WHAT IS THE REAL IMPAIRMENT ON ESOPHAGEAL MOTILITY IN PATIENTS WITH GASTROESOPHAGEAL REFUX DISEASE?

Angela FALCÃO, Ary NASI, Jeovana BRANDÃO, Rubens SALLUM and Ivan CECCONELLO

ABSTRACT – Context - Impairment of esophageal motility is a common finding in patients with gastroesophageal reflux disease (GERD) as reduced lower esophageal sphincter (LES) basal pressure. A very low LES pressure might facilitate the occurrence of more gastroesophageal reflux whereas abnormal esophageal peristalsis may contribute to impaired esophageal clearance after reflux. Objective - Evaluate the esophageal motor function of the lower esophageal sphincter and esophageal body in the various forms of gastroesophageal reflux disease. Methods - The manometrics records of 268 patients, who had evaluation of the esophageal motility as part of the diagnostic gastroesophageal reflux disease were split into four groups, as follows: 33 patients who had no esophagitis; 92 patients who had erosive esophagitis; 101 patients who had short Barrett’s esophagus and 42 patients who had long Barrett’s esophagus. Results - The group who had long Barrett’s esophagus showed smaller mean LES pressure and higher percentage of marked LES hypotonia; in the distal segment of the esophageal body the this group showed higher percentage of marked hypocontractility of the distal segment (<30 mm Hg); this same group showed higher percentage of esophageal motility disorders. Conclusions - The most intense esophageal motility disorders and lower pressure of lower esophageal sphincter were noted in the group with long Barrett’s esophagus. Those with reflux esophagitis and short Barrett’s esophagus had esophageal motility impairment, intermediate among patients with esophagitis and long Barrett’s esophagus. Patients with typical symptoms of gastroesophageal reflux but without esophagitis by endoscopy study showed no impairment of esophageal motility.


Declared conflict of interest of all authors: none

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surgery, patients with achalasia, esophageal or fundic varices, esophageal cancer, collagen diseases or previous ingestion of corrosive agents. All drugs that might interfere with esophageal motor function (i.e., nitrates, metoclopramide, and calcium-channel blocking agents) were discontinued at least 48 hours before the study.

Endoscopy was performed in all patients to assess the degree of esophageal mucosal injury. Barrett’s esophagus was confirmed both endoscopically and histologically. The degree of mucosal injury was graded according to the Los Angeles classification(24).

The 268 selected patients were divided into the following groups:
- No esophagitis group (NE): 33 patients showing only typical clinical complaints of GERD (heartburn and regurgitation), without esophagitis at endoscopy;
- Erosive esophagitis group (EE): 92 patients with erosive esophagitis (LA classification);
- Short Barrett’s esophagus group (short BE): 101 patients with short BE (< 3 cm);
- Long Barrett’s esophagus group (long BE): 42 patients with long BE (> 3 cm).

Standard water-perfusion esophageal manometry was performed with a Polygraph HR and a low-compliance perfusion system (Microcapillary Infusion System for Esophageal Manometry, both from Synetics Medical AB, Stockholm, Sweden) and with an 8-lumen catheter of 75 cm total length and 4.5 mm diameter with eight capillary channels (0.8 mm of thickness) having each one hole for capturing the pressure. The procedure of esophageal manometry was performed according to a standard protocol, which is widely known in the specific literature(6) and adopted in our laboratory by the station pull-through technique. All patients were studied in the supine position and performed 10 swallows of a 5 mL bolus of water at room temperature with an interval of at least 30 s between successive swallowing(20).

The following parameters were (i) LES - total length (in cm), LES resting pressure (in mm Hg) measured at the mid respiratory level, percentage of severe LES hypotonia (when LES pressure was lower than or equal to 6 mm Hg); (ii) Esophageal body - esophageal peristaltic amplitude (in mm Hg) at 3 and 18 cm above the upper LES margin, evaluation of the swallow complex propagation with identification of esophageal disinhibition as: diffuse esophageal spasm (DES) was defined as simultaneous contractions in the esophageal body in 20% or more of wet swallows; ineffective esophageal motility (IEM) was defined as 30% of contractions in the distal esophagus are of low amplitude (<30 mm Hg) and/or 30% of contractions are not transmitted(26, 32) and simultaneous contractions of the medial and distal segments in all the studied complexes (100%).

