Consistency between the endoscopic Kyoto classification and pathological updated Sydney system for gastritis: A cross-sectional study

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Abstract

Background: Two methods are used to evaluate gastritis: the updated Sydney system (US) with pathology and Kyoto classification, a new endoscopy-based diagnostic criterion for which evidence is accumulating. However, the consistency of their results is unclear. This study investigated the consistency of their results.

Methods: Patients who underwent esophagogastroduodenoscopy and were evaluated for Helicobacter pylori infection for the first time were eligible. The association between corpus and antral US scores (neutrophil activity, chronic inflammation, atrophy, and intestinal metaplasia) and Kyoto classification scores (atrophy, intestinal metaplasia, enlarged folds, nodularity, and diffuse redness) was assessed.

Results: Seven-hundred-seventeen patients (mean age, 49.2 years; female sex, 57.9%; 450 H. pylori-positive and 267 H. pylori-negative patients) were enrolled. All endoscopic gastritis cases in the Kyoto classification were associated with high corpus and antral US scores for neutrophil activity and chronic inflammation. A subanalysis was performed for H. pylori-positive patients. Regarding atrophy and intestinal metaplasia, endoscopic findings were associated with US scores. Enlarged folds, nodularity, and diffuse redness were associated with high corpus US scores for neutrophil activity and chronic inflammation, but with low antral US scores for atrophy and intestinal metaplasia. The Kyoto classification scores were also associated with the pathological topographic distribution of neutrophil activity and intestinal metaplasia.

Conclusions: Among H. pylori-positive individuals, endoscopic and pathological diagnoses were consistent with atrophy and intestinal metaplasia. Enlarged folds, nodularity, and diffuse redness were associated with pathological inflammation (neutrophil activity and chronic inflammation) of the corpus; however, they were inversely associated with pathological atrophy and intestinal metaplasia. The endoscopy-based Kyoto classification of gastritis partially reflects pathology.

Introduction

Gastric cancer is one of the major cancers worldwide, and an accurate diagnosis of Helicobacter pylori (H. pylori)-associated gastritis is crucial in clinical practice, because H. pylori-associated gastritis indicates the early phase of gastric carcinogenesis.1–4 Assessment methods for H. pylori-associated gastritis include

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pathology, endoscopic findings, serum pepsinogen, and *H. pylori* antibody. Among them, pathology based on the updated Sydney system (USS) is common and well-established.1,5

Conversely, due to recent advances in endoscopic equipment and procedures, diagnostic performance for gastritis through endoscopy has improved.9 In addition, the Kyoto classification was advocated in the Japan Gastroenterological Endoscopy Society in 2014, which aimed to unify the endoscopic diagnostic criteria for gastritis. The Kyoto classification has been vigorously studied and showed an association between gastritis and *H. pylori* infection6–8,10 and gastric cancer risk.11–13 These factors have contributed to the development of endoscopic diagnostics for gastritis.

It is vital to determine whether the Kyoto classification is consistent with pathology. This is because if it is sufficiently consistent with pathology, endoscopic diagnosis of gastritis could reduce the burden of pathological diagnosis and risk of bleeding due to biopsy. Recently, Nomura et al. evaluated the diagnostic values between pathology and endoscopic findings (atrophy, enlarged folds, nodularity, diffuse redness, and regular arrangement of collecting venules [RAC]).14,15 They reported that no single endoscopic feature was observed that is highly specific for histological atrophy and inflammation and suggested that combinations of endoscopic findings can improve diagnostic accuracy. In contrast, several reports have shown that endoscopic atrophy and intestinal metaplasia are associated with pathological atrophy and intestinal metaplasia, respectively.16–19 We also showed that the Kyoto classification was associated with the pathological topographic distribution of neutrophil activity, which is related to the risk of cancer.20 However, only a few studies on the consistency between the Kyoto classification and pathology based on the USS are available. Therefore, we investigated the relationship between the Kyoto classification and the USS in a cross-sectional manner and evaluated the consistency between endoscopic findings and pathology.

