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Gastric Mucosal Changes Evaluated by Double-contrast Upper Gastrointestinal Radiography after *Helicobacter pylori* Eradication

Rika Nakano[1], Akira Sato[1,2], Yumiko Oomori[1], Hitomi Suzuki[1], Kaori Kabata[1], Sho Matsubara[1]

Abstract

Objective: Double-contrast upper gastrointestinal radiography (UGI-XR) has been used for screening gastric cancer worldwide. However, gastric mucosal change after eradication of *Helicobacter pylori (H. pylori)* on UGI-XR is poorly understood. We investigated gastric mucosal changes after *H. pylori* eradication on UGI-XR.

Methods: The width of gastric folds and the state of mucosal surface before and after *H. pylori* eradication were evaluated in 104 subjects by UGI-XR. Gastric mucosal surface (GMS) findings were classified into four types according to the degree of abnormality in the mucosal pattern: A, normal; B, enlarged and mildly irregular-shaped gastric area; C, obviously enlarged with considerable irregular gastric area; and D, irregular rugged mucosal surface.

Results: During a 16.1-months follow-up period, the enlarged folds improved in 62/91 subjects (68%), and the width of the gastric folds decreased from 6.4 mm (mean) to 3.7 mm ($p<0.0001$). Gastritis change of GMS changed in all types; however, the improvement to type A with normalization of fold width was lower in type C (2.6%, $p=0.047$) and type D (0%, $p=0.029$) than in type B (16.1%).

Conclusion: *H. pylori*-induced chronic gastritis changed after *H. pylori* eradication in 70% of the subjects who underwent UGI-XR, and UGI-XR is useful for evaluating gastric mucosal change after *H. pylori* eradication. In subjects with type C and type D GMS, the rate of change to a normal mucosa on UGI-XR was low, which suggested earlier *H. pylori* eradication, prior to developing type C and type D mucosal patterns.

Keywords *Helicobacter pylori*, double-contrast upper gastrointestinal radiography, atrophic gastritis, enlarged gastric folds

Helicobacter pylori (H. pylori) induced atrophic gastritis that leads to gastric cancer, and eradication of *H. pylori* can reduce the risk of gastric cancer development[1–3]. From these results, *H. pylori* eradication treatment has been covered by health insurance in Japan since 2001. Gastric cancer is the third cause of cancer death in Japan, with reports of high prevalence of *H. pylori* infection[4] and increasing number of subjects receiving *H. pylori* eradication treatment. Although the risk of cancer development is reduced after eradication of *H. pylori*, the risk still remains, and cancer screening is required even after eradication. Double-contrast upper gastrointestinal radiography (UGI-XR) has been used as a standard gastric cancer screening method, and is officially recommended as a cancer screening method in Japan because of its usefulness in reducing the risk of gastric cancer mortality[5]. In addition it is useful for detecting *H. pylori* induced chronic gastritis (*H. pylori* gastritis), which is one of the major risk factors for gastric cancer development[6,7]. However, few studies have been carried out regarding the change of gastric mucosa on UGI-XR after *H. pylori* eradication, and it is still not fully understood. We therefore conducted a retrospective study to investigate the gastric mucosal changes on UGI-XR after *H. pylori* eradication.

[1] Sasaki Foundation Shonan Health Examination Center ; [2] Division of Gastroenterology, Department of Internal Medicine, St. Marianna University School of Medicine Yokohama City Seibu Hospital
Contact : Rika Nakano, Department of Radiology, Sasaki Foundation Shonan Health Examination Center, 10–4 Takaracho, Hiratsuka, Kanagawa 254–0034, Japan. Tel : +81–463–21–3811 ; Fax : +81–463–21–3814 ; E-mail : rnakano@po.kyoundo.jp

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Methods

Subjects

We included 104 health check-up subjects (mean age 54.1 years, at the time of *H. pylori* eradication), who had UGI-XR before and after a successful *H. pylori* eradication therapy, which was performed between September 2013 and March 2017 (**Table 1**). None of the subjects had a history of gastric cancer or gastrectomy and none had used gastric acid suppressants. The diagnosis of the *H. pylori* infection was based on a *H. pylori* antibody titer ≥ 10 U/mL measured using an enzyme immunoassay kit (E-plate Eiken *H. pylori* antibody II; Eiken Chemical, Tokyo, Japan).

