17]. Conversely, chronic active inflammation of the stomach, regardless of the existence of gastric atrophy, directly induces histologically diffuse-type cancer, which tends to develop in the non-atrophic stomach and is thus usually morphologically depressed or ulcerated[14,15,17,18]. The natural history of *H. pylori*-related chronic gastritis can be classified into four stages (Groups A-D), based on the establishment of *H. pylori* infection or CAG[20,21]. In the present study, the screening performance of transnasal EGD according to each of the four stages of *H. pylori*-related chronic gastritis was also investigated in comparison with standard transoral EGD. No gastric cancers were detected among subjects with an *H. pylori*-negative healthy stomach (Group A), while establishment of *H. pylori* infection (Group B) was associated with the development of gastric mucosal neoplasias. The incidence of gastric mucosal neoplasias increased significantly as the extent of CAG increased from Group B to Group C. In Group B (subjects with *H. pylori*-infected non-atrophic stomach), the detection rate of gastric mucosal neoplasia was significantly lower with transnasal EGD than with standard transoral EGD, representing the detection rate of gastric cancer. Types of cancers detected in Group B were predominantly depressed or ulcerated type morphologically and diffuse type histologically, supporting the reported clinicopathological characteristics of cancers developing from a non-atrophic stomach[14,15,17]. The present results clearly indicate that the screening performance of transnasal EGD is low for detecting the above-mentioned types of cancer developing against a background of the non-atrophic stomach. Meanwhile, in Groups C and D, comprising subjects with extensive CAG, no significant differences in detection rates of gastric mucosal neoplasia were seen between the two EGDs. As postulated in the multistep model of stomach carcinogenesis, a major proportion of cancers develop from the stomach mucosa with extensive CAG together with intestinal metaplasia in regions with a high risk for cancer, including Japan[14,15,17,18]. Consistent with this, 83.0% of gastric mucosal neoplasias (82.9% of cancers) developed in Groups C and D. In these groups, intestinal-type cancer predominated histopathologically and 50% of detected neoplasias were morphologically elevated or protruding, compatible with clinicopathological findings of cancer developing from extensive CAG[14-17]. Based on the observed detection rates for the two EGDs, screening performance of transnasal EGD appears comparable to that of standard transoral EGD in detecting this major type of cancer. However, the significantly smaller size of detected cancers and the significantly higher percentage of early cancers among cancers detected by standard transoral EGD suggest great room for improvement in the diagnostic performance of transnasal EGD for cancer screening in subjects with extensive CAG. Meanwhile, the present study has some limitations. Firstly, in our country gastric cancer screening is being carried out as a public health service and a non-negligible number of people underwent the screening by endoscopy. Thus, the detection rate of gastric mucosal neoplasia is to some extent under the influence of the time intervals between the previous EGD and the EGD performed in the present study. In both groups of the two EGDs, around 55% of the study subjects underwent the cancer screening by EGD in the previous year. The proportion of the subjects who underwent EGD within the last 3 years was 11% and 18% in transnasal and standard transoral EGD, respectively. As for the remaining subjects, no information about the previous EGD is available. Secondly, in general the incidence of gastric neoplasia is higher in males compared to females. In the present study, the number of male subjects included in the transnasal EGD group was significantly higher than in the transoral EGD group. Thus, the screening performance of transnasal EGD might have been overestimated, although it still remains suboptimal compared with that of standard transoral EGD. Since tolerability, acceptability and safety of transnasal EGD with a small-diameter endoscope are better than standard transoral EGD, transnasal EGD has been increasingly used for gastric cancer screening[30-32]. However, the present results indicate that the screening performance of transnasal EGD remains suboptimal, even in subjects with extensive CAG, which represents a key route of stomach carcinogenesis in Japan. Furthermore, in screening for the small proportion of cancers developing from the *H. pylori*-infected non-atrophic stomach, small-diameter endoscopes are clearly

inadequate compared with standard endoscopes. Evaluation of the accuracy of transnasal EGDs in cancer screening must await the results of long-term follow-up studies. However, the present findings offer compelling evidence that the introduction of small-diameter endoscopes into cancer screening first requires improvements in the low image quality of transnasal EGD due to low resolution, low luminous intensity and narrow angle of view.