**Methods**

**Study design and oversight.** This retrospective cross-sectional study was conducted at Toyoshima Endoscopy Clinic, an outpatient endoscopy-specialized clinic located in Tokyo, an urban area in Japan. This study was performed in accordance with the ethical guidelines for medical studies in Japan. Written informed consent was obtained from patients at the time of esophagogastroduodenoscopy to use their data for research purposes. The study design was described in a protocol prepared by Toyoshima Endoscopy Clinic and was approved by the Certified Institutional Review Board, Hattori Clinic on September 4, 2020 (approval no. S2009-U04). The study’s protocol was published on our institute’s website (http://www.ichou.com) so that patients could opt out of the study. All clinical investigations were conducted in accordance with the ethical guidelines of the Declaration of Helsinki.

**Study population.** This study included patients who underwent esophagogastroduodenoscopy and were evaluated with *H. pylori* infection for the first time in their life at Toyoshima Endoscopy Clinic from December 2013 to August 2019. Patients who received *H. pylori* eradication therapy were excluded. The study patients were pathologically diagnosed with gastritis using biopsy samples obtained from the gastric mucosa. Patients underwent serum *H. pylori* antibody test or urea breath test (UBT) to diagnose *H. pylori* infection.

**Diagnosis of *H. pylori* infection.** A positive *H. pylori* infection was defined based on positive histology of the gastric mucosa or a positive UBT. A combination of negative histology and a negative UBT or a combination of negative histology and serum antibody levels (E-plate Eiken *H. pylori* antibody II, Eiken Chemical, Tokyo, Japan) <10 U/mL was defined as a negative *H. pylori* infection. A combination of negative histology and serum antibody levels >10 U/mL without performing UBT was defined as unavailable *H. pylori* status. In the case of a discrepancy when there was a discrepancy between the results of a UBT and a serum antibody test, the result of the UBT was considered the standard.8

**Kyoto classification for gastritis.** One expert endoscopist reviewed all images and scored them according to the Kyoto classification. The endoscopic Kyoto classification score for gastritis consists of the following five endoscopic findings: atrophy, intestinal metaplasia, enlarged folds, nodularity, and diffuse redness.13 Representative endoscopic findings based on the Kyoto classification are shown in Figures 1 and 2.

Endoscopic atrophy was classified according to the extent of mucosal atrophy, as reported according to the Kimura and Takemoto classification.2 Non-atrophy and C-1 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 (Fig. 1).

Endoscopic intestinal metaplasia typically appears as slightly elevated and grayish-white plaques surrounded by mixed patchy pink and pale areas of the mucosa, forming an irregular uneven surface. Villous patterns, whitish colors, and rough surfaces are useful indicators for the endoscopic diagnosis of intestinal metaplasia.21 Intestinal metaplasia score 0 was defined as the absence of intestinal metaplasia; intestinal metaplasia score 1 as the presence of intestinal metaplasia within the antrum, and intestinal metaplasia score 2 as intestinal metaplasia extending into the corpus (Figs. 1a–c and 2a–f).

An enlarged fold is defined as a width ≥5 mm that is not flattened or is only partially flattened by stomach insufflation. The absence and presence of enlarged folds were scored as enlarged fold scores of 0 and 1, respectively (Figs. 1a and 2g).

Nodular gastritis is characterized by a mililiary pattern resembling “goosebumps,” which is mainly located in the antrum.22 The absence and presence of nodularity were scored as nodularity scores of 0 and 1, respectively (Figs. 1c and 2h).

Diffuse redness refers to uniform redness with continuous expansion observed in non-atrophic mucosa, mainly in the corpus. RACs are findings in which collecting venules are arranged in the corpus. From a distance, it appears as numerous dots; up close, it has the appearance of a regular pattern of starfish-like shapes. The absence of diffuse redness or RAC throughout the fundic gland area, presence of mild diffuse redness or diffuse redness partially with RAC, and severe diffuse redness or diffuse redness without RAC were scored as diffuse redness scores of 0, 1, and 2, respectively (Figs. 1a and 2i,j).
Updated Sydney system score. Biopsy specimens were obtained from two sites: the greater curvature of the corpus and antrum. One experienced gastrointestinal pathologist diagnosed \textit{H. pylori} density, neutrophil activity, chronic inflammation, atrophy, and intestinal metaplasia score based on the USS on hematoxylin and eosin staining. The scores were graded on a scale of 0–3 (none, 0; mild, 1; moderate, 2; severe, 3). Neutrophil activity and chronic inflammation were defined as the densities of polynuclear neutrophil leukocytes and mononuclear leukocytes in the mucosa, respectively. Pathological atrophy was defined as the loss of normal glandular tissue in the mucosa. Pathological intestinal metaplasia was defined as a phenotypic change from normal epithelial cells of the gastric mucosa to an intestinal phenotype.

