Factors Affecting Esophageal Motility in Gastroesophageal Reflux Disease

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Background: There are conflicting data concerning the effect of gastroesophageal reflux disease (GERD) on esophageal motor function.

Hypothesis: Duration of GERD might affect severity of symptoms, grade of esophageal mucosal injury, and esophageal motor behavior.

Design: Retrospective study of a defined cohort.

Settings: Two referral centers, one of them academic, for esophageal gastrointestinal motility disorders.

Patients: One hundred forty-seven patients with documented GERD.

Main Outcome Measures: Symptoms, grade of mucosal injury on esophagoscopy, esophageal manometry, ambulatory esophageal pH monitoring, and esophagogram.

Results: Patients with GERD had significantly decreased lower esophageal sphincter resting pressure (P=.02), lower amplitude of esophageal peristalsis at all levels of measurement (P<.001), and more delayed esophageal transit (P=.007) compared with control subjects. Patients with dysphagia, severe esophagitis, and Barrett esophagus presented with a longer history of the disease, significantly worse esophageal motor function (P<.01), and more prolonged esophageal transit than patients without the above features of the disease. Impairment of esophageal peristalsis and lower esophageal sphincter resting pressure were significantly inversely related to the duration of the disease (P<.001). Also, delay of esophageal transit was significantly related to the duration of the disease (P=.002) and inversely related to the amplitude of esophageal peristalsis (P<.001). Unlike the manometric variables, the extent of reflux, as assessed by ambulatory 24-hour esophageal pH monitoring, was not related to the duration of the disease.

Conclusion: A long history of GERD is more commonly associated with presence of dysphagia, delayed esophageal transit, severe esophagitis, presence of Barrett esophagus, and impaired esophageal motility.

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the resting LES, LES relaxation at swallow, and amplitude of
through the cardia into the stomach. Esophageal transit was defined as the time

tichRRULCEPceeHRAACKLRTIAAUKS BHOT, lesiGNO, were excluded from the

to the DeMeester scoring system,5 and only patients with

ty of symptoms. Duration of the disease was defined as the

glass diseases, and diabetic neuropathy), were excluded from the

intestine, were those with an abnormal result of esophageal pH monitoring, which was
defined as a composite score above 14.72 and esophageal
intrinsic pH of less than 4 for more than 4% of the record-
ing time during 24-hour pH measurement.3 All patients in-
cluded in the study fulfilled the criterion of an abnormal re-
sult of esophageal pH monitoring as mentioned already. Before
manometry and esophageal pH monitoring, any medication with
gastrokinetic and antisecretory properties was discontinued for
at least 3 and 7 days, respectively.

statistical analysis

Unless otherwise stated, data are expressed as the median and
range. Statistical analysis included linear correlation of the du-
ration of symptoms with the LES pressure and the amplitude
of esophageal peristalsis at 5, 10, and 15 cm proximal to the
LES. Correlation of the acid reflux measures with the ampu-
tude of esophageal peristalsis and the LES resting pressure, and
with the duration of symptoms, was also performed in the same
manner. Mann-Whitney test for unpaired values was applied to
compare the various clinical and laboratory measures be-
tween patients with and without dysphagia and those with and
without Barrett esophagus. Also, the same test was applied to
assess differences in the manometric, esophageal pH monitor-
ing, and esophageal transit data between different degrees of
esophagitis. P values of less than .05 were considered statisti-
cally significant.

results

There were 95 male and 52 female patients, with a me-
dian age of 51 years (range, 20-78 years), who partici-
pated in the study. The duration of the reflux symptoms ranged from 3 to 52 years (median, 16 years). Twenty-
seven patients (12 male, 15 female) reported grades II and
III dysphagia. They all had been receiving conser-

vative treatment with PPIs, mostly intermittently and at
maintenance doses for 1.8 to 7.2 years. For patients with a GERD history of less than 10 years, there was positive
correlation of the duration of the disease and the length of
treatment with PPIs (P = .005).

Laboratory Assessment

At esophagoscopy, there were 32 patients (21.8%) with-
out esophagitis, while 40 (27.2%) had grade I, 45 (30.6%)
had grade II, and the remaining 30 (20.4%) had grade III
esophagitis. Most of the patients with grade III esophagi-
tis were those who had failed to fully comply with PPI main-
tenance treatment. Twenty patients had short-segment (6
[30%]) or long-segment (14 [70%]) Barrett esophagus. On
the esophagogram, 114 patients (77.6%) had a sliding non-
reducing hiatal hernia, while esophageal transit was sig-
nificantly slower than in controls (18 seconds [7-55 sec-
onds] vs 14 seconds [6-31 seconds]; P = .007). Compared
with controls, patients had significantly lower LES resting
pressure (12 mm Hg [3-41 mm Hg] vs 21 mm Hg [12-31