Evaluation of UGI-XR

Radiological findings of the sufficiently extended gastric body, or antrum, in the dorsal position on double contrast examination of UGI-XR were assessed by a gastrointestinal radiologist (SM). Gastric fold with a width of 4.5 mm or more was defined as enlarged according to Nakajima *et al.*[8] and the change of the gastric mucosal surface (GMS) was classified according to the degree of abnormality in the mucosal pattern based on the reports of Yamamichi *et al.*[9]. They were classified into four types (type A: defined as having no abnormal mucosal pattern, a gastric area that was not visualized or was recognized as small and round-shaped with a homogenous pattern (**Fig. 1a**); type B: defined as having a slightly enlarged and slightly irregular gastric area (**Fig. 1b**); type C: defined as having an obviously enlarged gastric area with considerable irregularity (**Fig. 1c**); type D: defined as an absent gastric area or irregularly enlarged area showing cobblestone-like appearance (**Fig. 1d**).

Table 1. Baseline Characteristics of Subjects

	Subjects of the study
n	104
male/female	41/63
age mean; range (years)	54.1; 34–69
fold width; normal/enlarged/disappeared	8/91/5
fold width; mean, range (mm)	6.4, 2.2–7.6
type of the change in gastric mucosal surface; A/B/C/D	8/31/38/27
observation period mean; range (months)	16.1; 4–47

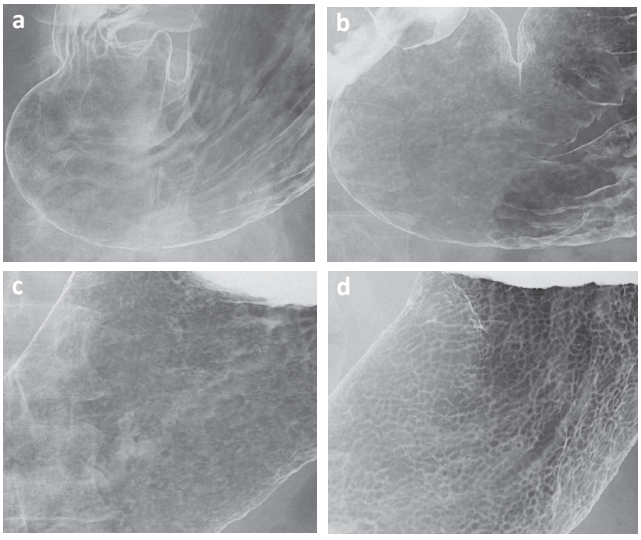

Fig. 1. Typical Images of the Gastric Mucosal Surface of Chronic *Helicobacter pylori* Gastritis by Double-contrast Upper Gastrointestinal Radiography

a. Type A: No abnormal mucosal pattern with a small, round shape, and homogenous gastric area. b. Type B: The gastric area is obscurely visualized in an irregular shape with a mixture of micro nodule and barium fleck. c. Type C: The gastric area is obviously enlarged showing multiple small granular prominences. d. Type D: The gastric surface is irregularly rugged with a cobblestone-like appearance.

Statistical analyses

The statistical analyses were performed with R2.8.1 software using Spearman's rank correlation coefficient, Student's *t*-test, Kruskal–Wallis test, and Chi-squared test.

Results

After *H. pylori* eradication, improvement of fold width and gastric mucosal surface were observed in many subjects. Typical cases are shown in **Fig. 2**.

Gastric folds

Before *H. pylori* eradication, 91 subjects showed fold enlargement and 5 subjects showed fold disappearance (**Table 2**). After eradication, a decrease in the fold width of the enlarged folds was already seen in cases even 4 months after eradication. There was no gender difference in the decrease of fold width after eradication. Decrease of fold width (reduction by 1 mm or more) was seen in 62 (68%) of 91 subjects with enlarged folds. Both male and female subjects improved to achieve a normal fold width range (<4.5 mm), 19 of 38 (50%) and 30 of 53 (57%), respectively. The mean fold width decreased from 7.4 mm to 4.0 mm in males, from 5.7 mm to 3.6 mm in females, and from 6.4 mm to 3.7 mm in all subjects, ($p<0.0001$).