Outcomes and statistical analysis. We investigated the association between the Kyoto classification score and the USS score among the entire study population and subgroups of \textit{H. pylori}-positive and \textit{H. pylori}-negative patients. The association between serum anti-\textit{H. pylori} antibody titers and the Kyoto classification and USS scores were also analyzed. We arbitrarily defined serum antibody <3 and $\geq$100 U/mL as 2.9 and 100 U/mL, respectively.

The Mann–Whitney \textit{U} test, Kruskal–Wallis test, and Steel–Dwass test were used for statistical calculations. Statistical significance was defined as a two-sided \textit{P} value <0.05. Calculations were performed using the statistical software Ekuseru-Toukei 2015 (Social Survey Research Information Co., Ltd., Tokyo, Japan).
Figure 2  Representative endoscopic findings based on the Kyoto classification (intestinal metaplasia, enlarged folds, nodularity, and diffuse redness). (a–c) Intestinal metaplasia 1. Intestinal metaplasia is limited to the antrum. (d–f) Intestinal metaplasia 2. Intestinal metaplasia extends to the corpus. (g) Enlarged folds 1. (h) Nodularity 1. (i) Diffuse redness 1. (j) Diffuse redness 2. (a, d, g, i, j) Greater curvature of the corpus. (b, e) Lesser curvature of the corpus. (c, f, h) The antrum.
Results

Patient characteristics. Of the 726 patients, 5 patients with unknown status for *H. pylori* infection were excluded, and 721 were registered. A flowchart of patient diagnoses of *H. pylori* infection is presented in Supporting information, Figure S1.

Table 1  Baseline characteristics of the study patients

|                      | Total   | *H. pylori* negative | *H. pylori* positive |
|----------------------|---------|----------------------|---------------------|
| N                    | 721     | 267                  | 454                 |
| Age, mean (±SD)      | 49.2 ± 13.3 | 46.2 ± 13.6         | 51.0 ± 12.8         |
| Female sex, %        | 57.8    | 64.8                 | 53.7                |
| Kyoto classification score |
| Atrophy              | 0.98    | 0.28                 | 1.39                |
| Intestinal metaplasia | 0.39    | 0.07                 | 0.57                |
| Enlarged folds       | 0.26    | 0.03                 | 0.39                |
| Nodularity           | 0.21    | 0.02                 | 0.33                |
| Diffuse redness      | 0.99    | 0.09                 | 1.52                |
| Updated Sydney system score |
| Neutrophil activity  |
| Corpus               | 0.50    | 0.01                 | 0.79                |
| Antrum               | 0.47    | 0.00                 | 0.74                |
| Chronic inflammation |
| Corpus               | 1.13    | 0.15                 | 1.69                |
| Antrum               | 1.08    | 0.20                 | 1.59                |
| Atrophy              |
| Corpus               | 0.14    | 0.05                 | 0.20                |
| Antrum               | 0.13    | 0.06                 | 0.18                |
| Intestinal metaplasia |
| Corpus               | 0.10    | 0.02                 | 0.15                |
| Antrum               | 0.10    | 0.03                 | 0.14                |