The groups were compared according to the different manometric parameters, and to the demographic data (age and gender).

For statistical analysis we used the Pearson’s chi-square test (estimated by the Monte Carlo method), the non-parametric Kruskal-Wallis’ test with the Bonferroni’s multiple comparisons tests. All numeric measurements are reported as mean plus or minus one standard deviation (mean ± 1 SD). A significance level (level of rejection of the null hypothesis) of 0.05 (%) was considered for Pearson’s chi-square and Kruskal-Wallis’ tests; for the Bonferroni’s multiple comparisons the 5% significance level was divided by the number of comparisons. Was used the SPSS version 13.0 software for Windows system.

RESULTS

Demographics data
The mean age (± 1 SD) was 41.5 years (± 12.0) in the no-erosive, 47.0 years (± 14.1) in erosive esophagitis, 47.3 years (± 15.3) in short Barrett’s esophagus and 48.5 years (± 16.0) in long Barrett’s esophagus groups and they were similar (P = 0.157). There was a higher percentage of male patients in short Barrett’s esophagus (65.3%) and long Barrett’s esophagus groups (71.4%) (P = 0.008) and predominantly female patients in the no-erosive (69.7%) and erosive esophagitis group (58.7%) (P<0.001) (Table 1).

| TABLE 1. The demographics date analyzed in the four study groups |
|-----------------|-----|-----|-----|-----|
|                 | NE  | EE  | SBE | LBE |
| Age             | 41.36 | 46.98 | 47.32 | 48.43 |
| (± 2.16)        | (± 1.48) | (± 1.52) | (± 2.49) |
| Gender          |     |     |     |     |
| Male            | 30.40% | 41.40%* | 61.20%* | 71.40%* |
| Female          | 69.50%* | 58.50%* | 38.70% | 28.50% |

Distribution of the demographics date analyzed in the four study groups: NE (no esophagitis), EE (erosive-esophagitis), SBE (short Barrett’s esophagus) and LBE (long Barrett’s esophagus).

(*) = P significant

Manometric data
The Table 2 shows details of mean (± 1 SD) LES length, LES resting pressure and proximal (18 cm above LES) and distal (3 cm above LES) esophageal peristaltic amplitude. The table also displays the percent distribution of short LES (total LES length below 2 cm), marked LES hypotonia (MRP<6 mm Hg), marked hypotonia in the distal esophagus (amplitude below 30 mm Hg) and esophageal disinhibition.

The patients with erosive esophagitis, short and long Barrett’s esophagus had lower LES length 3.3 (± 0.9), 3.4 (± 1.2), 3.1 (± 1.3) respectively; P = 0.623. However, the patients with long Barrett’s esophagus had a higher percentage of the shorter LES length (11.9%) when compared with erosive esophagitis and short Barrett’s esophagus groups (5.4%, 9.9% respectively - P<0.001). The no-erosive group did not show any change.

The long Barrett’s esophagus group had LES resting pressure (LESRP) lower [9.6 (± 5.8)] than the groups with erosive esophagitis [13.4 (± 7.9)] and short Barrett’s esophagus [12.6 (± 6.8)] (P = 0.006). The no-erosive group showed a mean value greater [19.9 (± 7.3)] than the other groups (P<0.001).

With respect to the presence of LES marked hypotonia (LESRP < 6 mm Hg), the long Barrett’s esophagus group had a higher percentage of marked LES hypotonia (30.9%)...
compared to erosive esophagitis (10.9%, \( P = 0.006 \)) and short Barrett’s esophagus groups (8.9%, \( P = 0.001 \)) which were similar (\( P = 0.809 \)) (Figure 1).