Gastric mucosal surface (GMS)

Before eradication, gastritis change of GMS (type B, C, and D) was observed in 96 subjects (**Table 3**). After eradication, a total of 65 subjects (67.7%) changed into other types of GMS. The change of type was seen in types (B, C, and D), and there was no gender difference in the rate of change. However, the rate of change to achieve a type A mucosal pattern differed by the type, and was the highest in type B (type B, 35.5%; C, 10.8%; D, 0%, $p=0.0006$) (**Table 4**). And the improvement rate to normalization of the fold width with change to type A GMS classification was lower in type C (1/38: 2.6%, $p=0.047$) and type D (0/27: 0%, $p=0.029$) than in type B (5/31: 16.1%) (**Fig. 3**).

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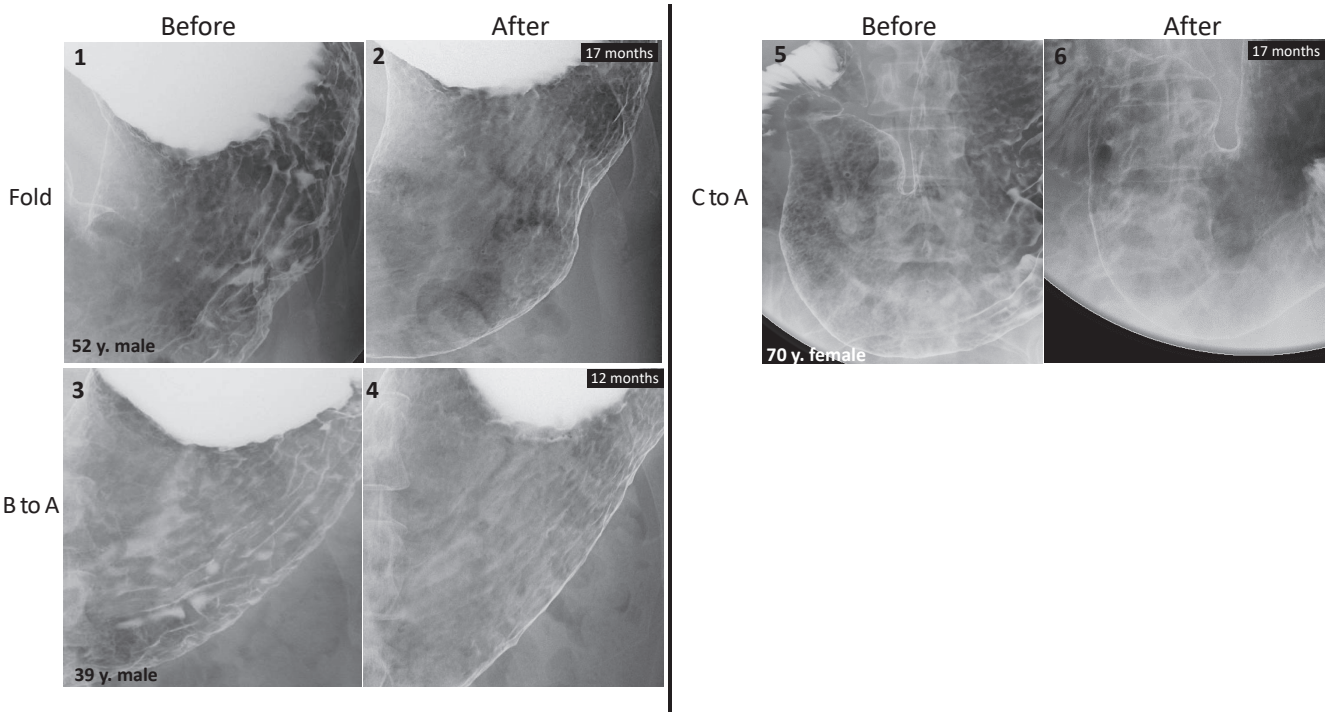

Fig. 2. The Enlarged and Meandering Gastric Fold Reduction

Gastric fold reduced in width from 12.6 mm to 2.4 mm after *H. pylori* eradication (1, 2). Irregular shaped gastric area with micro nodule and barium fleck changed to a fine granular homogenous pattern (type B to A: 3, 4). Enlarged gastric area showing small granular prominence became obscure (type C to A: 5, 6).