Special attention should be paid to the screening of individuals with *H. pylori* infection of the non-atrophic stomach. This group of subjects as a whole is not considered to be at high risk of cancer, with an annual incidence rate of around 0.1% in Japan[20,21,33]. However, considering the rapid growth and high malignant potential of the diffuse-type cancer that tends to arise in this group, together with the subtle endoscopic findings present in the early stage, use of high-performance endoscopy is strongly recommended. We have recently reported that a group of subjects with non-atrophic stomach at high risk for diffuse-type cancer can be identified using serum pepsinogen (PG) levels (PG I > 70 ng/mL; PG I / II ratio $\leqslant$ 3.0)[33]. We believe that cancer screening in such individuals should be performed cautiously using standard transoral EGD. In the near future, high-performance, small-diameter endoscopes will surely be developed and are likely to contribute greatly to the establishment of highly efficient cancer screening programs. However, with the currently available small-diameter endoscopes, cancer screening should be performed meticulously based on ample experience with standard transoral EGD and also with full knowledge of the limitations and characteristics of small-diameter endoscopes.

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COMMENTS

Background

Transnasal esophagogastroduodenoscopy (EGD) is more acceptable for patients and has been increasingly applied for gastric cancer screening. Previous studies showed that the diagnostic accuracy of transnasal EGD was equivalent to that of standard transoral EGD for the detection of esophagogastric lesions. However, the screening performance of transnasal EGD for gastric mucosal neoplasias must be determined carefully because of its lower luminous intensity and lower quality of endoscopic images.

Research frontiers

In the present study, the diagnostic ability of transnasal and standard transoral EGD for gastric cancer screening has been evaluated from various points of view. Especially, the screening performance of both EGDs has been investigated according to the stages of *Helicobacter pylori* (*H. pylori*)-related chronic gastritis.

Innovations and breakthroughs

The results have clearly demonstrated that the diagnostic performance of transnasal EGD remains suboptimal for cancer screening, particularly in subjects with *H. pylori*-infected non-atrophic stomach.

Applications

Based on the present results, special attention should be paid to the cancer screening of the subjects with *H. pylori*-infected non-atrophic stomach, who are at high risk for diffuse-type cancer, and transoral EGD is strongly recommended for such individuals. The results of the authors' previous study have already revealed that such individuals can be identified using serum pepsinogen levels.

Peer review

Nakata *et al* compared the diagnostic performances of transnasal and standard transoral EGD in gastric cancer screening of asymptomatic healthy subjects. A total of 3324 subjects including 1382 screened by transnasal EGD and 1942 screened by standard transoral EGD were enrolled. They concluded that the diagnostic performance of transnasal endoscopy is suboptimal for cancer screening, particularly in subjects with H. pylori-related atrophic gastritis. This is a well-written paper describing an extensive experience in the use of transnasal endoscopy for gastric cancer screening.

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RESEARCH ARTICLE Open Access

Postprandial fullness correlates with rapid inflow of gastric content into duodenum but not with chronic gastritis

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Abstract

Background: The aim of this study is evaluating the correlation of postprandial fullness with chronic gastritis or rapid inflow of gastric content into duodenum, based on double-contrast barium X-ray imaging.

Methods: 253 healthy subjects who underwent upper gastrointestinal barium X-ray examination were analyzed. Chronic gastritis was judged from mucosal atrophy and hypertrophic thickened folds on barium X-ray images. For the gastric excretion, the tips of barium flow on the single-contrast frontal barium X-ray images of the stomach were classified into four categories; V type (all the barium remained in the stomach), V-H type (some barium had flowed into the duodenum but the tip of barium remained in the proximal half of the duodenal bulb), H-V type (some barium had flowed into the duodenum and the tip of barium was in the distal half of duodenal the bulb, but no barium was observed in the descending part of the duodenum), and H type (some barium had flowed into the descending part of the duodenum). The chi-square test and Cochran-Mantel-Haenzel test were used for evaluation.