There was no significant difference between groups in the proximal esophageal peristaltic amplitude (18 cm above the LES) (\( P = 0.103 \)). In the distal segment (3 cm above the LES) the short and long Barrett’s esophagus groups showed lower amplitude contractions [74.2 (\( \pm 31.9 \)); 69.6 (\( \pm 35.3 \))] respectively] (\( P = 0.001 \)). The erosive esophagitis [92.4 (\( \pm 48.0 \))] showed a lower amplitude compared to the no-erosive group [116.1 (\( \pm 41.0 \))] (\( P < 0.001 \)).

The long Barrett’s esophagus group had a higher percentage of marked hypocontractility of the distal esophageal contraction (amplitude below 30 mm Hg) (14.3%) when compared to other groups (EE = 1.1% and SBE = 4.9%) (\( P = 0.003 \)). The no-erosive group did not show any change (Figure 2).

Concerning esophageal peristalsis the long Barrett’s esophagus group had a higher percentage of esophageal motility disorders (16.7%) when compared to other groups (EE = 3.0% and SBE = 5.9%) (\( P = 0.001 \)). The NE group showed no change (Figure 3).

### TABLE 2.
Distribution of the manometric variables analyzed in the four study groups

<table>
<thead>
<tr>
<th>MANOMETRICS VARIABLES</th>
<th>Study Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NE</td>
</tr>
<tr>
<td>Mean LES total length (cm)</td>
<td>3.9 (± 0.9)</td>
</tr>
<tr>
<td>% of short LES (total length &lt;2 cm)</td>
<td>0%</td>
</tr>
<tr>
<td>LES resting pressure (MRP – mm Hg)</td>
<td>19.9 (± 7.3)</td>
</tr>
<tr>
<td>% LES Marked hypotonia (MRP &lt;6 mm Hg)</td>
<td>0%</td>
</tr>
<tr>
<td>Mean proximal esophageal peristaltic amplitude (mm Hg)</td>
<td>56.5 (± 18.4)</td>
</tr>
<tr>
<td>Mean distal esophageal peristaltic amplitude (mm Hg)</td>
<td>116.1 (± 41.0)*</td>
</tr>
<tr>
<td>% Marked hypocontractility in the distal esophagus (&lt;30 mm Hg)</td>
<td>0%</td>
</tr>
<tr>
<td>% Esophageal dismotility</td>
<td>0%</td>
</tr>
</tbody>
</table>

Manometric variables analyzed in the four study groups: NE (no esophagitis), EE (erosive esophagitis), SBE (short Barrett’s esophagus) and LBE (long Barrett’s esophagus). mm Hg: millimeters of mercury; cm: centimeters; LES: lower esophageal sphincter; MRP: mean resting pressure; (*) = \( P \) significant.
**DISCUSSION**

In this case series, age was similar in all groups, a fact also observed by other authors\(^7\), \(^25\), \(^37\). However, in some studies, older age was observed in patients with Barrett’s esophagus\(^3\), \(^36\). There was a higher percentage of male patients both in short and long Barrett’s esophagus groups and female predominance in the no erosive and erosive esophagitis groups. Although Oliveira et al.\(^27\) found a slight predominance of males in the group with erosive esophagitis (62.2%).

The LES is the first defense against the GER and is considered the most important factor in the physiopathology of GERD\(^10\). Changes in structure and function of the esophagogastric junction and LES may predispose to the development of GERD\(^22\), \(^31\).

In our study, patients with long Barrett’s esophagus had both lower LES resting pressure and a higher percentage of marked hypotonia, also found by Clark et al.\(^10\) that identified LES marked hypotonia in greater frequency in patients with short and long Barrett’s esophagus when compared to a control group. We also observed a higher percentage of shorter LES in patients with long Barrett’s esophagus, as an indicator of a more severe antireflux barrier impairment. Therefore, there is a clear association of lower LES pressure and short LES length and esophageal mucosa injury, especially in relation to Barrett’s esophagus\(^4\), \(^13\), \(^17\), \(^23\), \(^26\), \(^27\), \(^37\).

The esophageal body pressure and the normal peristaltic movement can be considered as factors that have an influence on the complete bolus transit\(^9\).

