

ORIGINAL ARTICLE

Helicobacter pylori eradication improved the Kyoto classification score on endoscopy

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Key words

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Abstract

Background and Aim: Endoscopy-based Kyoto classification predicts the risk of *Helicobacter pylori* infection and gastric cancer; however, the change in score following *H. pylori* eradication remains unknown. We retrospectively compared the Kyoto score before and after *H. pylori* eradication.

Methods: *H. pylori*-positive patients who underwent baseline esophagogastroduodenoscopy (EGD), successful *H. pylori* eradication, and surveillance EGD were enrolled. The Kyoto score is a sum of scores for atrophy (Kimura-Takemoto atrophic-border classification none or C-I: 0, C-II or C-III: 1, O-I to O-III: 2), intestinal metaplasia (none: 0, antrum: 1, corpus and antrum: 2), enlarged folds (absence: 0, presence: 1), nodularity (absence: 0, presence: 1), and diffuse redness (none: 0, mild: 1, severe: 2) and ranges from 0 to 8.

Results: Eighty-three patients (mean age: 54.9 years; 65.1% women) were enrolled. The mean duration from successful eradication to surveillance EGD was 256 days. The Kyoto score significantly decreased from 3.90 to 2.78 following *H. pylori* eradication ($P < 0.001$). Scores for endoscopic atrophy (from 1.43 to 1.46, $P = 0.638$) and endoscopic intestinal metaplasia (from 0.53 to 0.47, $P = 0.543$) did not change; however, there was significant improvement in the scores for enlarged folds (from 0.14 to 0.00, $P = 0.002$), nodularity (from 0.18 to 0.04, $P = 0.002$), and diffuse redness (from 1.61 to 0.82, $P < 0.001$).

Conclusion: The Kyoto classification score decreased following *H. pylori* eradication. A decrease in the scores for enlarged folds, nodularity, and diffuse redness contributed to the decrease in Kyoto score.

Introduction

According to the Globocan 2018 data, 1 million new cases of gastric cancers are detected worldwide. Gastric cancer is the third leading cause of mortality, with 780 000 deaths.¹ The major cause of gastric cancer is *Helicobacter pylori* infection,^{2–4} and *H. pylori* eradication decreases the risk of gastric cancer.^{5–9} *H. pylori* eradication induces various molecular biological changes.^{10–12} In clinical practice, *H. pylori* eradication is confirmed based on changes in the urea breath test and the *H. pylori* serum antibody test.^{13–15} Recently, several studies have reported changes in endoscopic findings following *H. pylori* eradication in patients.^{16–18}

Endoscopy is essential to diagnose gastritis, evaluate the presence or absence of *H. pylori* infection, and assess the risk of gastric cancer.^{19–21} The Kyoto classification of gastritis is an endoscopy-based classification proposed by the Japan Gastroenterological Endoscopy Society in 2013. It was introduced to

estimate the risk of *H. pylori* infection and gastric cancer on endoscopy. The Kyoto classification score comprises parameters such as atrophy, intestinal metaplasia, enlarged folds, nodularity, and diffuse redness. The Kyoto classification score was reportedly associated with the risk of *H. pylori* infection and gastric cancer^{15,22–25}; however, the change in Kyoto score before and after *H. pylori* eradication remains unknown. Research on the Kyoto score before and after *H. pylori* eradication might contribute to updating the Kyoto score in the future. Therefore, we compared the Kyoto classification score before and after *H. pylori* eradication.

Methods

Study design and participants. This retrospective study was approved by the Ethical Review Committee of the Hattori

Clinic on 6 September 2019 (approval no. S1909-U06). Written informed consent was obtained from all participants. All clinical investigations were conducted according to the ethical guidelines of the Declaration of Helsinki.