Results: Chronic gastritis was observed in 72 subjects, among which 21 subjects (29.2%) presented with postprandial fullness. For the remaining 181 subjects without chronic gastritis, 53 subjects (29.3%) complained of postprandial fullness. There is no significant correlation between chronic gastritis and postprandial fullness ($p = 0.973$). For the rapid flow of gastric content into duodenum, all the 253 subjects comprised 136 subjects with V type (in the stomach), 40 subjects with V-H type (in the proximal half of the duodenal bulb), 21 subjects with H-V type (in the distal half of the duodenal bulb), and 56 subjects with H type (in the descending part of the duodenum). Postprandial fullness was present in 30 subjects with V type (22.1%), 9 subjects with V-H type (22.5%), 8 subjects with H-V type (38.1%), and 27 subjects with H type (48.2%). There is a distinct correlation between postprandial fullness and gastric barium excretion on barium X-ray imaging ($p = 0.002$).

Conclusions: Bothersome postprandial fullness correlates with rapid inflow of gastric content into duodenum, but not with chronic gastritis.

Background

Postprandial fullness is defined as an unpleasant sensation like prolonged persistence of food in the stomach. In the Rome III criteria which classifies functional gastrointestinal disorders (FGIDs) into four categories (i.e., functional dyspepsia, belching disorders, nausea/vomiting disorders, and rumination syndrome in adults), bothersome postprandial fullness is described as a major symptom of functional dyspepsia [1,2]. Postprandial fullness, as well as early satiety, is a popular gastrointestinal symptom which occurs to not only FGID patients but also to healthy subjects. However, in both situations, the underlying mechanisms of postprandial fullness remain unclear.

It can be easily imagined that gastritis may cause unpleasant sensation of postprandial fullness. However,

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despite the many studies evaluating an association between FGID symptoms and gastritis [3-6], studies focusing on the correlation of postprandial fullness and gastritis have been very few. Marzio *et al.* reported that *Helicobacter pylori* infection is not associated with upper abdominal complaints including postprandial fullness and early satiety [7], and Karamanolis *et al.* also reported that the status of *Helicobacter pylori* infection does not correlate with the symptoms of functional dyspepsia [8]. In our study, not *Helicobacter pylori* infection but chronic gastritis itself was precisely diagnosed on the basis of gastric atrophy and/or hypertrophic thickened folds in double-contrast barium X-ray images of the stomach [9,10]. Based on radiologically accurate diagnosis, we tried to evaluate correlation between gastritis and postprandial fullness.

The sensation of a full stomach (satiety) has been reported to be dependent on the volume of the integrated meal, as well as the caloric content and viscosity of the meal [11]. Even the ingestion of water alone could lead to a sensation of satiety [11,12]. Based on these reports, the sensation of satiety seems likely to correlate positively with residual volume in the stomach. We therefore hypothesized that gastric content emptying might influence the sensation of postprandial fullness. Namely, we speculated that subjects with slow gastric content emptying such as those with gastroptosis (downward displacement of the stomach) would tend to have more gastric residue, and thereby be apt to cause the sensation of postprandial fullness. In our study, noncaloric barium was used for the orally taken content, and injection of a spasmolytic agent was performed to relax the muscles of the gastrointestinal walls. Stimulant effect of caloric content upon gastrointestinal movement [12] or autonomic peristalsis of the stomach could thus be excluded.

Consequently, our study examined the correlation of bothersome postprandial fullness with gastric barium excretion, which is followed by rapid inflow of barium into the duodenum. Although the relative density of barium contrast medium is much heavier than normal food, the result of this study using noncaloric barium should reflect the effect of rapid inflow of gastric content into duodenum to some extent.

Methods

Subjects

Subjects comprised 285 individuals (273 men and 12 women) who underwent medical check-ups at the Health Department, Human Resources Division, Nippon Steel Corporation in 2008. All of them underwent upper gastrointestinal double-contrast barium X-ray examination for screening of gastric cancer. For evaluation of serum anti-*H. pylori* antibody, we used a commercial EIA kit called E-plate EIKEN *H. pylori* antibody (Eiken Chemical Co.,LTD., Tokyo, Japan) according to the previous report [13]. This study was approved by the Working Group of Research Ethics, Human Resources Division of Nippon Steel Corporation. All the data were completely anonymized, and were handled carefully according to the Declaration of Helsinki.