Table 2  The updated Sydney system score based on endoscopic gastritis

|                      | Endoscopic atrophy | Endoscopic intestinal metaplasia | Enlarged folds | Nodularity | Diffuse redness |
|----------------------|--------------------|----------------------------------|----------------|------------|----------------|
|                      | (-)    | (+)    | (-)    | (+)    | (-)    | (+)    | (-)    | (+)    |
| N                    | 253    | 468    | 548    | 173    | 536    | 185    | 564    | 157    | 342    | 379    |
| Neutrophil activity  |
| Corpus               | 0.103***| 0.714  | 0.427***| 0.728  | 0.375***| 0.859  | 0.406***| 0.834  | 0.158***| 0.807  |
| Antrum               | 0.104***| 0.662  | 0.403***| 0.669  | 0.379***| 0.723  | 0.398***| 0.713  | 0.210***| 0.698  |
| Chronic inflammation |
| Corpus               | 0.274***| 1.583  | 0.982***| 1.578  | 0.879***| 1.838  | 0.920***| 1.860  | 0.437***| 1.744  |
| Antrum               | 0.296***| 1.497  | 0.945***| 1.494  | 0.910***| 1.560  | 0.946***| 1.541  | 0.571***| 1.531  |
| Pathological atrophy |
| Corpus               | 0.004***| 0.220  | 0.064***| 0.393  | 0.122*  | 0.207  | 0.139   | 0.160  | 0.041***| 0.236  |
| Antrum               | 0.012***| 0.199  | 0.052***| 0.390  | 0.147   | 0.093  | 0.155   | 0.068  | 0.113   | 0.152  |
| Pathological intestinal metaplasia |
| Corpus               | 0.000***| 0.160  | 0.033***| 0.329  | 0.080** | 0.173  | 0.099   | 0.121  | 0.015***| 0.185  |
| Antrum               | 0.012***| 0.146  | 0.033***| 0.308  | 0.104   | 0.087  | 0.122*  | 0.019  | 0.109   | 0.090  |

P values were calculated using the Mann–Whitney U test by comparing the updated Sydney system scores between presence and absence of endoscopic gastritis.

*P < 0.05.
**P < 0.01.
***P < 0.001.

The baseline characteristics of the study patients are shown in Table 1. The average age was 49.2 years, and 57.8% of the study population were females. There were 267 and 454 subjects who were *H. pylori*-negative and *H. pylori*-positive, respectively. The average Kyoto scores were 0.98 for atrophy, 0.39 for intestinal metaplasia, 0.26 for enlarged fold, 0.21 for nodularity, and 0.99 for diffuse redness. The average USS scores in the corpus and antrum were 0.50 and 0.47 for neutrophil activity, 1.13 and 1.08 for chronic inflammation, 0.14 and 0.13 for atrophy, and 0.10 and 0.10 for intestinal metaplasia, respectively.

Association between Kyoto classification and updated Sydney system score. Table 2 shows the association between the absence or presence of endoscopic findings and the USS scores in all patients. All endoscopic findings in the Kyoto classification for gastritis were associated with high scores of pathological inflammation (i.e. neutrophil activity and chronic inflammation) in both the corpus and antrum. Endoscopic atrophy and intestinal metaplasia were associated with high scores of pathological atrophy and intestinal metaplasia in both the corpus and antrum. Nodularity was associated with a low score of pathological intestinal metaplasia in the antrum. Table S1 shows the association between the quantitative Kyoto classification and the USS scores in all patients. The results evaluated by the quantitative Kyoto classification scores were similar to those evaluated by the absence or presence of endoscopic findings.

The association between the Kyoto classification and updated Sydney system score among *H. pylori*-positive patients. Table 3 shows the association between the absence or presence of endoscopic findings in the
Kyoto classification and pathology

Table 3  Among *Helicobacter pylori* positive patients, the updated Sydney system score based on endoscopic gastritis