This cohort study included *H. pylori*-positive patients who underwent baseline esophagogastroduodenoscopy (EGD), treatment for *H. pylori* eradication, and surveillance EGD after successful eradication at the Toyoshima Endoscopy Clinic from May 2016 to August 2019. EGDs were performed either for screening or evaluation of the existing symptoms by 22 different endoscopists. Successful eradication was confirmed by the urea breath test. The exclusion criteria were patients with a history of gastric cancer, those who had undergone surgical gastrectomy, or those who had achieved *H. pylori* eradication. We also excluded patients who underwent baseline EGD more than 3 months prior to initiation of treatment for *H. pylori* eradication, those who underwent surveillance EGD less than 4 weeks after *H. pylori* eradication, and those who failed to achieve *H. pylori* eradication.

We collected the data on age, gender, body mass index, smoking habit, drinking habit, family history of gastric cancer, use of aspirin, indication for examination, and the duration between *H. pylori* eradication and surveillance EGD as the patient's baseline characteristics.

Endoscopic examination. An Olympus Elite system and an Olympus scope including GIF-HQ290, GIF-H290Z, GIF-H260, GIF-XP290N, or GIF-260N (Olympus, Tokyo, Japan) were used. Sedation with midazolam and/or pethidine was induced based on the patient's willingness.^{26,27} The choice of oral or nasal endoscopy was based on patient preference and tolerability.²⁸ The T-File System (STS-Medic Inc., Tokyo, Japan) was used for filing endoscopic images and documentation of the endoscopic findings. The Kyoto classification score was evaluated and was entered into the database of the T-File System by each endoscopist.

Endoscopy-based Kyoto classification score. The Kyoto classification score for gastritis is based on total scores for the following five endoscopic parameters, ranging from 0 to 8: atrophy, intestinal metaplasia, enlarged folds, nodularity, and diffuse redness with or without regular arrangement of collecting venules (RAC). A high score indicates an increased risk of gastric cancer and *H. pylori* infection.²⁰

Endoscopic atrophy was classified according to the extent of mucosal atrophy, as described by Kimura and Takemoto.^{29–31} Nonatrophic and C-I were scored as atrophy score 0, C-II and C-III as atrophy score 1, and O-I to O-III as atrophy score 2.

Intestinal metaplasia typically appears grayish-white with slightly elevated plaques surrounded by mixed patchy pink and pale areas of the mucosa, forming an irregular uneven surface. Villous appearance, whitish mucosa, and rough mucosal surface are helpful indicators for the endoscopic diagnosis of intestinal metaplasia.^{32,33} Intestinal metaplasia score of 0 was defined as the absence of intestinal metaplasia, 1 as the presence of intestinal metaplasia within the antrum, and 2 as intestinal metaplasia extending into the corpus. Intestinal metaplasia score is calculated based on the diagnosis established using white-light imaging.

An enlarged fold is defined as a width of 5 mm or more that is not flattened or only partially flattened by stomach insufflation. The absence and presence of enlarged folds were scored 0 and 1, respectively.

Nodular gastritis is characterized by a miliary pattern resembling "goose flesh," which is mainly located in the antrum. The absence and presence of nodularity were scored as 0 and 1, respectively.

Diffuse redness refers to uniform redness with continuous expansion observed in the nonatrophic mucosa mainly in the corpus.²⁹ An RAC in the corpus appears like numerous dots. On close observation, it demonstrates a regular pattern of starfish-like shapes. The absence of diffuse redness, presence of mild diffuse redness or diffuse redness with RAC, and severe diffuse redness or diffuse redness without RAC were scored as 0, 1, and 2, respectively.

Pathological examination. We obtained biopsy specimens from two sites—the greater curvature of the corpus and the antrum in patients prior to *H. pylori* eradication. One experienced gastrointestinal pathologist diagnosed the specimens based on the updated Sydney System in hematoxylin and eosin staining. We defined the updated Sydney System score of 0 for both specimens as histological negative. We defined the updated Sydney System score of ≥ 1 for at least one specimen as histological positive.