Upper gastrointestinal X-ray examination

Ten minutes after intramuscular injection of spasmolytic agent (7.5 mg of prifinium bromide), the subject drank 150 ml of barium in one gulp. X-ray images were then taken as follows; 1) double-contrast image of the upper and lower esophagus in the right anterior oblique standing position, 2) single-contrast image of the stomach in the frontal standing position, 3) double-contrast image of the stomach in the supine position, 4) single-contrast image of the stomach in the prone position, 5) double-contrast image of the stomach in the right anterior oblique supine position, 6) double-contrast image of the stomach in the prone position, 7) double-contrast image of the stomach in the left anterior oblique supine position, 8) double-contrast image of the stomach in the left anterior oblique half-standing position, and 9) double-contrast image of the stomach in the frontal standing position.

Symptoms of postprandial fullness

As for evaluation of postprandial fullness, we used the question "Does your stomach feel heavy after meals?" from Frequency Scale for the Symptoms of GERD (FSSG) [14]. According to the answer to this question administered prior to the upper gastrointestinal barium X-ray examination, the subjects were classified into two groups: postprandial fullness-positive (+) and postprandial fullness-negative (-).

Evaluation of chronic gastritis

Chronic gastritis was defined as gastric atrophy with enlarged areae gastricae or hypertrophic gastritis with thickened folds on the greater curvature [9]. Both atrophic and hypertrophic gastritis were typically observed in the stomach with chronic *H. pylori* infection [9,10], and were precisely evaluated based on the double-contrast stomach images on the barium X-ray examination (Figure 1).

Evaluation of rapid inflow of gastric barium into duodenum on upper gastrointestinal X-ray examination

Based on the flow of barium during the examination, all subjects were classified into one of the following four categories: V, V-H, H-V, and H type. Soon after the subject drank 150 ml of barium, the single-contrast and frontal X-ray image was taken in the standing position.