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mm Hg; \( P = .02 \) and amplitude of esophageal peristalsis at all levels of measurement (5 cm above LES: 58 mm Hg [11-114 mm Hg] vs 96 mm Hg [48-135 mm Hg], \( P < .001 \); 10 cm above LES: 50 mm Hg [10-93 mm Hg] vs 89 mm Hg [42-131 mm Hg], \( P < .001 \); 15 cm above LES: 34 mm Hg [6-81 mm Hg] vs 66 mm Hg [34-96 mm Hg], \( P = .03 \). All of the manometric measures (LES pressure and amplitude of esophageal peristalsis at all levels) were significantly inversely related to the duration of the disease (Figure 1 and Figure 2). Also, the delay of esophageal transit was significantly related to the duration of the disease (Figure 3A) and, as expected, inversely related to the amplitude of peristalsis at the distal esophagus (Figure 3B). Unlike the manometric measures, the extent of reflux at ambulatory 24-hour esophageal pH monitoring, as expressed by the DeMeester score of 69 (34-127) and the percentage of time with pH less than 4 (16% [4.5%-45%]), was not related to the duration of the disease. Also, none of the manometric variables nor those of esophageal transit were related to the duration of treatment with PPIs.

**CORRELATION OF LABORATORY DATA TO CLINICAL PRESENTATION**

Patients with dysphagia tended to be significantly older and have a longer history of disease, lower amplitude of esophageal peristalsis, and lower LES resting pressure as compared with those without dysphagia. Furthermore, the former subset of patients presented with more severe esophagitis, greater incidence of Barrett esophagus, and slower esophageal transit than the latter one (Table 1).

**CORRELATION OF CLINICAL AND LABORATORY DATA TO ENDOSCOPIC FINDINGS**

Severity of esophagitis was significantly related to the duration of disease. Patients with grade III esophagitis had the longest history of reflux disease. Also, patients with grade II esophagitis had significantly lower amplitude of esophageal peristalsis at all levels, lower LES pressure, and greater extent of reflux than those with grade I or no esophagitis at all. Patients with grade III esophagitis presented with even more impaired esophageal peristalsis, lower LES pressure, and greater extent of reflux. Similarly, the more severe the esophagitis, the more prolonged was the esophageal transit (Table 2). No relationship between the extent of reflux as measured by esophageal pH monitoring and the severity of esophagitis was detected.
CORRELATION OF CLINICAL AND LABORATORY DATA TO PRESENCE OF BARRETT ESOPHAGUS

Patients with Barrett esophagus were older and had a longer history of disease and greater incidence of dysphagia than those without. Furthermore, the former group of patients had significantly more severe esophagitis, lower amplitude of esophageal peristalsis and LES resting pressure, greater extent of reflux, and more delayed esophageal transit than the latter one (Table 3).

COMMENT

It has been suggested that amplitude of esophageal contractions is not significantly altered in patients with GERD, even in the presence of severe inflammation, although impairment of LES tone is secondary to esophagitis. Furthermore, it has been reported that healing of macroscopic mucosal lesions with conservative treatment does affect esophageal body motility and that antireflux operations have little influence on esophageal motility pattern. In contrast to our observations, recent data indicate a strong relationship between esophageal exposure to acid and motility impairment. In particular, esophageal motility deteriorates and the prevalence of a mechanically defective LES increases, as mucosal injury progresses, although there are patients with severe mucosal lesions who still have a competent sphincter. The fact that the severity of reflux esophagitis and esophageal motility impairment are related to the duration and frequency of the reflux episodes, as shown in a previous study by our group, may be explained by the presence of acid-sensitive receptors in the esophageal mucosa, as proposed by Bontempo et al.

According to the findings of the present study, which are in agreement with the latter hypothesis, there is a strong relationship between severity of mucosal injury on the one hand and presence of dysphagia and extent of esophageal motility impairment on the other, in GERD. In particular, dysphagia, although not commonly encountered, was detected almost exclusively in patients with severe esophagitis, while delay of esophageal transit was significantly related to the grade of mucosal injury. Furthermore, severity of mucosal inflammation was inversely related to the amplitude of esophageal peristalsis and the LES resting pressure. Our findings partly confirm those reported by Grande et al, according to which dysphagia is related to esophageal motor impairment, rather than to mucosal inflammation.