Statistical analysis. Comparison of the Kyoto classification score before and after *H. pylori* eradication was performed using the Wilcoxon signed-rank sum test. We evaluated the first-degree polynomial equation with Kyoto score as the objective variable and duration of years after *H. pylori* eradication as an explanatory variable using the least-squares method. The association between histological and endoscopic diagnoses was analyzed using the two-sided Cochran-Armitage trend test. The intra- and interobserver variations between the diagnoses for diffuse redness scored by the endoscopists were analyzed by the kappa value.

Significance was indicated by a *P* value less than 0.05. Calculations were performed using the statistical software Ekuseru-Toukei 2015 (Social Survey Research Information Co., Ltd., Tokyo, Japan).

Results

Eighty-three patients were finally eligible, after excluding 11 patients whose baseline EGD was conducted more than 3 months before initiation of therapy for *H. pylori* eradication and two patients who underwent posteradication EGD within 4 weeks. The mean age of the patients was 54.9 years, and women comprised 65.1% of the cohort. The mean duration between *H. pylori* eradication and surveillance EGD was 256 days (range 33–504 days) (Table 1).

The Kyoto score significantly decreased from 3.90 ± 1.69 to 2.78 ± 1.33 following *H. pylori* eradication ($P < 0.001$, Fig. 1). The scatter plot shows the duration of years between successful *H. pylori* eradication and surveillance EGD, *x*, and the Kyoto score, *y*, for each of the 83 patients (Fig. 2). The approximation of the best-fitting line was $y = -1.1x + 3.7$. Comparison of each

Table 1 Patient characteristics

| | Before eradication | After eradication |
|---|--------------------|-------------------|
| <i>n</i> | 83 | |
| Age (year), mean (SD) | 54.9 (13.0) | |
| Female gender (%) | 65.1 | |
| Body mass index (kg/m ²), mean (SD) | 21.9 (3.41) | |
| History of smoking (%) | 8.43 | |
| Regular alcohol consumption (%) | 27.7 | |
| Family history of gastric cancer (%) | 7.23 | |
| Regular intake of aspirin (%) | 2.41 | |
| Indication | | |
| Screening/evaluation for symptoms | 69/14 | |
| Sedative use in EGD (%) | 94.0 | 100 |
| Per oral/per nasal EGD | 78/5 | 82/1 |
| Duration after <i>Helicobacter pylori</i> eradication (year), mean (SD) | | 0.704 (0.312) |

EGD, esophagogastroduodenoscopy.

endoscopic parameter before and after *H. pylori* eradication showed that the atrophy score and the intestinal metaplasia score did not change, while the scores for enlarged folds, nodularity, and diffuse redness score were significantly reduced ($P = 0.002$, 0.002 , and <0.001 , respectively, Table 2).

We show representative images before and after *H. pylori* eradication in Figure 3.

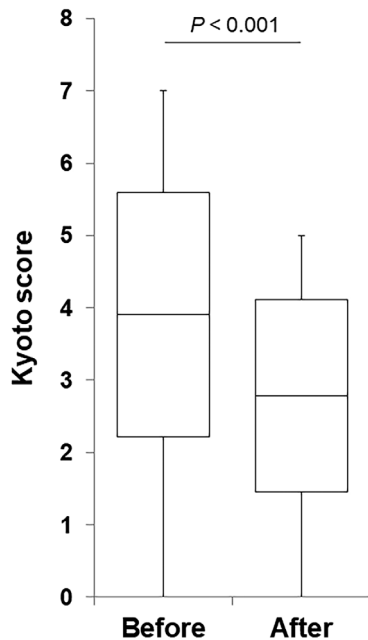


Figure 1 Kyoto classification score before and after *Helicobacter pylori* eradication. Box plots depicting the average Kyoto score. The P value was calculated using the Wilcoxon signed-rank sum test.

