GUIDELINES IN FOCUS

Gastroesophageal reflux disease: nonpharmacological treatment

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DESCRIPTION OF THE EVIDENCE COLLECTION METHOD
A search was performed in the EMBASE, SciELO / LILACS, PubMed / Medline and Cochrane Library databases using the following words: gastroesophageal reflux, gerd, heartburn, nerd, gero, esophagus, esophagitis, extra-esophageal, asthma, atypical symptoms, chest pain, cough, globus sensations, hoarseness, otorhinolaryngology diseases, pain, respiratory tract diseases, laryngitis, anti-ulcer agents, enzyme inhibitors, proton pumps, lansoprazole, omeprazole, proton pump inhibitors, rabeprazole, continuous, on-demand, surgery, fundoplication, Nycomed, and Medley; received speaker fees sponsored by AstraZeneca and Nycomed; received financial support for organizing educational activities sponsored by Nycomed, Aché and AstraZeneca. Rezende Filho J received speaker fees sponsored by Nycomed. Mion O received speaker fees sponsored by AstraZeneca. Stelmach R received speaker fees; financial support to organize teaching activities and to perform research; and consulting fees sponsored by AstraZeneca, Aché and Medley. Dantas RO received speaker fees sponsored by AstraZeneca. Zaterka S received financial support for teaching and consulting activities sponsored by Jansen-Cilag. Navarro T received speaker fees; financial support for teaching and consulting activities, and performed research sponsored by AstraZeneca.

CONFLICT OF INTEREST
Chinzon D received reimbursement for attending conferences sponsored by Jansen and, also received speaker and consulting fees sponsored by Jansen, AstraZeneca and Medley. Lemme EMO received speaker fees sponsored by AstraZeneca and received grants for research sponsored by Nycomed. Moraes Filho JPP received reimbursement for attending a symposium sponsored by AstraZeneca,
A total of 5,000 publications were retrieved. Using the filters: humans, randomized controlled trial, randomized AND controlled AND trial, clinical AND trial, clinical trials, random*, random allocation, therapeutic use, epidemiologic methods, cohort studies, cohort AND study*, prognos*, first AND episode, cohort, we selected 73 studies to support this Guideline.

**DEGREE OF RECOMMENDATION AND STRENGTH OF EVIDENCE**

A: Experimental or observational studies of best consistency.

B: Experimental or observational studies of lower consistency.

C: Case reports (non-controlled studies).

D: Opinion without critical evaluation, based on consensuses, physiological studies or animal models.

**OBJECTIVE**

Due to high prevalence, variety of the clinical presentation forms and economic impact, consequences of loss of quality of life and clinical-laboratory research costs, the implementation of international consensus meetings has been encouraged. On the other hand, the diagnosis and therapeutic management of gastroesophageal reflux disease (GERD) has varied from center to center, which is an important factor in the search for scientific evidence on the issue, prompting the implementation of this Guideline, which seeks to answer four key clinical questions of the non-pharmacological treatment of GERD.

1. **Does the nonpharmacological treatment produce results in GERD?**

**Obesity**

Body mass index (BMI) > 25 is a risk factor for erosive GERD (B). There is an association between reflux symptoms and obesity (OR: 2.6) (B). BMI is associated with reflux (OR per 5 units: 1.9) (B). BMI > 25 is a risk factor (OR: 1.41) for GERD (B). Obesity is associated with GERD (B). Weight decrease does not reduce the manifestations of reflux (B). In patients with mean BMI of 42.5 kg/m², there is no association with the prevalence of GERD (B). Obesity predisposes to gastroesophageal reflux, and weight loss improves postprandial reflux and reduces pH time < 4 (B).

**Smoking**

Smoking is a risk factor for non-erosive GERD (B) and for reflux symptoms (B). Smokers have more reflux episodes than nonsmokers, but a 24-hour abstinence does not reduce the pH time < 4 (B).

24-hour smoking abstinence reduces the number of reflux episodes, but does not affect the total acid exposure (B). Individuals abstaining from smoking for 48 hours have increased esophageal acid exposure (B). Smoking is associated with GERD (B).

**Alcohol**

Alcohol intake is a risk factor for erosive GERD (B). Frequent consumption of alcohol is a risk factor for reflux symptoms (B). The habits of drinking wine or beer increase the risk of reflux (B). Alcoholic consumption is a risk factor for erosive GERD (OR: 2.42 to 2.85) (B).

**Coffee**

Coffee consumption is associated with GERD (OR: 1.23) (B).

**Diet**

The consumption of sweets and white bread is associated with symptoms of reflux (B). Fruit consumption has a protective effect on reflux symptoms (B). Frequent consumption of alcohol is a risk factor for reflux (B). The habits of drinking wine or beer increase the risk of reflux (B). Alcohol consumption is a risk factor for erosive GERD (OR: 2.42 to 2.85) (B).