Despite the aforementioned data, the assumption that both extent and duration of gastroesophageal reflux may adversely influence esophageal motility, although attractive, is neither fully documented nor universally accepted. In regard to severity of GERD, the results reported by Shiino et al and those found in the present study agree in that the extent of acid reflux, as assessed on esophageal pH monitoring, was not related either to the duration and severity of symptoms or to the delay of esophageal transit, the grade of mucosal injury, the presence of Barrett esophagus, or even the impairment of esophageal peristalsis and LES resting pressure. Hence, it can be speculated that impairment of esophageal motor function may be detected independently of the extent of reflux present at a given time and that, since severe esophageal mucosal injury is established, further esophageal motor deterioration is not dependent on the extent of ongoing reflux.

In contrast to the findings of Shiino et al and Armstrong et al, those of the present study showed a strong relationship between duration of GERD symptoms and severity of esophageal motor impairment. We found a strong inverse correlation between the length of history of GERD and the grade of esophageal mucosal injury, as well as the amplitude of esophageal peristalsis and LES resting pressure. Furthermore, patients with dysphagia had a more prolonged history of the disease than those without. Also, the former subset of patients exhibited more severe esophagitis, greater esophageal motor impairment, and more delayed esophageal transit. In addition, GERD history was longer in patients with Barrett esophagus than in those without. Also, impairment of esophageal motility was greater and esophageal transit more delayed in the former group of patients.

Discrepancy between the assumptions concerning influence of GERD duration on esophageal motor function
### Table 1. Clinical and Laboratory Data in Patients With and Without Dysphagia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With Dysphagia (n = 27)</th>
<th>Patients Without Dysphagia (n = 120)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, No. M/F</td>
<td>12/15</td>
<td>83/27</td>
<td>.03</td>
</tr>
<tr>
<td>Age, y*</td>
<td>61 (39-76)</td>
<td>49 (20-78)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Duration of disease, y*</td>
<td>21 (6-51)</td>
<td>14 (3-52)</td>
<td>.002</td>
</tr>
<tr>
<td>Esophagitis, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>3</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Grade I</td>
<td>5</td>
<td>35</td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>7</td>
<td>38</td>
<td></td>
</tr>
<tr>
<td>Grade III</td>
<td>12</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>Barrett esophagus, No.</td>
<td>10/20</td>
<td>10/120</td>
<td>.01</td>
</tr>
<tr>
<td>Amplitude of peristalsis, mm Hg*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cm Proximal to LES</td>
<td>27 (11-69)</td>
<td>68 (15-114)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>10 cm Proximal to LES</td>
<td>21 (10-57)</td>
<td>56 (10-93)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>15 cm Proximal to LES</td>
<td>14 (6-50)</td>
<td>43 (7-81)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LES resting pressure, mm Hg*</td>
<td>9 (3-27)</td>
<td>13 (3-41)</td>
<td>.05</td>
</tr>
<tr>
<td>DeMeester score*</td>
<td>77 (39-127)</td>
<td>68 (34-119)</td>
<td>.14</td>
</tr>
<tr>
<td>Esophageal transit time, s*</td>
<td>33 (11-95)</td>
<td>17 (7-39)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviation: LES, lower esophageal sphincter.

*Data are given as median (range).

### Table 2. Clinical and Laboratory Data According to Grading of Esophagitis

<table>
<thead>
<tr>
<th>Variable</th>
<th>Grade 0 (n = 32)</th>
<th>Grade I (n = 40)</th>
<th>Grade II (n = 45)</th>
<th>P Value†</th>
<th>Grade III (n = 30)</th>
<th>P Value ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, No. M/F</td>
<td>21/11</td>
<td>33/7</td>
<td>27/18</td>
<td>&lt;.05</td>
<td>14/16</td>
<td>&lt;.05</td>
</tr>
<tr>
<td>Age, y</td>
<td>43 (20-71)</td>
<td>47 (23-72)</td>
<td>58 (27-78)</td>
<td>.03</td>
<td>63 (32-77)</td>
<td>.02</td>
</tr>
<tr>
<td>Duration of disease, y*</td>
<td>7.5 (3-27)</td>
<td>13 (3-31)</td>
<td>19 (3-52)</td>
<td>&lt;.001</td>
<td>29 (5-51)</td>
<td>.01</td>
</tr>
<tr>
<td>Amplitude of peristalsis, mm Hg*</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cm Proximal to LES</td>
<td>79 (17-114)</td>
<td>70 (17-111)</td>
<td>48 (11-110)</td>
<td>&lt;.001</td>
<td>34 (18-92)</td>
<td>.004</td>
</tr>
<tr>
<td>10 cm Proximal to LES</td>
<td>62 (10-92)</td>
<td>60 (11-93)</td>
<td>36 (10-86)</td>
<td>&lt;.001</td>
<td>28 (11-70)</td>
<td>.004</td>
</tr>
<tr>
<td>15 cm Proximal to LES</td>
<td>54 (9-80)</td>
<td>48 (6-81)</td>
<td>30 (6-78)</td>
<td>&lt;.001</td>
<td>19 (7-51)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LES resting pressure, mm Hg*</td>
<td>17 (6-41)</td>
<td>17 (6-35)</td>
<td>10 (3-32)</td>
<td>.006</td>
<td>7 (3-36)</td>
<td>.02</td>
</tr>
<tr>
<td>DeMeester score*</td>
<td>59 (36-95)</td>
<td>64 (34-119)</td>
<td>77 (38-105)</td>
<td>.002</td>
<td>77 (44-127)</td>
<td>.6</td>
</tr>
<tr>
<td>Esophageal transit time, s*</td>
<td>16 (8-48)</td>
<td>15 (8-53)</td>
<td>20 (7-46)</td>
<td>.4</td>
<td>27 (14-44)</td>
<td>.003</td>
</tr>
</tbody>
</table>

