Does the nissen fundoplication procedure improve esophageal dysmotility in patients with Barrett’s esophagus?

**A fundoplicatura a nissen melhora a dismotilidade esofágica em pacientes com esôfago de barrett?**

**INTRODUCTION**

Esophageal dysmotility (ED) is a motor disorder to be sought and well evaluated before performing anti-reflux surgery. ED can be found in patients with gastro-esophageal reflux disease (GERD) and Barrett’s esophagus (BE).

Increasing evidence indicates that there may be a direct impact of reflux on the inhibitory and excitatory intramural neurons that regulate both peristaltic function and the strength of the esophageal contraction amplitude.

The most frequent esophageal motility disorders found in BE and GERD patients are lower esophageal sphincter (LES) hypotonia, ineffective esophageal motility (IEM), diffuse esophageal spasm (DES), esophageal body (EB) hypomotility and aperistalsis. However, BE can also be a consequence of an already manifested ED, with an increase in the reflux of acid and bile salt content into the esophagus when there are impairments in the esophageal clearance, thus contributing to the development of BE, in a vicious cycle of inflammation and impaired motility leading to a more severe disease.

**ABSTRACT**

Objective: to evaluate esophageal dysmotility (ED) and the extent of Barrett’s esophagus (BE) before and after laparoscopic Nissen fundoplication (LNF) in patients previously diagnosed with BE and ED. Methods: twenty-two patients with BE diagnosed by upper gastrointestinal (GI) endoscopy with biopsies and ED diagnosed by conventional esophageal manometry (CEM) were submitted to a LNF, and followed up with clinical evaluations, upper GI endoscopy with biopsies and CEM, for a minimum of 12 months after the surgical procedure. Results: sixteen patients were male (72.7%) and six were females (27.3%). The mean age was 55.14 (± 15.52) years old, and the mean postoperative follow-up was 26.2 months. The upper GI endoscopy showed that the mean length of BE was 4.09 cm preoperatively and 3.91 cm postoperatively (p=0.042). The evaluation of esophageal dysmotility through conventional manometry showed that: the preoperative median of the lower esophageal sphincter resting pressure (LESRP) was 9.15 mmHg and 13.2 mmHg postoperatively (p=0.006). The preoperative median of the esophageal contraction amplitude was 47.85 mmHg, and 57.50 mmHg postoperatively (p=0.408). Preoperative evaluation of esophageal peristalsis showed that 13.6% of the sample presented diffuse esophageal spasm and 9.1% ineffective esophageal motility. In the postoperative, 4.5% of patients had diffuse esophageal spasm, 13.6% of aperistalsis and 22.7% of ineffective motor activity (p=0.133). Conclusion: LNF decreased the BE extension, increased the LES resting pressure, and increased the amplitude of the distal esophageal contraction; however, it was unable to improve ED.

**Keywords:** Esophageal Dysmotility. Barrett’s esophagus. Esophageal Manometry. Nissen fundoplication. Esophageal benign diseases.
Laparoscopic Nissen fundoplication (LNF) has been proposed for patients with GERD and BE as an effective and safe therapeutic alternative, especially in cases where inadequate control of reflux symptoms is found during clinical treatment²⁰-²². Although this may be true, there is still insufficient data related to the changes in esophageal motility and its evolution after surgical treatment of GERD and BE²³-²⁵. However, when successful, LNF provides less exposure to acid and bile salt content, reducing esophageal erosion and, consequently, diminished the metaplastic process present in BE²⁶, ²⁷.

The aim of the present study is to evaluate esophageal dysmotility and the extent of BE before and after LNF in patients previously diagnosed with BE and ED.

**MATERIALS AND METHODS**

**Study design**

This study was carried out at the Clinics Hospital at the University of São Paulo Medical School (HC-FMUSP), in São Paulo, SP, Brazil. Participants were identified at the Barrett’s esophagus outpatient clinic in the period between January 2010 and January 2015. All procedures performed were in accordance with the ethical standards of the institutional research committee of the institution and, with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This research project was approved by the Ethics Committee for Research of the FMUSP (N0.2.399.947) CAAE: 77125917.8.0000.0068.

Twenty-two individuals with symptoms of heartburn and regurgitation, diagnosed with BE via upper GI endoscopy and confirmed by the presence of a metaplastic columnar epithelium, containing goblet cells (intestinal metaplasia) at histopathological examination, with esophageal dysmotility via conventional esophageal manometry (CEM) and who also underwent a LNF, were included in the study. The extent of Barrett’s epithelium, in centimeters, was assessed before and after surgery. Patients who presented recurrence of reflux symptoms or fundoplication complications, such as twisted or slipped valve, identified in a postoperative upper GI endoscopy were excluded from the study. Preoperative and postoperative CEM studies were performed by two of the study researchers not involved in the clinical management of the patients. At the time of the postoperative manometric assessment, the patients had at least 12 months of follow-up after surgery in order to determine the real impact of the LNF on their ED. All patients underwent a 24-hour pH-metry test to evaluate the effective control of reflux, in the postoperative follow-up of NLF. They were considered normal by the DeMeester score below 14.74.