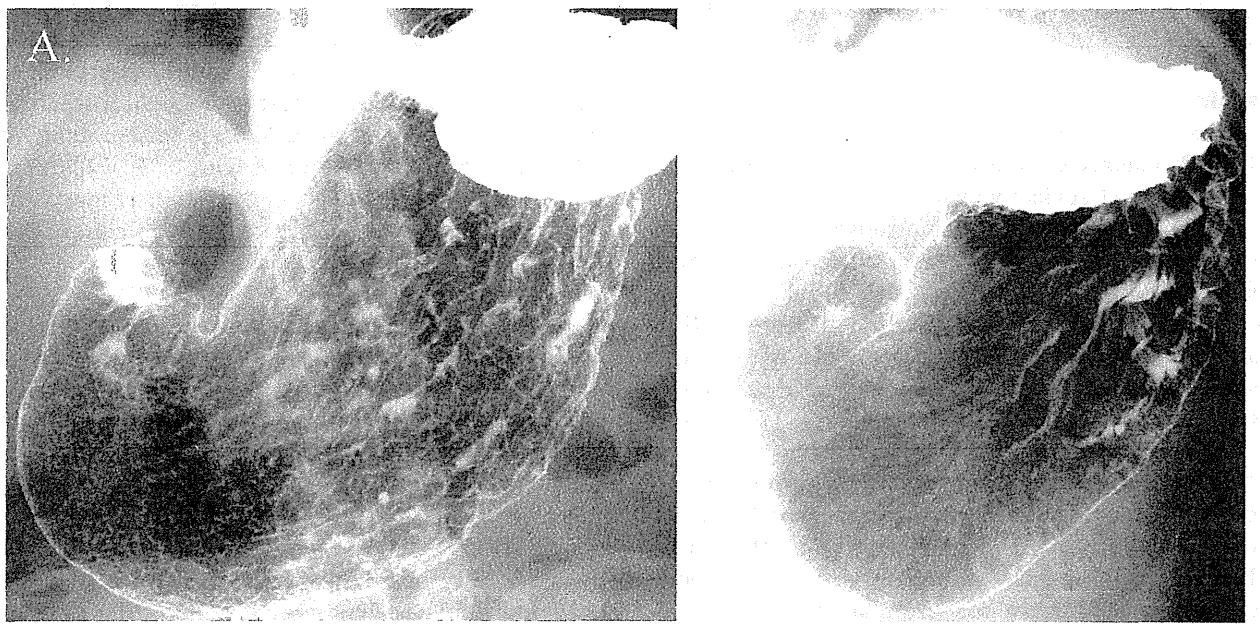

Figure 1 The typical two types of chronic gastritis observed in the double-contrast barium X-ray images. (A) Atrophic gastritis with enlarged areae gastricae. (B) Hypertrophic gastritis with thickened folds on the greater curvature.

At this moment, the tips of barium flow were classified as follows (Figure 2);

V type (in the stomach): all the barium remained in the stomach (i.e., no barium had flowed into the duodenum).

V-H type (in the proximal half of the duodenal bulb): some barium had flowed into the duodenum, but the tip of barium remained in the proximal half of the duodenal bulb.

H-V type (in the distal half of the duodenal bulb): some barium had flowed into the duodenum and the tip of barium was in the distal half of duodenal the bulb, but no barium was observed in the descending part of the duodenum.

H type (in the descending part of the duodenum): some barium had flowed into the descending part of the duodenum.

Statistical methods

We used JMP software (SAS Institute, NC, USA) for statistical analyses. We did not separate the sexes, since the sample size of women was too small. Correlations between age and categorical variables were compared using the χ^2 test and Fisher's exact test. To evaluate relationships between postprandial fullness and gastric barium excretion or chronic gastritis on barium X-ray images, the χ^2 test, Fisher's exact test, and Cochran-Mantel-Haenszel test adjusted for age were used. Two-

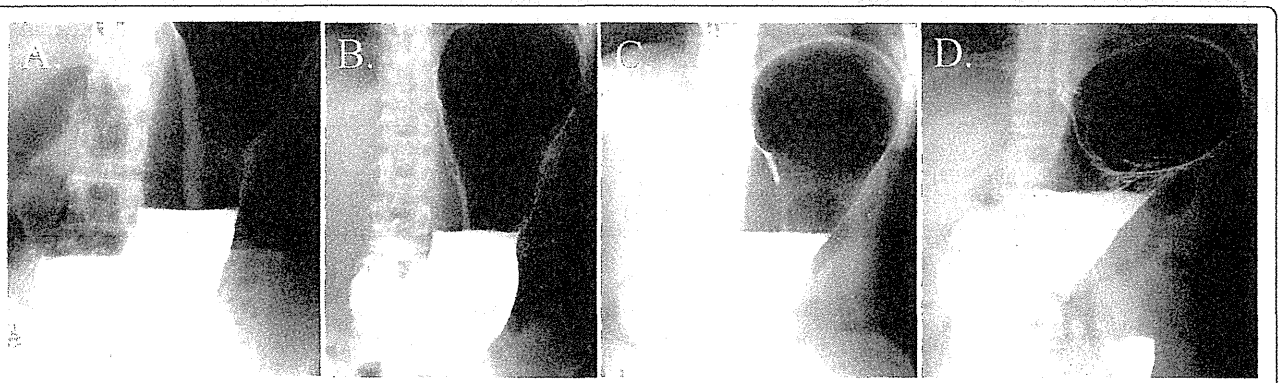

Figure 2 The degrees of gastric barium excretion based on the tip of barium flow in a single-contrast frontal view of the stomach in the standing position. (A) V type (in the stomach). (B) V-H type (in the proximal half of the duodenal bulb). (C) H-V type (in the distal half of the duodenal bulb). (D) H type (in the descending part of the duodenum).

sided p-values <0.05 were considered as statistically significant.

Results

Characteristics of the study subjects

Of the 285 subjects, we excluded 30 subjects with poor X-ray images (1 subject with previous gastric resection, 26 subjects with uncontrollable spastic movement of stomach, 2 subjects with massive gastric residue, and 1 subject with inadequate position change due to hemiplegia) and 2 subjects with insufficient information obtained from the questionnaire. Mean age for the remaining 253 subjects (241 men and 12 women) was 48.6 ± 7.04 years (range, 32-69 years).