Abbreviation: LES, lower esophageal sphincter.

*Data are given as median (range).

†Grade II vs grades 0 and I.
‡Grade III vs grade II.
§Indicates not calculated.
||Grade I vs grade 0, P = .009.

### Table 3. Clinical and Laboratory Data in Patients With and Without Barrett Esophagus

<table>
<thead>
<tr>
<th>Variable</th>
<th>Patients With Barrett Esophagus (n = 20)</th>
<th>Patients Without Barrett Esophagus (n = 127)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex, No. M/F</td>
<td>7/13</td>
<td>88/39</td>
<td>.05</td>
</tr>
<tr>
<td>Age, y*</td>
<td>61 (29-72)</td>
<td>49 (20-78)</td>
<td>.005</td>
</tr>
<tr>
<td>Duration of disease, y*</td>
<td>23 (3-49)</td>
<td>15 (3-52)</td>
<td>.03</td>
</tr>
<tr>
<td>Esophagitis, No.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Grade 0</td>
<td>3</td>
<td>29</td>
<td></td>
</tr>
<tr>
<td>Grade I</td>
<td>0</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Grade II</td>
<td>8</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>Grade III</td>
<td>9</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Amplitude of peristalsis, mm Hg*</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 cm Proximal to LES</td>
<td>31 (11-77)</td>
<td>67 (11-114)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>10 cm Proximal to LES</td>
<td>25 (10-68)</td>
<td>55 (10-93)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>15 cm Proximal to LES</td>
<td>18 (6-47)</td>
<td>40 (6-81)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>LES resting pressure, mm Hg*</td>
<td>7 (3-27)</td>
<td>13 (3-41)</td>
<td>.02</td>
</tr>
<tr>
<td>DeMeester score*</td>
<td>78 (39-127)</td>
<td>67 (34-119)</td>
<td>.06</td>
</tr>
<tr>
<td>Esophageal transit time, s*</td>
<td>27 (7-46)</td>
<td>17 (8-55)</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Abbreviation: LES, lower esophageal sphincter.

*Data are given as median (range).
reported by Shiino et al and those exhibited in the present study might be explained by several differences in patient groups between the 2 studies. First, our group included exclusively patients with documented GERD who were referred for surgical management, in contrast to the patients in Shiino and coworkers’ study, which also included patients who were referred to determine the presence of GERD. That means that patients in the present series had generally more severe reflux disease than those of Shiino et al. Indeed, mean acid reflux score was significantly higher in our series (70 vs 43). Second, more than half of our patients had severe mucosal inflammation on endoscopy, while the vast majority of patients in the Shiino et al series had either normal esophageal mucosa on endoscopy or no endoscopy at all. Finally, duration of GERD symptoms was significantly shorter in the Shiino et al series (median, 60 months) than in ours (median, 150 months).

Taking into account that the longer the duration of GERD, the more severe the esophageal body dysfunction, and considering that esophageal body motility is a major determining factor for the necessity and timing of surgical management in patients with GERD, we propose that patients with reflux who have a long history of the disease should be promptly offered antireflux surgery, instead of maintenance conservative treatment with PPIs. Esophageal body motor function was deteriorated by time in the present series, although all patients had been receiving long-term medical treatment. This means that, even if macroscopic mucosal lesions finally become healed during treatment with PPIs, functional improvement is not always achieved, as already reported by others.

In conclusion, esophageal body motility and, consequently, esophageal clearance function are inversely related to duration of GERD. It seems that this inverse correlation exists in late rather than early stages of the disease, and that medical treatment fails to prevent esophageal motor dysfunction. We suggest that surgical treatment of patients with GERD be performed before severe esophageal body dysmotility develops, and independent of LES functional status.

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