|                      | Endoscopic atrophy | Endoscopic intestinal metaplasia | Enlarged folds | Nodularity | Diffuse redness |
|----------------------|--------------------|----------------------------------|----------------|------------|----------------|
|                      | (–)    | (+)    | (–)   | (+)    | (–)   | (+)    | (–)   | (+)    | (–)   | (+)    | (–)   | (+)    |
| Neutrophil activity  |        |        |        |        |        |        |        |        |        |        |        |        |
| Corpus               | 0.667  | 0.798  | 0.786  | 0.786  | 0.717*** | 0.893** | 0.733  | 0.730  | 0.742  | 0.737  | 0.559*** | 0.845  |
| Antrum               | 0.684  | 0.745  | 0.747  | 0.728  | 0.733  | 0.750  | 0.742  | 0.737  | 0.769  | 0.733  |           |        |
| Chronic inflammation |        |        |        |        |        |        |        |        |        |        |        |        |
| Corpus               | 1.590  | 1.704  | 1.719  | 1.648  | 1.572*** | 1.881** | 1.590  | 1.591  | 1.593*** | 1.895  | 1.323*** | 1.789  |
| Antrum               | 1.474  | 1.602  | 1.610  | 1.557  | 1.590  | 1.591  | 1.601  | 1.572  | 1.703*  | 1.563  |           |        |
| Pathological atrophy |        |        |        |        |        |        |        |        |        |        |        |        |
| Corpus               | 0.026* | 0.216  | 0.099***| 0.384  | 0.190  | 0.216  | 0.217  | 0.166  | 0.054** | 0.237  |           |        |
| Antrum               | 0.026  | 0.190  | 0.086***| 0.342  | 0.227* | 0.097  | 0.236**| 0.060  | 0.356*  | 0.131  |           |        |
| Pathological intestinal metaplasia |        |        |        |        |        |        |        |        |        |        |        |        |
| Corpus               | 0.000* | 0.166  | 0.054***| 0.333  | 0.134  | 0.181  | 0.166  | 0.125  | 0.022** | 0.186  |           |        |
| Antrum               | 0.026  | 0.153  | 0.051***| 0.310  | 0.176  | 0.091  | 0.206***| 0.020  | 0.341***| 0.092  |           |        |

*P* values were calculated using the Mann–Whitney *U* test by comparing the updated Sydney system scores between presence and absence of endoscopic gastritis.

*P* < 0.05.

**P** < 0.01.

***P** < 0.001.

Kyoto classification for gastritis and the USS scores among *H. pylori*-positive patients.

Endoscopic atrophy was associated with high scores of pathological atrophy and intestinal metaplasia in the corpus (*P* = 0.049 and 0.037, respectively). Endoscopic intestinal metaplasia was associated with high scores of pathological atrophy and intestinal metaplasia in both the corpus and antrum (all *P* < 0.001). Enlarged folds were associated with high scores of neutrophil activity and chronic inflammation in the corpus (*P* < 0.001) and with a low score of pathological atrophy in the antrum (*P* = 0.018). Nodularity was associated with high scores of neutrophil activity and chronic inflammation in the corpus (*P* = 0.015 and *P* < 0.001, respectively) and with low scores of pathological atrophy and intestinal metaplasia in the antrum (*P* = 0.009 and *P* < 0.001, respectively). Diffuse redness was associated with high scores of pathological inflammation, atrophy, and intestinal metaplasia in the corpus, but with low scores of chronic inflammation, atrophy, and intestinal metaplasia in the antrum.

Table 4 shows the association between quantitative Kyoto classification scores and the USS scores among *H. pylori*-positive patients. Regarding the pathological topography of neutrophil activity, the neutrophil activity scores in the corpus were higher than those in the antrum in patients with a Kyoto classification atrophy score 2, enlarged fold score 1, nodularity score 1, and diffuse redness score 2 (*P* = 0.040, 0.003, 0.018, and <0.001, respectively). In patients with a Kyoto classification diffuse redness score 0, the neutrophil activity score in the corpus was lower than that in the antrum (*P* = 0.006). Regarding the pathological topography of intestinal metaplasia, the pathological intestinal metaplasia score in the corpus was higher than that in the antrum in patients with a Kyoto classification intestinal metaplasia score 2 (*P* = 0.045).

The association between the Kyoto classification and updated Sydney system scores among *H. pylori*-negative patients. Table 5 shows the association between the absence or presence of endoscopic findings in the Kyoto classification for gastritis and the USS scores among *H. pylori*-negative patients.