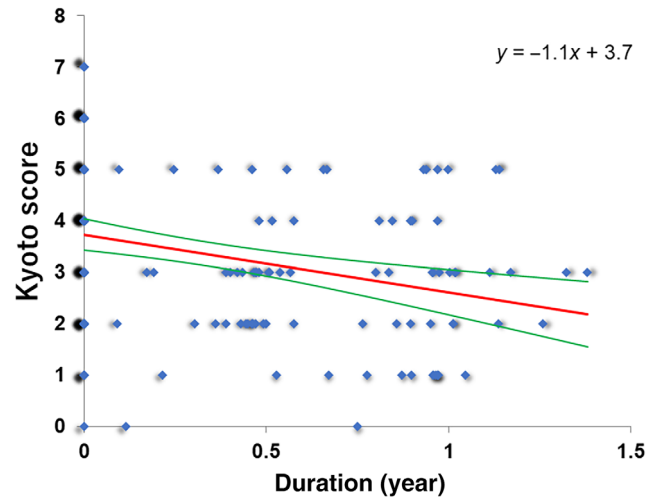


Figure 2 Scatter plot of the Kyoto score based on the duration of surveillance esophagogastroduodenoscopy after *Helicobacter pylori* eradication. The red line is a fitting line. Green curves are the confidence interval upper and lower limit values.

Pathological examination was performed in 70 patients prior to *H. pylori* eradication. The endoscopic atrophy and intestinal metaplasia scores were associated with histological atrophy and intestinal metaplasia, respectively, as shown in Tables 3 and 4.

The kappa values for intra- and interobserver variability were 0.93 and 0.89, respectively. The reproducibility was graded as excellent.

Discussion

Our previous review indicated that enlarged folds had a relatively high positive predictive value (56.2–86.0%) for current *H. pylori* infection.^{19,34–36} Nodularity had low sensitivity (6.4–32.1%) but excellent specificity (95.8–98.8%).^{34,36,37} Diffuse redness had a high positive predictive value (65.6–91.5%).^{34–36} RAC had a good sensitivity for absence of infection (86.7–100%).^{34,35,38,39} In this study, we found that the Kyoto score significantly decreased after *H. pylori* eradication. A decrease in the scores for

Table 2 Kyoto classification score before and after *Helicobacter pylori* eradication

| | Before eradication | After eradication | P value |
|--|--------------------|-------------------|-----------|
| Atrophy score, mean (SD) | 1.43 (0.65) | 1.46 (0.59) | 0.638 |
| Intestinal metaplasia score, mean (SD) | 0.53 (0.79) | 0.47 (0.79) | 0.543 |
| Enlarged folds score, mean (SD) | 0.14 (0.35) | 0.00 (0.00) | 0.002 |
| Nodularity score, mean (SD) | 0.18 (0.39) | 0.04 (0.19) | 0.002 |
| Diffuse redness score, mean (SD) | 1.61 (0.58) | 0.82 (0.39) | <0.001 |

The P value was calculated using the Wilcoxon signed-rank sum test.