**Manometry study**

The esophageal manometry measurements were performed using a CEM device with a polyvinyl catheter of 75 cm of length and 45 mm of diameter, with 8 capillary channels. The catheter was perfused with water at a flow rate of 0.6 mL/min/channel through a pneumohydraulic perfusion system of low complacency.

Esophageal manometry assessed LES resting pressure (LESRP), esophageal peristaltic function and esophageal contraction.

The ED alterations evaluated were: LES hypotonia, diffuse esophageal spasm (DES), ineffective esophageal motility (IEM), distal esophageal body (EB) aperistalsis, distal EB hyper and hypocontractility.

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 having 30% of contractions in the distal esophagus with low amplitude (<30 mmHg) and/ or having 30% of contractions that are not transmitted; aperistalsis was defined when 100% of wet swallows are followed by simultaneous esophageal contractions; esophageal body (EB) hypocontractility was defined as an EB pressure below 64 mmHg, EB hypercontractility was defined as an EB pressure above 180 mmHg. LES hypotonia was defined as LESRP below 14 mmHg²⁸-³⁰. The LES baseline tone was assessed using the mean airway resting pressure²⁸.

Conventional esophageal manometry (CEM) was used instead of a high-resolution manometry (HRM) due to the fact that, in the preoperative evaluation, the Digestive Surgery Division did not have yet a high-resolution manometry device.
**Statistical analysis**

Data analysis included an initial descriptive exploration of the data including mean, standard deviation, median, 25th and 75th percentile of the quantitative variables and proportion with a 95% confidence interval (95% CI) for the qualitative ones. The Fisher exact test and Pearson Chi-Square tests were used for association analysis in the contingency table. The Shapiro-Wilk Normality Test was used to evaluate quantitative variables in a normal distribution. The paired Wilcoxon test and paired Student’s t-test was used to compare if the preoperative position measurements were the same as the postoperative, considering the dependence found between the times. All the tests performed took into consideration a bidirectional of 0.05 and a 95% confidence interval (CI) and were performed with computational support of the software Stata 12.0 for Windows and Excel 2010 (Microsoft Office).

**RESULTS**

All patients included had no reflux or dysphagia symptoms in the first 12 months of follow-up, without the use of proton pump inhibitors (PPI). Overall, sixteen patients were male (72.7%) and six females (27.3%). The mean participant age was 55.14 (± 15.52) years preoperatively and 58.81 (± 13.79) postoperatively. The mean postoperative follow-up time was of 26.2 (± 9.27) months. Reduction or absence of acid reflux was observed in all patients evaluated at 24-hour pH-metry after anti-reflux surgery with a mean DeMeester score of 2.45 (± 3.32), and no deaths occurred during the study period.

A decreased length of columnar mucosa was observed in the upper GI endoscopy, from 4.09 cm (± 2.50) preoperatively to 3.91 cm (± 2.34) in the postoperative evaluation (p=0.042).

In the CEM, the analysis of the LES resting pressure showed increase in its median (25th; 75th) values, going from 9.15 (5.78; 11.93) mmHg in the preoperative evaluation to 13.20 (11.00; 16.28) mmHg in the postoperative evaluation (p=0.013). Besides, percentage of LES hypotonia decreased from 86.3% to 54.5% after LNF (p= 0.021).

The median (25th; 75th) values of the distal esophageal body pressure (EBP) increased from 47.85 (35.65; 60.43) mmHg in the preoperative stage to 57.50 (34.10; 80.45) mmHg in the postoperative evaluation (p=0.408) (Table 1).

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**Table 1. Length of the Barrett’s esophagus and manometry findings for lower esophageal sphincter resting pressure and esophageal body pressure.**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Evaluation</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Preoperative</td>
<td>Postoperative</td>
</tr>
<tr>
<td>BE length (cm)</td>
<td>4.09 ± 2.50</td>
<td>3.91 ± 2.34</td>
</tr>
<tr>
<td>LESRP</td>
<td>Median (25th; 75th)</td>
<td>Median (25th; 75th)</td>
</tr>
<tr>
<td></td>
<td>9.15 (5.78; 11.93)</td>
<td>13.20 (11.00; 16.28)</td>
</tr>
</tbody>
</table>
| LES hypotonia         | Preoperative N (%)          | Postoperative N (%) | 0.021 (***)
|                       | 19 (86.3)                   | 12 (54.5)   |
| EBP                   | Median (25th; 75th)         | Median (25th; 75th) | 0.408 ** |
|                       | 47.85 (35.65; 60.43)        | 57.50 (34.10; 80.45) |

BE: Barrett’s esophagus; LESRP: lower esophageal sphincter resting pressure; EBP: esophageal body pressure; (*) Paired t-Student test; (**) Wilcoxon test. (*** ) Pearson Qui-Square test.
When we analyzed the presence of ED, preoperative evaluation showed that 13.6% of the samples presented diffuse esophageal spasm (DES) and 9.1% ineffective esophageal motility (IEM). In the postoperative phase, 4.5% of the patients displayed DES, 22.7% showed IEM and 13.6% aperistalsis. There was no significant difference between the preoperative and postoperative evaluation either together (p = 0.195) or when analyzing each ED separately (p = 0.133) (Table 2).