All endoscopic findings in the Kyoto classification for gastritis were associated with high scores for chronic inflammation in both the corpus and antrum. Endoscopic atrophy and intestinal metaplasia were associated with high neutrophil activity scores in the corpus, while pathological atrophy and intestinal metaplasia were associated with high neutrophil activity scores in both the corpus and antrum. Furthermore, diffuse redness was associated with high scores for pathological atrophy in both the corpus and antrum.

The association of serum anti-*H. pylori* antibody titers with the Kyoto classification and updated Sydney system scores. We present the mean serum anti-*H. pylori* antibody titers based on the Kyoto classification score and the USS score in Figures S2 and S3, respectively.

The serum antibody levels were associated with all endoscopic findings in the Kyoto classification for gastritis. Serum antibody titers were associated with high scores for pathological inflammation in both the corpus and antrum and high scores for pathological atrophy and intestinal metaplasia in the antrum.

Discussion

In *H. pylori*-positive subjects, our main findings are as follows. First, atrophy and intestinal metaplasia were consistent between endoscopy and pathology. Second, enlarged folds, nodularity, and diffuse redness were significantly associated with pathological...
inflammation in the corpus. Interestingly, enlarged folds, nodularity, and diffuse redness were inversely associated with pathological atrophy. Nodularity and diffuse redness were inversely associated with pathological intestinal metaplasia.

Enlarged folds are associated with altered parietal cells, long foveolar of the corpus mucosa, suppressed acid secretion, increased serum gastrin, high serum *H. pylori* antibody titer, and increased serum pepsinogen I and II, especially pepsinogen II.23–27

Table 4  Among *Helicobacter pylori* positive patients, the updated Sydney system score based on the Kyoto classification score

|                         | Endoscopic atrophy | Endoscopic intestinal metaplasia | Enlarged folds | Nodularity | Diffuse redness |
|-------------------------|--------------------|----------------------------------|----------------|------------|----------------|
|                         | 0 1 2              | 0 1 2                            | 0 1 2          | 0 1 2      | 0 1 2          |
| Neutrophil activity     |                    |                                  |                |            |                |
| Corpus                  | 0.667†††           | 0.739†                     | 0.852           | 0.786     | 0.783          | 0.788          | 0.717*** | 0.893          | 0.748*| 0.862          | 0.559*** | 0.515          | 0.878          |
| Antrum                  | 0.684†             | 0.736                      | 0.753           | 0.747     | 0.700          | 0.745          | 0.733     | 0.751          | 0.742| 0.737          | 0.769     | 0.606          | 0.745          |
| Chronic inflammation    |                    |                                  |                |            |                |
| Corpus                  | 1.590              | 1.648                      | 1.755           | 1.719††† | 1.467          | 1.758          | 1.572*** | 1.882          | 1.593*** | 1.895          | 1.323*** | 1.364          | 1.832          |
| Antrum                  | 1.474              | 1.589                      | 1.614           | 1.610     | 1.583          | 1.541          | 1.590     | 1.593          | 1.601| 1.572          | 1.703     | 1.576          | 1.561          |

Pathological atrophy

|                         |                    |                                  |                |            |                |
| Corpus                  | 0.026***           | 0.071                      | 0.350           | 0.093††† | 0.183          | 0.505          | 0.190     | 0.215          | 0.217| 0.166          | 0.054†     | 0.121          | 0.248          |
| Antrum                  | 0.026***           | 0.077                      | 0.294           | 0.086††† | 0.483          | 0.255          | 0.227†    | 0.097          | 0.236**| 0.060          | 0.356     | 0.152          | 0.129          |

Pathological intestinal metaplasia

|                         |                    |                                  |                |            |                |
| Corpus                  | 0.000***           | 0.050                      | 0.273           | 0.054††† | 0.167          | 0.434          | 0.134     | 0.180          | 0.166| 0.125          | 0.022†     | 0.091          | 0.195          |
| Antrum                  | 0.026***           | 0.061                      | 0.237           | 0.051††† | 0.467          | 0.214          | 0.176     | 0.050          | 0.205***| 0.020          | 0.341††     | 0.061          | 0.095          |