A videofluoroscopic study associated with manometric showed that non-peristaltic contractions or distal esophageal body contractions less than 30 mm Hg would not be effective to complete occlusion of the esophageal lumen and the complete emptying of the liquid bolus (contrast), suggesting that these changes would lead to an inefficient esophageal clearance\(^22\), \(^34\). Another study compared a combined multichannel intraluminal impedance with esophageal manometry (MII-EM) evaluates the functional aspects of esophageal contractions by simultaneously measuring bolus transit and esophageal contraction showed that the major factors to determine the complete bolus transit are the normal esophageal body pressure and normal peristalsis\(^9\).

In our study, the mean contraction amplitude in the proximal segment (18 cm above the LES) were normal in all groups. These data suggest that hypocontractility caused by GERD is located in the more distal esophagus when reflux exposure is more intense\(^14\), \(^15\).

However, the mean of the distal contraction amplitude was lower in short and long Barrett’s esophagus groups. Moreover, there was no observed hypocontractility in the no-esophagitis group, which was also observed by Dantas et al.\(^15\). One must consider, however, that the swallows were performed with water (in bolus) and in the supine position. It is known that there may be a variation in amplitudes of contraction and peristalsis in response to swallowing with water, but the 10 swallows performed during the manometry has been accepted as the minimum necessary for an adequate assessment\(^20\).

The percentage of esophageal body marked hypocontractility (amplitude below 30 mm Hg) was found almost only in patients with Barrett’s esophagus, particularly in the long Barrett’s esophagus group. The difference was significantly higher when compared to erosive esophagitis group, as also observed by other authors\(^9\), \(^25\), \(^37\).

The impairment of esophageal motility is a common finding in patients with GERD. More than half of patients with GERD have change of the esophageal peristalsis, which are those with higher reflux and poor esophageal clearance\(^18\). It has been demonstrated that the decrease in the esophageal contraction amplitude may occur in patients without esophagitis but these changes are infrequent in these patients\(^13\).

Our data found that only groups with erosive esophagitis and both short and long Barrett’s esophagus had some abnormal esophageal peristalsis. There was a relationship between the frequency of these amendments and intensity of mucosal injury, with a higher percentage of involvement in the long Barrett’s esophagus group.

This fact coincides with the findings of Meneguetti et al.\(^20\) and Jorge et al.\(^6\) who also concluded that as the amount of mucosal damage increased from group without esophagitis to Barrett’s esophagus, both esophageal motility and acid clearance worsened, suggesting that esophageal mucosal damage may contribute to esophageal dysmotility and worsening reflux\(^9\) and that there is a direct relationship between the impairment of motor function and severity of esophageal reflux esophagitis\(^4\), \(^30\).

In our study, functional changes were uncommon in the patients without esophagitis and more frequent and severe in patients with Barrett’s esophagus, but it is difficult to explain why most patients with reflux esophagitis and even Barrett’s esophagus showed no motor disorders.

These findings further suggest that the inflammatory process of GERD extending from the mucosa to the muscular layer resulting in hypocontractility\(^30\), \(^38\) and compromising the esophageal motility of several patients, but not in all. This would also explain why the results of surgical treatment of patients with long Barrett’s esophagus are worse than in patients with erosive esophagitis\(^12\), \(^30\).

Finally, it should also be noted that patients were evaluated only once, so that the manometric alterations may be represented by a single time of clinical history of each one. Patients with GERD should be considered as a wide spectrum in which it is possible to move from one group to another in different degrees of esophagitis\(^28\). This does not mean that all patients will develop varying degrees of esophagitis, but we can say that without proper treatment, uncomplicated cases may progress to severe esophagitis or Barrett’s esophagus irreversibly\(^30\).
In conclusion, we observed that patients with typical symptoms of gastroesophageal reflux but without esophagitis by endoscopy study showed slight impairment of esophageal motor function. Those with EE and SBE showed an impairment of esophageal motor function intermediary between patients with esophagitis and LBE.

In patients with LBE we observed greater impairment of the LES as a lesser length, lower resting pressure and a higher percentage of severe hypotonia. This group also showed less contraction amplitude and a higher percentage of severe hypocontractility and changes in the distal esophageal peristalsis.
REFERÊNCIAS


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