Do endoscopic markers still play a role in the diagnosis of celiac disease?

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Background: A number of changes in the duodenum are associated with celiac disease (CD), and can be identified endoscopically. Their accuracy becomes crucial as CD markers. This study aimed to determine the diagnostic value of endoscopic markers and to find ways of applying them in the diagnosis of CD.

Methods: Seven hundred and sixty-five consecutive patients referred for upper gastrointestinal endoscopy during 18 months were enrolled in the study. The second part of the duodenum was inspected carefully, and biopsies were taken in all patients to detect histologic changes suggestive of CD.

Results: Endoscopic features suggestive of CD were observed in 69 (10.6%) patients; of these, 7 (10.1%) patients were finally diagnosed to have CD. Of the remaining 578 patients in whom the endoscopic markers were not seen, 2 (0.3%) patients were found to have CD. The overall sensitivity, specificity, PPV and NPV of the markers for the diagnosis of CD were 77%, 91%, 10% and 99%, respectively. Of the 9 patients who had CD, 5 had typical symptoms of CD and 4 had atypical features of CD.

Conclusions: Owing to high NPV of endoscopic markers, a careful observation of the second part of duodenum plays an important role in the diagnosis of CD. In patients in whom endoscopic markers are observed, biopsies are indicated; routine duodenal biopsy in all patients cannot be advocated.


Celiac disease (CD) is an immune-mediated enteropathy, triggered by the ingestion of gluten-containing grains in genetically susceptible persons. CD was first described with classic symptoms of malabsorption syndrome such as diarrhea, steatorrhea and weight loss. However, we now know more about the clinical manifestations of CD.1,2 The variability in clinical presentation is a major challenge in early detection of CD often leading to delay in diagnosis which may result in serious complications.3 Timely diagnosis of CD and strict dietary treatment is important, which could prevent complications.4

A considerable number of celiac patients have upper gastrointestinal symptoms for a long duration before CD is correctly diagnosed, and most of them undergo esophagogastro duodenoscopy (EGD). Thus, EGD can play an important role in early detection of the disease. Over the past 2 decades, a number of changes in the duodenum, which are associated with CD and can be identified endoscopically, have been recognized.5 These include grooves (fissures) in the mucosa between folds, lace pattern, punctate whitish spots, reduction of folds and smaller size or flattened folds. When we consider these findings as CD markers, their accuracy assumes importance. Though there are few studies in this field, the diagnostic value of these endoscopic markers and particularly their clinical utility is still unclear.6,7

Small bowel biopsy is the gold standard for diagnosing CD. However, it is not clear whether routine duodenal biopsy is advisable in all patients.

This study aimed to determine the diagnostic value of endoscopic markers and to find ways of applying them in the diagnosis of CD.

Methods
This study was performed at Poursina Hakim Research Institute (a referral center of gastrointestinal and liver diseases in Isfahan, Iran). During a period of 18 months, 765 consecutive patients who were referred to our clinic to undergo EGD for various indications were evaluated.

A complete medical history was taken and patients were divided into three groups according to their signs and
symptoms at the time of endoscopy without considering the indication for endoscopy.

**Group 1:** typical presentation for CD – chronic diarrhea, steatorrhea, weight loss and anemia; **Group 2:** atypical gastrointestinal symptoms for CD – abdominal pain, gaseous abdomen, constipation, dyspepsia, epigastric pain, reflux and vomiting; and **Group 3:** associated disorders of CD – epilepsy, diabetes mellitus, failure to thrive, infertility, rheumatic disease, Crohn disease, ulcerative colitis, lymphoma and liver disease.

All endoscopies were performed using Pentax EPM-3300; EG 2940 scope by a single experienced gastroenterologist and the recordings were reviewed by another expert. Lidocaine spray was routinely used before endoscopy and intravenous midazolam was also used when needed. The endoscopist carefully observed the second part of the duodenum (D2) for markers suggestive of CD including lace pattern, scalloping, grooves (fissures) in the mucosa between folds, and reduction or loss of folds. In all patients at least four biopsies were taken from D2 with a standard forceps for histopathology. The tissue was fixed in 10% natural formalin and sent for examination. Sections were stained with hematoxylin and eosin, and reviewed by a single pathologist who was not aware of the patient’s endoscopic findings. Histological abnormality was classified according to the Marsh classification of 1992, revised in 1997.8

Diagnosis of CD was based on small intestinal biopsy specimens showing the appropriate histopathologic features and clinical improvement on a gluten-free diet according to the revised ESPGAN 1990.9

Informed consent were obtained from all the patients for authorization to use their medical records for research purposes, with approval of the protocol by the ethics committee of our institute.