<table>
<thead>
<tr>
<th>Variables</th>
<th>Preoperative n (%)</th>
<th>Postoperative n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ED</td>
<td>5 (22.7)</td>
<td>9 (40.9)</td>
<td>0.195 **</td>
</tr>
<tr>
<td>DES</td>
<td>3 (13.6)</td>
<td>1 (4.5)</td>
<td></td>
</tr>
<tr>
<td>Aperistalsis</td>
<td>0 (0.0)</td>
<td>3 (13.6)</td>
<td>0.133 *</td>
</tr>
<tr>
<td>IEM</td>
<td>2 (9.1)</td>
<td>5 (22.7)</td>
<td></td>
</tr>
</tbody>
</table>

(**) Pearson Qui-Square test.

**DISCUSSION**

It is common knowledge that a clinically successful fundoplication is capable of providing satisfactory control of duodenal-gastro-esophageal reflux. However, the timing for indication of this surgical procedure, for patients with BE and ED, is still a challenge.

In our study, we observed a reduction in BE length, from 4.09 cm (± 2.50) preoperatively to 3.91 cm (± 2.34) postoperatively (p = 0.042). Other authors have also reported a regression of the esophageal intestinal metaplasia after fundoplication.

Our data showed that patients with preoperative esophageal hypercontractility evolved with normal postoperative esophageal contraction pressure. These data are similar to those described by Barreca et al., who observed a return to normal manometric patterns in 80% of patients after successful control of esophageal acid exposure. These authors further describe that high esophageal contractions may be associated with GERD and a Nissen fundoplication can effectively control GERD and should not be contraindicated.

Moreover, Riedl et al., described that anti-reflux surgery is effective in the treatment of GERD, regardless of the preoperative manometric findings and they also concluded that this type of surgery does not worsen the symptoms of preoperative dysphagia, as reported by other authors. However, Wilshire et al. showed that after Nissen fundoplication, dysphagia is linked to an abnormal hiatal functional anatomy, i.e. impaired relaxation of the high-pressure zone rather than motility changes.
Similarly, Yamamoto et al. retrospectively observed that the vast majority of patients with postoperative dysphagia had evidence of hiatal flow obstruction, which was linked to longer lengths of the high-pressure zone and higher relaxation pressures, rather than motor disorders of the esophageal body.

Gill et al. also evaluated esophageal motility through a manometric study before and after fundoplication. They found that, despite satisfactory GERD symptoms relief and increased LES and EB pressure, Nissen fundoplication led to an increase in aperistalsis episodes. These findings are in accordance with ours results, still it is difficult to establish a reliable comparison, because, unlike our study, Gill et al. did not evaluate patients with BE.

The “tailored” approach in patients with GERD who are candidates for surgery has not been suggested either especially for those in which preoperative manometry demonstrates ineffective peristalsis, in line with the available evidence that the outcome of anti-reflux surgery in patients with esophageal dysmotility is not affected by a total fundoplication approach. In addition, a higher incidence of recurrent reflux has been reported after Toupet or Lind fundoplication.

The importance of studying possible interventions that may affect ED is based on the fact that impaired motility compromises the esophageal clearance, increasing the exposure of the distal esophageal mucosa to acid and bile salts reflux content and, thus, accelerating the process of intestinal metaplasia observed in BE.

It is expected that a clinically successful fundoplication would lead to an increased LESRP due to the anti-reflux mechanism of this surgery. However, the main endpoints here are the effects of this procedure on the impaired EB contraction. Although we found a tendency for improvement in esophageal contraction with increased esophageal body amplitude after laparoscopic Nissen fundoplication, we also observed that the prevalence of ED, such as DES, IME and aperistalsis, increased after surgery.

We are aware that the main limitations of the current study are in the small number of patients evaluated and in the use of conventional manometry procedures instead of high-resolution manometry (HRM) to assess esophageal dysmotility. However, even with such limitations, we believe the current study presents important results regarding the long-term effects of Nissen fundoplication in patients with BE and ED.

CONCLUSION

In conclusion, LNF decreased the BE extension, increased the LES resting pressure, and increased the amplitude of the distal esophageal contraction; however, it was unable to improve ED.

In order to establish more solid conclusions regarding the real impact of the LNF on ED in patients with BE, it is of paramount importance that new studies are developed with a larger sample and longer follow-up period.
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2016;29(8):967-970.


Received in: 27/05/2020
Accepted for publication: 20/07/2020
Conflict of interest: no.
Funding source: none.

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