Gastric mucosal disease
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Chapter 3

Agreement between Endoscopic and Histological Scores of Gastric Atrophy

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ABSTRACT

Objective: To investigate the strength of agreement between the endoscopic atrophic border (EAB) and the histological score for atrophy.

Methods: A series of 298 dyspeptic Japanese patients underwent upper endoscopy. The grade of gastric atrophy was estimated according to EAB. Antral and corpus biopsy were taken and biopsies were evaluated semi-quantitatively according to the updated Sydney classification system including the score for atrophy. The StatExact software package was used to calculate the weighted kappa statistics.

Results: The strength of agreement between the endoscopic score of atrophy (EAB) and the histological score of atrophy was good with a weighted kappa value of 0.51 (95% confidence interval 0.44-0.59).

Conclusion: The strength of agreement between endoscopic and histological scores of atrophy is not worse than interobserver histological agreement between two pathologists. It is worthwhile to further research on the use of EAB to identify and score gastric atrophy.

Key Words: Atrophy, Endoscopic atrophic border, Histology, Weighted kappa value
Introduction

Gastric atrophy is defined as the loss of the specialized glandular structures\(^1\). Loss of these gastric glands may follow a multifocal distribution and usually be accompanied by intestinal metaplasia\(^2-3\). The clinicopathological importance of gastric atrophy is based upon its close association with gastric carcinoma\(^4-6\). It has been estimated that the risk of gastric cancer in patients with gastric atrophy is about 5-9 fold compared with the risk in subjects without atrophy\(^7-9\). So the significance of atrophy and intestinal metaplasia for the subsequent development of gastric cancer is widely accepted.

With respect to the quality of health care and the consequences for treatment of individual patients, it is important to improve the diagnostic methods of atrophic gastritis.

The updated Sydney system designed a visual analogue scale for grading of the different histopathological parameters including the score of atrophy, but without well-defined criteria, the visual analogue scale would not solve all difficulties\(^10-11\). The least likelihood of agreement was seen for atrophy particularly in the antrum and others have commented on the poor interobserver agreement on the recognition of atrophy. The assessment remains a problem. In our previous study\(^12\), the weighted kappa value of the interobserver histological agreement for atrophy between two pathologists was 0.49, which corresponded to moderate reproducibility. So the need remains for improvement of the criteria for grading atrophy.

Since 1969, Japanese have used endoscopy to visualize directly changes in the gastric mucosa of gastritis patients and developed an endoscopic scoring system for atrophy using the endoscopic atrophic border (EAB)\(^13-15\), which marks the transition between
non-atrophic gastritis and atrophic gastritis. The atrophic border is the boundary between the antral and fundic glandular territories, which is endoscopically recognized by discriminating between differences in color and height of the gastric mucosa. The area of atrophy is yellowish pale in color and transparent blood vessels, while that of non-atrophy is homogeneously reddish and smooth. Recently the close relationship between the EAB and gastric cancer was reported by Yoshimura et al. They found that most gastric cancer, especially the intestinal type, occurs on the distal side of EAB where severe atrophy is present\textsuperscript{16}.

In this study we investigated the relation between the EAB and histological score for atrophy, and to further improve the diagnosis of atrophy.
Materials and Methods

Patients
A series of 298 dyspeptic Japanese patients (187 men, and 111 women; mean age=55.97±13.07) from the department of Gastroenterology, Kure Kyosai Hospital, Japan were enrolled for this study during the period of 1994-1996.

Endoscopy and Biopsy
Upper gastrointestinal endoscopy was performed in all patients after an overnight fast. At least four biopsy samples were taken for histological examination, two from the greater curvature of the antrum and two from the upper middle corpus. The grade of gastric atrophy was estimated according to the endoscopic atrophic border (EAB), which was reported by Kimura & Takemoto in 1969 (Fig 1). This classification divides the extent of atrophy into a closed type (C-type) and an open type (O-type). The C-type means atrophic border remains on the lesser curvature of the stomach, while the O-type represents the atrophic border no longer exists on the lesser curvature but extends along the anterior and posterior walls of the stomach. The atrophic border crosses the angulus on the lesser curvature in the C1 pattern, the lower and middle parts of the corpus in the C2 pattern, and the upper part of the corpus in the C3 pattern. The atrophic border, which is parallel to the vertical axis of the stomach, is on the lesser curvature in the O1 pattern, on the anterior and posterior wall in the O2 pattern and on the greater curvature in the O3 pattern. The grade is defined as followings: none(C0), mild(C1, C2), moderate (C3, O1), severe (O2, O3). C1 represents highly localized antral gastritis, subsequent lines represents increasing extension through the lessor and greater
curvatures. O3 represents extensive atrophic gastritis, affecting almost the entire stomach. (see Fig 1)

**Histology**

Biopsies were stained with hematoxylin-eosin, and the following five features were evaluated semi-quantitatively in the specimens of antral and corpus of each patients:

- degree of inflammation
- neutrophilic infiltration
- glandular atrophy
- intestinal metaplasia
- \(H_p\) density. Each of the variables was graded as absent(=0), mild(1-2), moderate (3-4), severe(5-6), according to the updated Sydney classification system. Particular attention was paid to the glandular atrophy, which was defined as the loss of specialized gastric glandular tissue with or without replacement of intestinal metaplasia. Specially, it was defined as “mild”, if there was only focal (grade 1) or small areas( grade 2) of gastric glands missing. “moderate”, if there was up to 25 % ( grade 3) and 25%-50%(grade 4) of gastric glands missing, and “severe”, if the loss of glands was more than 50 % (grade 5) and complete or almost complete (grade 6). Glands replaced by metaplastic epithelium represented atrophy and were scored accordingly. All biopsy specimens were blindly examined by a pathologist (YL), who was unaware of clinical and endoscopic data of the patients. Totally 499 antral and 416 corpus specimens were evaluated. Some specimens were excluded from the study because they were of insufficient mucosal thickness for proper assessment of atrophy.