Table 5  Among *Helicobacter pylori* negative patients, the updated Sydney system score based on endoscopic gastritis

|                         | Endoscopic atrophy | Endoscopic intestinal metaplasia | Enlarged folds | Nodularity | Diffuse redness |
|-------------------------|--------------------|----------------------------------|----------------|------------|----------------|
|                         | 0 1 2              | 0 1 2                            | 0 1 2          | 0 1 2      | 0 1 2          |
| Neutrophil activity     |                    |                                  |                |            |                |
| Corpus                  | 0.000***           | 0.057                      |                 | 0.008*    | 0.071          | 0.012          | 0.000     | 0.011          | 0.000| 0.008          | 0.056     | 0.000          | 0.000          |
| Antrum                  | 0.000*             | 0.019                      |                 | 0.004     | 0.000          | 0.004          | 0.000     | 0.004          | 0.000| 0.000          | 0.000     | 0.000          | 0.000          |
| Chronic inflammation    |                    |                                  |                |            |                |
| Corpus                  | 0.033***           | 0.642                      |                 | 0.119***  | 0.786          | 0.139***       | 0.714     | 0.142***       | 0.800| 0.105***       | 0.833     | 0.154***       | 0.889          |
| Antrum                  | 0.085***           | 0.679                      |                 | 0.171***  | 0.786          | 0.190***       | 0.714     | 0.196*         | 0.600| 0.154***       | 0.889     | 0.154***       | 0.889          |
| Pathological atrophy    |                    |                                  |                |            |                |
| Corpus                  | 0.000***           | 0.250                      |                 | 0.024***  | 0.500          | 0.050          | 0.000     | 0.050          | 0.000| 0.036**        | 0.222     | 0.036**        | 0.222          |
| Antrum                  | 0.009***           | 0.264                      |                 | 0.012***  | 0.929          | 0.062          | 0.000     | 0.062          | 0.000| 0.024***       | 0.556     | 0.024***       | 0.556          |
| Pathological intestinal metaplasia |                    |                                  |                |            |                |
| Corpus                  | 0.000***           | 0.113                      |                 | 0.008***  | 0.286          | 0.023          | 0.000     | 0.023          | 0.000| 0.012          | 0.167     | 0.012          | 0.167          |
| Antrum                  | 0.009*             | 0.094                      |                 | 0.012***  | 0.286          | 0.027          | 0.000     | 0.027          | 0.000| 0.024          | 0.056     | 0.024          | 0.056          |

P values were calculated using the Mann–Whitney *U* test by comparing the updated Sydney system scores between presence and absence of endoscopic gastritis.

† *P* < 0.05.

** *P* < 0.01.

*** *P* < 0.001.

O Toyoshima et al. Kyoto classification and pathology

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Nodularity represents the aggregation of lymphoid follicles in the mucosa. A high serum \( H. \text{pylori} \) antibody titer is associated with nodularity.\(^7\) The congestion and dilation of the subepithelial capillary network with inflammation cause diffuse redness of the mucosal surface.\(^28\) Therefore, endoscopic enlarged folds, nodularity, and diffuse redness represent mucosal inflammation and reflect severe neutrophil activity and chronic inflammation.\(^5,29\) After the continuation of acute inflammation induced by \( H. \text{pylori} \) infection, atrophy and intestinal metaplasia appear, and active inflammation and \( H. \text{pylori} \) density decrease.\(^30\) The present study showed that enlarged folds, nodularity, and diffuse redness were inversely associated with pathological atrophy and intestinal metaplasia,\(^1,35\) which is consistent with our results.

Several reports have shown good reproducibility of the agreement between pathological diagnosis and endoscopic findings for atrophy and intestinal metaplasia.\(^17-19,32,33\) which is consistent with our results. However, there are still many studies that have reported opposite findings, especially for atrophy and intestinal metaplasia.\(^34\) Our study showed that pathological intestinal metaplasia was significantly higher in the corpus than that in the antrum when endoscopic intestinal metaplasia was present in the corpus (i.e., Kyoto classification intestinal metaplasia score 2). Pathological intestinal metaplasia in the corpus has been reported to be associated with a higher risk of gastric cancer than antral intestinal metaplasia; therefore, endoscopic determination of intestinal metaplasia in the corpus is beneficial.