Table 2. Gastric Fold Width Before and After Eradication of *Helicobacter pylori*

	male	female
n	41	63
age (mean)	54.4	53.9
before *H. pylori* eradication		
mean	7.4 mm	5.7 mm
normal/enlarged/disappeared	2/38/1	6/53/4
after *H. pylori* eradication		
mean	4.0 mm	3.6 mm
normal/enlarged/disappeared	21/19/1	36/23/4
improvement to normal from enlarged (%)	19 (50.0)	30 (56.6)

H. pylori: *Helicobacter pylori*

Table 3. Type of the Change in Gastric Mucosal Surface and Normal Fold Width Before and After Eradication of *Helicobacter pylori*

	Type of the change in GMS			
	A	B	C	D
before *H. pylori* eradication				
n (total: 104)	8	31	38	27
male/female (*n*)	4/4	16/15	13/25	8/19
age (years)	54.3	55	53.6	53.7
observation period (months)	13.3	13.8	16.9	18.4
normal fold width (*n*)	1	5	3	2
after *H. pylori* eradication				
n (total: 104)	24	54	23	3
male/female (*n*)	9/15	24/30	8/15	0/3
previous type, A/B/C/D	7/13/4/0	1/15/24/14	0/3/9/11	0/0/0/3
normal fold width (*n*)	20	25	17	0

After *H. pylori* eradication, GMS changed to other types in many subjects.
H. pylori: *Helicobacter pylori*. GMS: gastric mucosal surface

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Table 4. Change to Type A from Each of the Types After *Helicobacter pylori* Eradication

	Type of gastric mucosal surface			
	A	B	C	D
before *H. pylori* eradication (*n*)	8	31	38	27
type A after *H. pylori* eradication (*n*)	7	11	4	0
rate of change (%)	—	35.5 †	10.5 †	0 †
change to type A with normal fold width (*n*)	6	5	1	0

† $p=0.0006$. *H. pylori*: *Helicobacter pylori*

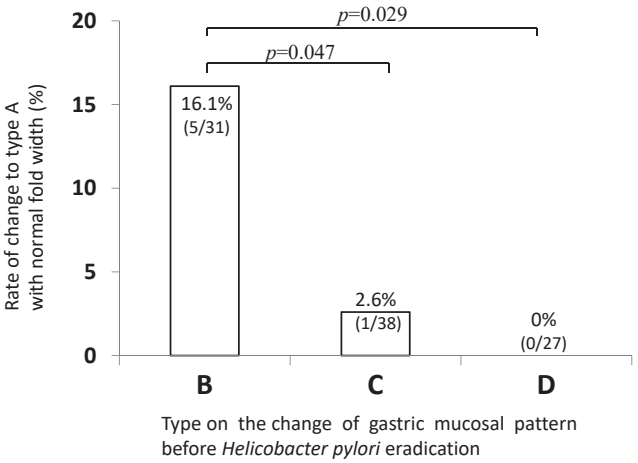

Fig. 3. Rate of Change in Gastric Mucosal Surface to Type A with Normal Fold Width Among Type B, C, and D

The rate was lower in type C (2.6%, $p=0.047$) and type D (0%, $p=0.029$) than in type B (16.1%).

