Gastroesophageal reflux disease (GERD) is a motility disorder with functional abnormalities of the lower esophageal sphincter (LES) and defective mechanisms of clearance of refluxed gastric contents. The efficiency of mechanical esophageal clearance depends on gravity, primary esophageal body peristalsis evoked by a swallow, and secondary peristalsis evoked by esophageal distension or acid reflux. Inefficiency of esophageal peristalsis may prolong mucosal exposure to refluxed gastric contents; delay in removing refluxed acid increases the contact time of acid with the esophageal mucosa, thus promoting esophagitis and its complications. However, around 60% of GERD patients do not have esophageal mucosal lesions, and are termed as having endoscopy-negative or nonerosive GERD. In most studies, the definition of nonerosive reflux disease (NERD) has included all patients with typical GERD symptoms (heartburn and acid regurgitation) and normal upper gastrointestinal endoscopy.

Motor disorders associated with GERD have been classified as nonspecific. These are characterized by 30% or more nontransmitted contractions, low amplitude waves (<30 mmHg in amplitude), or triple-peaked, retrograde, or prolonged contractions.

The term ineffective esophageal motility (IEM) has been coined recently to describe the pattern of peristaltic failure observed during manometric studies in patients with nonspecific motor disorders or atypical GERD symptoms, although a number of esophageal body motor abnormalities have been described previously in patients with reflux disease.
with GERD. IEM has been defined as the presence of contractions <30 mmHg in amplitude and/or a rate of nontransmission to the distal esophagus of 30% or more of swallows employed for the study of the esophageal body. Previous studies have also demonstrated that patients with IEM have significantly more recumbent and upright reflux, and delayed acid clearance than those without IEM.

Considering that reflux has been found to be more severe in patients with erosive than nonerosive GERD and that IEM delays esophageal clearance, it could be speculated that IEM is more common in patients with erosive GERD than in those with nonerosive disease. Since IEM is a frequent finding in patients with GERD, we compared the results of manometric patterns of the esophageal body in patients with erosive and nonerosive GERD.

**Methods**

One hundred patients with a chief complaint of heartburn and primary diagnosis of GERD referred to the GI motility department of RCGLD of Shahid Beheshti University (Taleqani Hospital), a teaching hospital and tertiary referral center, between January 2002 and January 2005, were prospectively enrolled in this study and their data were recorded. Heartburn was defined as a burning or tight sensation arising from the epigastrium and rising upwards retrosternally. Acid regurgitation was defined as a sensation of acid coming up from the throat into the mouth leaving a sour taste in the mouth. To avoid misdiagnosis, patients were asked to accurately describe their complaints of heartburn and/or acid regurgitation. Patients with predominant symptoms of heartburn and/or acid regurgitation occurring at least once per week for the past 6 months were considered to have GERD. Symptoms of patients were refractory to omeprazole 20 mg daily for two months. Proton pump inhibitor therapy was discontinued ten days before endoscopy and pHmetry.

All patients underwent upper GI endoscopy and, according to the endoscopic findings, were divided into two groups: erosive and nonerosive GERD. Esophagitis was graded according to the Los Angeles classification as Grades A to D.

The exclusion criteria were: presence of dysphagia, contraindications to performing endoscopy, and serious or acute cardiovascular, respiratory, digestive tract, or metabolic disease. Written, informed consent was obtained from each participant before enrollment. The protocol was approved by the ethics committee of the University Hospital.

**Esophageal manometry**

Patients were instructed to fast for 4 hours before the test. We used an 8-lumen, 4.5 mm diameter polyvinyl catheter with four proximal openings spaced at 5 cm intervals and at 90° angles, and the distal four side holes arranged radially at the same level. Each channel was perfused with distilled water at 0.6 mL/min, using a low-compliance pneumohydraulic capillary infusion system (Biomedics, California). Intraluminal pressures were recorded on a polygraph (PC Polygraph VIII, Synectics Medical, Sweden) and analyzed. LES recordings were obtained in the four distal ports using the slow pull-through technique, and LES pressure was the mean of end-expiratory maximum values. Response of the esophageal body to ten swallows of 3–5 mL of water was recorded at 5 cm and 10 cm above the LES. IEM was defined as contractions with an amplitude of <30 mmHg and/or with a rate of nontransmission to the distal esophagus in 30% or more of water swallows. Manometric abnormalities that did not meet criteria for established esophageal motility disorders was considered as nonspecific esophageal motility disorders (NEMD). Nutcracker esophagus was diagnosed in case of high amplitude peristaltic contractions (>180 mmHg).

**24-hour pH ambulatory monitoring**

Twenty-four-hour esophageal pH monitoring was performed as described by DeMeester et al. Using Digitrapper MKIII device (Synectics Medical, Medtronic ®). DeMeester score (DS) of more than 14.7 was taken to indicate abnormal acid reflux.

**Data analysis**

Data were expressed as mean (SD) values for quantitative variables and percentages for categorical variables. Statistical comparisons used χ², Fisher exact test, and t-test for normally distributed data, and Mann–Whitney for non-normally distributed data. The data were analyzed using SPSS version 13, and a p value <0.05 was considered significant.

**Results**

Seventy-seven patients (mean age 37.4 [12.1] years; 37 men) completed the study. Thirty-one of them (40.3%) had erosive GERD and 46 (59.7%) had nonerosive GERD. Twenty-three patients refused to undergo manometry and were excluded from the study. There were no differences in baseline parameters between the two groups (Table). Of the patients with erosive GERD, 20 had type A esophagitis (26%) and 11 had type B (14.3%).