Validation and age distribution of chronic gastritis

To validate our diagnosis of chronic gastritis judged from gastric atrophy and/or hypertrophic thickened folds (Figure 1), we analyzed another set of 30 subjects, who were tested positive for serum antibody against *H. pylori*. Among the 30 subjects with *H. pylori* infection, 29 subjects (97%) were diagnosed as chronic gastritis based on the double-contrast barium X-ray images. We therefore concluded that our diagnosis of atrophic and/or hypertrophic gastritis certainly reflects the chronic *H. pylori* infection.

Age distribution of subjects with chronic gastritis is shown in Table 1, which indicates a significant correlation between age and chronic gastritis (p = 0.005). It probably reflects the prevalence of *H. pylori* infection in Japanese population; older age is related to *H. pylori* infection and atrophic gastritis [15,16]. In contrast, age and postprandial fullness shows no significant correlation (p = 0.395; Table 2).

No correlation exists between chronic gastritis and postprandial fullness

Among all the 253 subjects, 72 subjects (28.5%) were diagnosed as chronic gastritis and 181 subjects (71.5%) had normal gastric mucosa. For the 72 subjects with chronic gastritis, 21 subjects (29.2%) reported postprandial fullness. For the 181 subjects without chronic gastritis, 53 subjects (29.3%) complained of postprandial fullness (Table 2). The χ^2 test and Cochran-Mantel-Haenszel test yielded p-values of 0.986 (odds ratio (OR), 1.006; 95% confidential interval (CI), 0.552-1.833) and 0.973 (OR, 0.989; 95% CI, 0.316-3.100) respectively, showing no significant correlation between chronic gastritis and postprandial fullness.

An obvious correlation exists between rapid inflow of gastric content into duodenum and postprandial fullness

Judged from rapid inflow of gastric content into duodenum on the upper gastrointestinal X-ray imaging, all subjects were divided into four categories; V, V-H, H-V, and H type (Figure 2). All the 253 subjects comprised 136 subjects with V type (53.8%), 40 subjects with V-H type (15.8%), 21 subjects with H-V type (8.3%), and 56 subjects with H type (22.1%) (Table 2). The sensation of postprandial fullness was present in 30 of the 136 subjects with V type (22.1%), 9 of the 40 subjects with V-H type (22.5%), 8 of the 21 subjects with H-V type (38.1%), and 27 of the 56 subjects with H type (48.2%). The χ^2 test yielded a p-value of 0.002 (OR, 3.290; 95% CI, 1.696-6.381), showing a distinct correlation between postprandial fullness and rapid inflow of gastric barium into duodenum (Table 2). This result strongly suggests that bothersome postprandial fullness is prone to be present in situations where intragastric content rapidly flows into the duodenum.

Discussion

In this study using the upper gastrointestinal barium X-ray images, we were unable to detect any relationship between postprandial fullness and chronic gastritis (atrophic and/or hypertrophic gastritis). Our result is consistent with previous reports, which denied the relation of *H. pylori* infection to postprandial fullness and early satiety [7,8]. Given the validation that our diagnosis of chronic gastritis mostly reflected the *H. pylori*

Table 1 Association of age groups and chronic gastritis.

	Chronic gastritis					
	Total (n = 253)	(+)	(-)			
	n (%)	n (%)	n (%)	OR (95% CI)	χ^2	*P*-value
Age (years)						
<39	13 (5.1)	1 (1.4)	12 (6.6)	reference		
40-44	67 (26.5)	12 (16.7)	55 (30.4)	2.618 (0.310-22.108)		
45-49	58 (22.9)	16 (22.2)	42 (23.2)	4.571 (0.549-38.075)		
50-54	67 (26.5)	22 (30.6)	45 (24.9)	5.867 (0.716-48.042)		
55-59	30 (11.9)	10 (13.9)	20 (11.0)	6.000 (0.680-52.902)		
60<	18 (7.1)	11 (15.3)	7 (3.9)	18.857 (1.989-178.803)	16.844	0.005

χ^2 test.