Discussion

Endoscopic and histological studies have reported that the mucosal change of atrophic gastritis improved after *H. pylori* eradication[10–12]. Studies on UGI-XR have also suggested the possibility of improvement of *H. pylori* gastritis after *H. pylori* eradication, in a cross-sectional study[13] and a few longitudinal studies with a limited number of subjects[14,15]. We investigated the mucosal change of *H. pylori* gastritis after *H. pylori* eradication in 104 subjects and obtained the following findings: (1) After *H. pylori* eradication, change to the mucosal findings of *H. pylori* gastritis occurred in nearly 70% of the subjects who had UGI-XR, and UGI-XR is useful for the evaluation of gastric mucosal changes after *H. pylori* eradication. (2) Both enlarged gastric folds and gastritis change of GMS improved to normal on UGI-XR in some subjects, but the improvement rate was low in subjects with type C and type D mucosal patterns.

Enlarged gastric fold is one of the major characteristics of *H. pylori* gastritis. Concerning the change of enlarged folds on UGI-XR after *H. pylori* eradication, Okuda *et al.*[14] reported that the fold width decreased in all seven subjects examined, and Yamasaki *et al.*[15] reported the improvement of the fold form in 12 of 14 subjects. In our study, nearly 70% of 96 subjects with enlarged folds showed decrease of fold width at 16.1 months after eradication, which was consistent with prior studies, and also showed that early decrease of fold width within 1 year after *H. pylori* eradication was frequent (36 subjects, mean: after 8.9 months). Enlarged folds are considered to be associated with the risk of developing gastric cancer[7,16], and Nishibayashi *et al.*[17] reported that enlarged folds are associated with increased oxidative DNA damage and an increased risk of gastric cancer with a stepwise increasing risk at fold width ≥5 mm, and extremely high risk at width ≥7 mm. In this study, 40 of 104 subjects had enlarged folds with width ≥7 mm before *H. pylori* eradication, and 18 of them improved to normal width (<4.5 mm) (data are not shown) after eradication. However, it is unknown whether the improvement of enlarged folds by *H. pylori* eradication is associated with decreased gastric cancer risk, and further studies are required to find out the significance of normalization of the fold width. As to the change of GMS after *H. pylori* eradication, Okuda *et al.*[14] reported reduction in the size of the gastric area in 4 of 6 subjects, and Yamasaki *et al.*[15] reported improvement to a normal pattern of GMS in 2 of 15 subjects after eradication. Furthermore, Yamamichi *et al.*[13] reported lower prevalence of atrophic gastritis on UGI-XR among subjects with *H. pylori* eradication than chronically *H. pylori*-infected subjects. Consistent to these reports, the change of gastric mucosal pattern was observed in 66 of 96 subjects after *H. pylori* eradication in the current study (**Table 3**), which indicated that UGI-XR is useful for the evaluation of the change of GMS after *H. pylori* eradication.

In a 16.1 months followed-up period, our study demonstrated that the rate of change to normal gastric mucosal surface after *H. pylori* eradication was low among subjects with type C and type D mucosal pattern. Although the observation period might relate with the result, it corresponds to the suggestion by Shiotani *et al.*[18] that the reversibility of the changes by *H. pylori* associated with atrophic gastritis depended upon the severity of the changes prior to *H. pylori* eradication. Furthermore, it is reported that patients with preexisting severe gastric atrophy are at an increased risk for gastric cancer development after *H. pylori* eradication[19–21]. Although further studies are needed, the low

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improvement rate of *H. pylori* gastritis in type C and type D mucosal patterns might possibly correlate to the risk of cancer development, and suggests the necessity of eradication of *H. pylori* prior to type C and type D mucosal pattern for the prevention of gastric cancer development.

Conclusion

H. pylori gastritis can be changed after *H. pylori* eradication in 70% of the subjects who had UGI-XR, and UGI-XR is useful for evaluating the change of gastric mucosal findings after *H. pylori* eradication as well as for screening cancer. In subjects with type C and D mucosal patterns, the improvement rate to normal mucosa seen on UGI-XR was low, which suggests the requirement of eradication prior to developing marked *H. pylori* gastritis.

Statement of Ethics

Informed consent was obtained from the subjects prior to the publication of this study.

This retrospective cohort study was conducted in accordance with the Declaration of Helsinki, and was approved by the Medical Ethics Committee and Institutional Review Board of Sasaki Foundation (#H30-3).

Disclosure Statement

The authors have no conflicts of interest to declare.

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