**Statistics**

The correlation and agreement between endoscopic and histologic findings in evaluating the grade of gastric atrophy were assessed by the weighted kappa value\(^{17}\) and its 95% confidence interval ( CI) using the StatExact software package. Weighted kappa values
were based on the idea that if more than one step difference existed, their disagreement should be given more weight than if they differed by only one step whilst taking chance into account. Values of weighted kappa less than 0.3 represented poor agreement, values between 0.3-0.5 were considered to represent moderate/good agreement, values between 0.5-0.7 represented good agreement and values exceeding 0.7 excellent agreement.

Results

The strength of agreement between the endoscopic score of atrophy (EAB) and the histological score of atrophy reached good reproducibility with a weighted kappa value of 0.51 (95% confidence interval: 0.44-0.59). (Table 1)

It is interesting to see to what extent and in which direction the final diagnosis differed from each other. Table 1 shows the difference between the endoscopic and histological findings. Complete agreement of atrophy on 0-6 grades in this study was 21% (62/298), one step disagreement occurred in 43% (127/298), two steps disagreements were found in 22% (67/298), and disagreement of more than two steps was seen in 14% (42/298).

Remarkably, the results in endoscopy more often were changed to a mild to moderate degree of atrophy than to a severe degree, while the degree in the histological findings is more often in moderate and severe degree.
Table 1. Cross tabulation of the endoscopic and histologic scores on atrophy

<table>
<thead>
<tr>
<th>Histology</th>
<th>C0</th>
<th>C1</th>
<th>C2</th>
<th>C3</th>
<th>O1</th>
<th>O2</th>
<th>O3</th>
<th>Total</th>
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<td>0</td>
<td>21</td>
<td>9</td>
<td>10</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>44</td>
</tr>
<tr>
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<td>6</td>
<td>7</td>
<td>4</td>
<td>3</td>
<td>0</td>
<td>0</td>
<td>20</td>
</tr>
<tr>
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<td>0</td>
<td>7</td>
<td>6</td>
<td>11</td>
<td>8</td>
<td>3</td>
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<td>35</td>
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<tr>
<td>3</td>
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<td>3</td>
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<td>11</td>
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<tr>
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<td>6</td>
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<td>10</td>
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<td>68</td>
<td>78</td>
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<td>15</td>
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</tbody>
</table>
Discussion

Correct and reliable histological diagnosis of atrophy has a great influence on clinical practice. Reliability in assessing atrophy in histological specimens is important because the progression is associated with an increased risk of gastric cancer. But as reported the intra- and interobserver agreement on the grading of gastric atrophy could not get the satisfied result, because no gold standard is available, and one must rely completely on the understanding the definition of atrophy and his experience. So it is urgent and necessary to find a better way to improve the judgement of atrophy.

Weighted kappa values are known to be much more rigorous criteria, which exclude the bias of agreement by chance. In our study, the strength of agreement between endoscopic and histological scores of atrophy is good with a weighted kappa value of 0.51. It should be emphasized that the results represent agreement not only the presence or absence of atrophy, but where present, on its grade of severity. All the variables in our study were graded using a visual analogue scale graded from 0 to 6. This visual analogue scale was designed to increase intra- and interobserver agreement in the estimation of severity of certain features of gastritis. And the grades on atrophy under endoscopy or histology are parallel.

Although the endoscopic and histological scores of atrophy revealed a good agreement, also there existed 14% disagreement of more than two steps. This apparent paradox may be partly explained by the quality of the biopsies obtained. Some were fragments of necrotic tissues, others were traumatised and many were not composed of mucosa which had been inadvertently sample. From experience, it is known that histologic atrophy may
be absent when endoscopic atrophy is present, and vice versa. Neither one could substitute another. The biopsy specimens from one site in the stomach only represent the local findings. Alternatively the sampling might be superficial and not adequate. So the biopsy may not reveal the true extent of gastritis. More insight was gained into the process of clinical diagnosis.

As the endoscopic atrophic border is the boundary of both atrophy and gland type, it is the reflection of the atrophic pattern in whole stomach. We combined the antral and corpus histological score together instead of evaluating the scores separately. So the histological results we used in the cross tabulations were the final combined scores.

The investigation of chronic gastritis has progressed rapidly, but still many points remain unsettled. A random observation of biopsy is of no meaning, and the strict comparison of endoscopic and histological finding is mandatory. In view of the relationship of this condition, the diagnosis of gastric atrophy should be made on the basis of both endoscopy and histology. To our knowledge, no study has yet been published concerning the agreement on endoscopic and histological findings of atrophy except in Japan\textsuperscript{18-21}. With the excellent development of fiber-gastroscopy, and endoscopists and pathologists acquaint themselves with the criteria well, it has become possible to get high agreement on atrophy. It is worthwhile to further research on the use of endoscopic atrophic border to identify and score gastric atrophy.
References


17. Cohen J. Weighted kappa: nominal scale agreement with provision for scaled disagreement or partial credit. Psychol Bull 1968;70:213-220


Fig 1. Schematic illustration of the extension of the endoscopic atrophic border and the patterns of endoscopically diagnosed atrophy, as represented by Kimura et al.