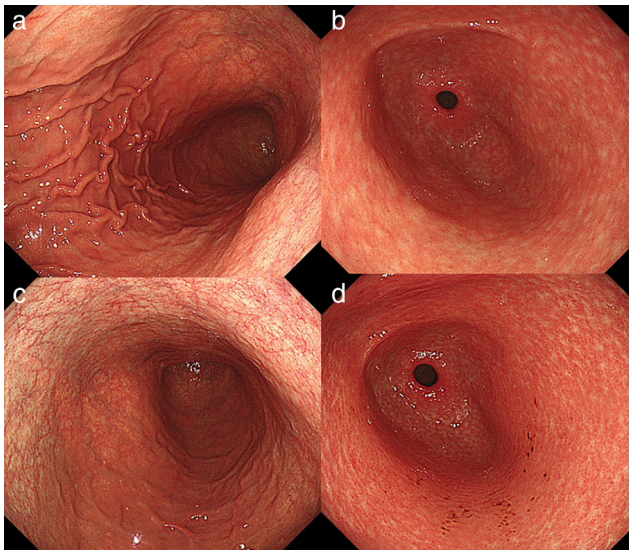


Figure 3 Representative images before and after *Helicobacter pylori* eradication. (a, b) Before eradication. A 37-year-old woman. Kyoto score: 6; atrophy score: 2; intestinal metaplasia score: 0; enlarged folds score: 1; nodularity score: 1; diffuse redness score: 2. (a) Corpus of the stomach. (b) Antrum of the stomach. (c, d) 296 days after eradication. Kyoto score: 4; atrophy score: 2; intestinal metaplasia score: 0; enlarged folds score: 0; nodularity score: 1; diffuse redness score: 1. (c) Corpus of the stomach. (d) Antrum of the stomach.

enlarged folds, nodularity, and diffuse redness contributed to the decrease in Kyoto score. Our results indicate that enlarged folds, nodularity, and diffuse redness without RAC predict current *H. pylori* infection. Enlarged folds,^{40,41} nodularity,^{42,43} and diffuse redness^{44,45} are induced by mucosal inflammation. Deactivation of mucosal inflammation following *H. pylori* eradication might have led to the findings of improvement on endoscopy.

Some meta-analyses mentioned that *H. pylori* eradication partially improved the pathological atrophy but did not improve the pathological intestinal metaplasia.^{46–48} Our study showed that the endoscopic atrophy and intestinal metaplasia scores were associated with histological atrophy and intestinal metaplasia, respectively. Kodama *et al.*⁴⁹ stated that an improvement in atrophy on endoscopy was seen 78 months after eradication. Nagata

Table 3 The relationship between histological and endoscopic atrophy

| | Pathological atrophy – | Pathological atrophy + | <i>P</i> value |
|----------------------|------------------------|------------------------|----------------|
| Endoscopic atrophy 0 | 7 | 0 | 0.018 |
| Endoscopic atrophy 1 | 23 | 5 | |
| Endoscopic atrophy 2 | 22 | 13 | |

P values were calculated by Cochran-Armitage trend test.

Table 4 The relationship between histological and endoscopic intestinal metaplasia

| | Pathological intestinal metaplasia – | Pathological intestinal metaplasia + | <i>P</i> value |
|------------------------------------|--------------------------------------|--------------------------------------|----------------|
| Endoscopic intestinal metaplasia 0 | 41 | 5 | 0.003 |
| Endoscopic intestinal metaplasia 1 | 8 | 5 | |
| Endoscopic intestinal metaplasia 2 | 6 | 5 | |

P values were calculated by Cochran-Armitage trend test.

*et al.*¹⁶ observed mottled patchy erythema in 54% of the patients 26 months after eradication, and histologic intestinal metaplasia was seen in 87% of the mottled patchy erythema. Yoshii *et al.*³⁶ reported that endoscopic atrophy and intestinal metaplasia had similar high diagnostic odds ratios for current and past *H. pylori* infection. As previously reported, our results suggest that endoscopic atrophy and intestinal metaplasia might not improve over a short period of time.

This study has several limitations. First, this was a retrospective cohort study conducted at a single institute. Second, our study revealed that *H. pylori* eradication decreased the Kyoto score by 1.1 per year; however, the mean duration of observation was only 256 days. Long-term observation is desirable in the future. Third, a mini lecture improved the accuracy of diagnosis for *H. pylori* infection based on the Kyoto classification,³⁷ and our study showed excellent reproducibility for the diffuse redness score; however, the reproducibility of the Kyoto classification score has not been sufficiently validated.

In conclusion, we confirmed that the Kyoto classification score decreased following *H. pylori* eradication. Among the Kyoto classification parameters, enlarged folds, nodularity, and diffuse redness might be indicators of successful *H. pylori* eradication.

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