Table 2 Characteristics of study subjects stratified by the sensation of postprandial fullness.

	Postprandial fullness					
	Total (n = 253)	(+)	(-)			
	n (%)	n (%)	n (%)	OR (95% CI)	χ^2	*P*-value
Age (years)						
<39	13 (5.1)	4 (5.4)	9 (5.0)	reference		
40-44	67 (26.5)	15 (20.3)	52 (29.1)	0.649 (0.175-2.406)		
45-49	58 (22.9)	20 (27.0)	38 (21.2)	1.184 (0.324-4.329)		
50-54	67 (26.5)	24 (32.4)	43 (24.0)	1.256 (0.349-4.514)		
55-59	30 (11.9)	8 (10.8)	22 (12.3)	0.818 (0.196-3.416)		
60<	18 (7.1)	3 (4.1)	15 (8.4)	0.450 (0.081-2.488)	5.178	0.395†
Chronic gastritis						
(+)	72 (28.5)	21 (28.4)	51 (28.5)	reference		
(-)	181 (71.5)	53 (71.6)	128 (71.5)	1.006 (0.552-1.833)	0.001	0.973† †
Gastric barium excretion						
V	136 (53.8)	30 (40.5)	106 (59.2)	reference		
V-H	40 (15.8)	9 (12.2)	31 (17.3)	1.026 (0.440-2.390)		
H-V	21 (8.3)	8 (10.8)	13 (7.3)	2.174 (0.825-5.733)		
H	56 (22.1)	27 (36.5)	29 (16.2)	3.290 (1.696-6.381)	14.806	0.002†

† χ^2 test.

† † Cochran-Mantel-Haenszel test adjusted for age.

infection, we concluded that no association exists between postprandial fullness and chronic gastritis.

Our novel finding was that subjects with rapid inflow of gastric content into duodenum have significant correlation with consciousness of postprandial fullness (Table 2). Counter to our expectations, the sensation of postprandial fullness does not tend to occur in subjects categorized in V type, where most of the subjects with gastroptosis are included. On the contrary, postprandial fullness tends to be present in situation where intragastric content flows rapidly into the duodenum. Based on these results, we speculate that the gastroduodenal shape should be one of crucial factors for postprandial fullness, as gastric barium excretion considerably depends on the shapes of stomach and duodenum.

Previous studies have reported that satiety signals arise from the stomach [17], and are transmitted to the central nervous system through vagal and/or splanchnic nerves via chemoreceptors and mechanoreceptors in the gastric wall [18,19]. Several reports have also suggested that pressure on gastric wall may induce dysplastic symptoms including satiation [20-22]. However, these reported mechanisms do not seem applicable to our results, as there should be no difference in effects on gastric wall among four types of gastroduodenal shapes, which represents four types of gastric barium excretion (V, V-H, H-V, and H type in Figure 2). Although the mechanisms underlying postprandial fullness remain unclear, we speculate that some mechanical or chemical stimuli affecting intestinal wall (duodenum and/or small intestine) may play critical roles in causing the sensation of postprandial fullness.

A recent study reported that higher body mass index (BMI) as well as gastric volume during fasting is clearly associated with reduced satiety [23]. A larger scale study including BMI should thus be performed, as there might be some correlation between gastric shape and BMI. In the near future, we are planning to take a large cross-sectional study of about 7,000 healthy subjects, in which not only chronic gastritis and gastric barium excretion but also BMI, age, sex, serum anti-*H. pylori* IgG, serum pepsinogen I and II levels [24], smoking habit, alcohol drinking, etc. will be evaluated. Our novel finding will be strictly verified in the forthcoming larger scale study based on multivariate analyses. At long last, some animal model should be also necessary to validate the correlation between rapid inflow of gastric content into duodenum and the sensation of postprandial fullness.

Conclusion

There is a distinct correlation between postprandial fullness and gastric barium excretion on upper gastrointestinal X-ray imaging: bothersome postprandial fullness is prone to be present in situations where intragastric content rapidly flows into the duodenum. On the contrary, no correlation exists between postprandial fullness and chronic gastritis judged from mucosal atrophy and hypertrophic thickened folds on barium X-ray images.