In patients with erosive GERD, 14 had abnormal manometry (12 IEM and 2 nutcracker esophagus, and among those with nonerosive GERD, 14 had abnormal manometry (13 IEM and 1 NEMD; p=0.18; Table). Low LES pressure was present in 14 patients with erosive GERD (45.2%) and in 21 of those with nonerosive GERD (45.7%) (p=0.97). Abnormal acid reflux was seen in 10
Ineffective esophageal motility in GERD

Foroutan, Doust, Jodeiri

In summary, IEM could be an integral part of GERD and need not always be associated with lesions. The results of our study suggest that IEM alone is unlikely to be the cause of GERD.

Discussion

The present study examined the relevance of IEM with the presence of esophagitis in GERD patients. Our analyses showed that the frequency of IEM was not greater in patients with erosive GERD as compared with those with nonerosive GERD.

Motor disorders in GERD are low waves and/or failed contractions. The mean amplitude of peristaltic waves in GERD is lower than that observed in an asymptomatic control group. Ineflective esophageal propulsion of a bolus occurs when the amplitude of peristaltic waves is <30 mmHg. Patients with esophagitis have a greater percentage of failed primary peristaltic waves and a lower amplitude of contractions, which parallels increasing severity of reflux disease. These abnormalities are responsible for the ineffective removal of refluxed contents, longer contact of acid with the esophageal mucosa, and possibly mucosal lesions.

Several studies have investigated the relation of IEM with esophagitis with varied results. Kruse-Anderson et al found fewer propagated contractions and lower amplitude of contraction in patients with esophagitis I and II when compared with controls. In their study, patients with reflux without esophagitis had esophageal contractions similar to that of controls. In contrast to these results and in conformity with our study, Lemme et al reported a similar prevalence of IEM in nonerosive and erosive GERD patients, which was 38% in both the groups. This was different from the findings observed in patients with long Barrett esophagus (56.7%) and a healthy control group (10%). Only patients with complicated GERD showed a greater prevalence of IEM. Ho et al observed that patients with IEM did not have an increased incidence of esophagitis on endoscopy than those with normal manometry. No correlation was found between esophagitis on endoscopy and esophageal motility.

Lemme et al found no difference in the severity of IEM between patients with erosive and nonerosive GERD. In addition, they did not find any difference between both the groups in the number of low amplitude (<30 mmHg) or nontransmitted waves.

We have shown that the incidence of abnormal acid reflux was not different between the erosive and nonerosive GERD groups. This result is consistent with that of Simren et al, who suggested that IEM had little influence on esophageal clearance during upright acid reflux, and only severe esophageal motility disturbances were associated with prolonged esophageal clearance in those with supine reflux.

Some hypotheses have been proposed for the failure of IEM to impair acid clearance.

Firstly, the definition of IEM may not be entirely appropriate. It is based on the concept that pressure waves in the distal esophagus <30 mmHg in amplitude are associated with failure of bolus clearance, measured radiologically or scintigraphically. However, careful inspection of the data reveals that the rate of failed clearance with waves that have an amplitude of 21–30 mmHg is only 56% and it is not until wave amplitudes fall below 21 mmHg that consistent failure of clearance occurred. Thus, ineffective motility associated with pressure waves >21 mmHg might not be expected to impair volume clearance.

Secondly, gravity may be a major factor in bolus clearance. Previous studies have shown that gravity contributes little to esophageal acid clearance in the presence of normal peristalsis, but it is important in patients with severe esophageal dysmotility such as those with scleroderma. In those studies volume clearance was assessed in the supine position, and not in the upright position. Also, in the presence of moderate IEM, there is no difference between clearance times in the upright and supine positions. However, when IEM is severe, esophageal clearance takes longer in the supine than in the upright position.

Our study has a number of limitations. In our study none of the patients had severe esophagitis. Our patients had received omeprazole for 2 months, but had not responded to this treatment.

In summary, IEM could be an integral part of GERD and need not always be associated with lesions. The results of our study suggest that IEM alone is unlikely to be the cause of GERD.

Table. Demographic data, manometric findings and DeMeester scores in erosive and nonerosive GERD patients

<table>
<thead>
<tr>
<th>Variables</th>
<th>Erosive GERD (n=31)</th>
<th>Nonerosive GERD (n=46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (M/F)</td>
<td>15/16</td>
<td>22/24</td>
</tr>
<tr>
<td>Age (years)</td>
<td>39.1 (13.8)</td>
<td>36.2 (10.7)</td>
</tr>
<tr>
<td>Abnormal esophageal motility (n %)</td>
<td>14 (45.2%)</td>
<td>14 (30.4%)</td>
</tr>
<tr>
<td>IEM (n %)</td>
<td>12 (38.7%)</td>
<td>13 (28.3%)</td>
</tr>
<tr>
<td>LES pressure (mmHg)†</td>
<td>13.1 (10.1)</td>
<td>12.4 (8.3)</td>
</tr>
<tr>
<td>Low LES pressure (n %)</td>
<td>14 (45.2%)</td>
<td>21 (45.7%)</td>
</tr>
<tr>
<td>Total DS for acid reflux†</td>
<td>28.9 (46.2)</td>
<td>27.7 (43.6)</td>
</tr>
<tr>
<td>Abnormal acid reflux based on DS (n %)</td>
<td>10 (32.3%)</td>
<td>19 (41.3%)</td>
</tr>
</tbody>
</table>

LES: lower esophageal sphincter; IEM: ineffective esophageal motility; DS: DeMeester score. Values are given as mean (SD).
major determinant of abnormal esophageal acid exposure and could not be a prerequisite for the development of esophagitis, as esophageal injury is not always associated with IEM. The actual role of IEM in GERD needs further clarification.

References