Our data analyses which include sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) were carried out using the statistical software package SPSS 11.5.

### Results

Of 765 patients who were referred, 118 did not return for follow up and were excluded. Thus, 647 patients (mean [SD] age of 42.0 [16.7] years, range: 5–82 years; 313 men) were evaluated.

Endoscopic features suggestive of CD were observed in 69 (10.6%) patients; of these 7 (10.1%) patients were finally diagnosed to have CD. Of the remaining 578 patients in whom the endoscopic markers were not seen, 2 patients (0.3%) were found to have CD.

The overall sensitivity, specificity, PPV and NPV of the CD markers were 77%, 91%, 10%, and 99%, respectively (Table 1). The most sensitive markers were grooves and lace pattern (22.2%). Lace pattern had also the highest PPV and specificity (18.1% and 98.5%, respectively). Grooves between folds and lace pattern had the highest NPV (98.8%).

The accuracy of endoscopic markers according to symptoms are presented in Table 2. Group 1 had the highest sensitivity of 55% and the highest NPV of 99.2%, whereas group 3 has the highest specificity of 90.2 % and

### Table 1. Diagnostic value of endoscopic markers in the diagnosis of celiac disease

<table>
<thead>
<tr>
<th>Endoscopic marker</th>
<th>Celiac disease</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grooves between folds</td>
<td>2</td>
<td>12</td>
<td>22.2</td>
<td>98.1</td>
<td>14.2</td>
</tr>
<tr>
<td>Scalloping folds</td>
<td>1</td>
<td>12</td>
<td>11.1</td>
<td>98.1</td>
<td>7.6</td>
</tr>
<tr>
<td>Lace pattern</td>
<td>2</td>
<td>9</td>
<td>22.2</td>
<td>98.5</td>
<td>18.1</td>
</tr>
<tr>
<td>Reduced folds</td>
<td>1</td>
<td>17</td>
<td>11.1</td>
<td>97.3</td>
<td>5.5</td>
</tr>
<tr>
<td>Mild reduction or loss of folds</td>
<td>1</td>
<td>12</td>
<td>11.1</td>
<td>98.1</td>
<td>7.6</td>
</tr>
</tbody>
</table>

PPV: Positive predictive value. NPV: Negative predictive value

### Table 2: Diagnostic value according to the signs and symptoms at the time of endoscopy

<table>
<thead>
<tr>
<th>Number (%)</th>
<th>Celiac disease</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 1</td>
<td>110 (17.0)</td>
<td>5</td>
<td>105</td>
<td>55.5</td>
<td>83.5</td>
</tr>
<tr>
<td>Group 2</td>
<td>471 (72.7)</td>
<td>0</td>
<td>471</td>
<td>0</td>
<td>26.1</td>
</tr>
<tr>
<td>Group 3</td>
<td>66 (10.3)</td>
<td>4</td>
<td>62</td>
<td>44.4</td>
<td>90.2</td>
</tr>
</tbody>
</table>

PPV: Positive predictive value. NPV: Negative predictive value

**Group 1:** typical presentation for celiac disease (CD); **Group 2:** atypical gastrointestinal symptoms for CD; **Group 3:** associated disorders of CD.
PPV of 6%.

In 9 patients who had CD, 5 had typical symptoms and 4 had associated diseases.

**Discussion**

We found a low sensitivity of endoscopic markers, which was lower than that observed in previous studies. However, these markers had a high NPV of 99%. The PPV for these markers ranged from 5.5% to 18.1%, and was not as high as their NPV.

Previous studies focused only on the sensitivity of these markers, and since the sensitivity was low, they suggested routine duodenal biopsies for every patient who undergoes EGD. In spite of disappointing sensitivity of endoscopic markers we believe that due to desirable NPV, careful observation of the second part of duodenum is one of the best ways to choose patients for taking biopsy.

Another important aspect is the clinical presentation; recent studies have stated that most patients do not have typical manifestation of CD, and have atypical symptoms. In our study, only half of the patients had typical manifestations of CD; the clinical manifestations were not helpful in diagnosing CD. However, when we considered them in addition to endoscopic markers, not only did the diagnostic value not improve but the sensitivity, specificity, NPV and PPV decreased. Only 3% of patients who presented with typical manifestation of CD had this disease. Therefore, clinical manifestations of patients are not helpful in selecting patients for taking biopsies.

We conclude that owing to high NPV of the endoscopic markers, careful observation of duodenum to find minimal changes in mucosa may play an important role in the diagnosis of CD. In patients in whom endoscopic markers are seen, biopsy is indicated. Clinical symptoms should not be considered as the basis for selecting patients for duodenal biopsies.

**References**


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