Regarding the topographic distribution of neutrophil activity, it has been reported that corpus-predominant activity has a higher risk of gastric cancer than antral predominant activity.\(^1,13,15\) In the present study, severe endoscopic atrophy, enlarged folds, and nodularity showed that neutrophil activity in the corpus was higher than that in the antrum. Each endoscopic feature was consistent with the risk of gastric cancer.

In the overall analysis including both \( H. \text{pylori} \)-negative and \( H. \text{pylori} \)-positive patients, pathological inflammation was associated with all endoscopic findings (atrophy, intestinal metaplasia, enlarged folds, nodularity, and diffuse redness). Pathological neutrophil activity and chronic inflammation are excellent indicators of \( H. \text{pylori} \) infection.\(^36,37\) All these endoscopic findings are also affected by \( H. \text{pylori} \) infection.\(^6-8,10\) \( H. \text{pylori} \) infection is thought to similarly affect endoscopic and pathological findings.

The strengths of this study are as follows. The first is a comprehensive survey of endoscopic findings in the Kyoto classification for gastritis, namely, new endoscopy-based diagnostic criteria for which evidence is accumulating. Second, this study included not only the entire analysis of \( H. \text{pylori} \)-negative and \( H. \text{pylori} \)-positive subjects (Tables 2 and S1), but also the subanalyses that were individually performed for \( H. \text{pylori} \)-positive and \( H. \text{pylori} \)-negative subjects (Tables 3, 4, and 5). Because endoscopic and pathological findings are strongly affected by \( H. \text{pylori} \) infection, the analysis results might depend on the positive rate of \( H. \text{pylori} \) infection. As a result, different tendencies were observed between the entire analysis and subanalyses of \( H. \text{pylori} \)-positive patients. We discovered that enlarged folds, nodularity, and diffuse redness were inversely associated with pathological atrophy and intestinal metaplasia, which pose a high risk for gastric cancer among \( H. \text{pylori} \)-infected patients. Third, endoscopic atrophy, intestinal metaplasia, and diffuse redness were evaluated not only as absent or present, but also as a three-step variable of 0/1/2 based on the Kyoto classification score. Furthermore, pathological gastritis was assessed separately in the corpus and antrum, and the topographic distribution of pathological gastritis was analyzed. Because the topographic distribution of neutrophil activity and intestinal metaplasia is strongly associated with gastric cancer risk,\(^1,15\) a detailed examination of the topographic distribution is meaningful.

This study had some limitations. This study had a retrospective design in a single institute. However, data were well-organized. This study only investigated endoscopic findings that were used in the Kyoto classification score. Further analysis is expected, including other findings related to gastric cancer, such as xanthoma,\(^38\) foveolar hyperplastic polyp,\(^39\) RAC,\(^40\) and fundic gland polyp.\(^41\) Although this study excluded patients who received prior \( H. \text{pylori} \) eradication therapy, it was found that the \( H. \text{pylori} \)-negative group included \( H. \text{pylori} \)-naive patients, patients with \( H. \text{pylori} \) that spontaneously disappeared, and patients who received unintentional \( H. \text{pylori} \) eradication by antibiotic treatment for other infectious diseases.\(^42\) Comparative studies between these groups will be required in the future.

Conclusions

Atrophy and intestinal metaplasia were consistent between the endoscopic and pathological diagnoses. Enlarged folds, nodularity, and diffuse redness were associated with pathological inflammation, namely, neutrophil activity, and chronic inflammation. Among \( H. \text{pylori} \)-positive individuals, enlarged folds, nodularity, and diffuse redness were inversely associated with pathological atrophy and intestinal metaplasia in the antrum. The endoscopic diagnosis of gastritis partially reflected the pathology.

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Supporting information

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Patient flowchart of diagnosis for *Helicobacter pylori* infection.

Figure S2. Serum anti-*Helicobacter pylori* antibody titer based on the Kyoto classification score.

Figure S3. Serum anti-*Helicobacter pylori* antibody titer based on the updated Sydney system score.

Table S1. The updated Sydney system score based on the Kyoto classification score.