**Posture**

Working in an inclined position is a risk factor for non-erosive GERD (B). GERD episodes are triggered by posture (B).

**Inclined head of the bed**

Sleeping with a wedge-shaped support is associated with less acid exposure than in the horizontal position (B). Raising the head of the bed (28 cm) reduces the number of reflux episodes and pH time < 5 (B).

**Night meals**

The later the night the meal is, the higher the rate of reflux episodes, especially in obese individuals and in those with erosive GERD (B). Going to bed immediately after dinner is associated with increased risk of GERD, especially within a time period of less than 3 hours (B).

**Physical exercise**

Physical activity seems to have a protective effect against GERD (B).

**Stress and fatigue**

GERD episodes are triggered by stress and fatigue (B). Stress is among the risk factors for GERD (B).
**Recommendation**

Although obesity (BMI > 25), smoking, alcohol consumption, coffee, sweets, proteins, excess food, inclined posture, stress and fatigue are associated with GERD, there is no consistent information to define that the resolution of these factors is followed by resolution or improvement of GERD. However, the elevation of the head of the bed and going to bed only after a minimum of three hours after the night meal are measures that reduce esophageal acid exposure.

**2. WHAT ARE THE INDICATIONS OF SURGICAL TREATMENT OF GERD?**

**Hiatal hernia**

**Parasophageal**

The laparoscopic Nissen fundoplication is equally effective in patients with GERD and paraesophageal hernia (B). There is improvement in abdominal pain, reflux, digestion score and quality of life score in patients with large paraesophageal hernias submitted to laparoscopic surgery (B). At the average follow-up period of 72 months, 93% of patients are free of GERD-related symptoms (B).

**Risk factor**

Hiatal hernia is a risk factor for erosive GERD (B). A hiatal hernia < 3 cm is a risk factor for non-erosive GERD, and a hiatal hernia > 3 cm, for erosive GERD and Barrett’s esophagus (B). The size of hiatal hernia, low pressures in the lower esophageal sphincter, esophageal acid exposure and number of reflux episodes are associated with esophagitis severity (B). Hiatal hernias > 2 cm are associated with Barrett’s esophagus and erosive GERD (B). The presence of hiatal hernia is associated with more severe esophagitis and predisposes patients with non-erosive GERD to more severe histological alterations (B). Patients with hiatal hernias have a high incidence of pathological reflux, regardless of the low pressure in the lower esophageal sphincter. Patients with pathologic reflux have esophageal propulsion failure and/or mechanical defects of the cardia associated with hiatal hernia (B).

**Prognosis**

Recurrence after fundoplication (Nissen or Toupet) is higher in large hernias (grades 3 and 4) (B). The permanent migration of the esophagogastric junction has more relevance in GERD prognosis than in sliding hiatal hernia, with reduction of the junction. Hiatal insufficiency and concentric hiatal hernia are determinant factors of irreversible cardia incontinence (B). In patients with GERD and hiatal hernia (31% erosive GERD and 75% lower sphincter dysfunction), reduction, crural closure, and Nissen fundoplication result in symptom improvement, at a 14-month follow-up (B). In patients with GERD (complicated or not), the presence of hiatal hernia determines significant increase in the PPI dose to achieve intraesophageal acid suppression (B).

**Recommendation**

Considering that:

- The presence of the permanent migration of esophagogastric junction and size of hiatal hernia (> 2 cm) are factors of worst prognosis for GERD;
- The presence of hiatal hernia requires higher doses of PPIs;
- The result of the laparoscopic fundoplication is adequate, including for paraesophageal hernia.

Hiatal hernias associated with GERD, especially those > 2 cm and fixed, should be treated surgically.

**Motility**

The Nissen fundoplication has good results in patients with normal esophageal motility, and the Toupet technique, in patients with esophageal dysmotility (B). There is no difference in postoperative symptoms in patients with or without esophageal dysmotility submitted to fundoplication (Nissen or Toupet) (A). The type of fundoplication should not be determined by the presence of dysmotility, as the postoperative dysphagia is not related to it (A). Preoperative dysmotility reflects a more severe disease, does not affect the postoperative outcomes, does not improve fundoplication and may occur after surgery (B).

**Recommendation**

Considering that:

- The preoperative dysmotility reflects a more severe disease, does not affect the postoperative outcomes, does not improve with fundoplication and may occur after surgery; no surgical treatment should be indicated using the parameter of esophageal dysmotility.

**Cost**

From the perspective of the National Health System, laparoscopic fundoplication is more cost-effective over eight years than PPI (B). Over five years, the cost of PPI is lower than the open surgery for GERD (B). Apparently, the Nissen fundoplication is more cost-effective in the treatment of GERD than treatment with PPI (B).

**Recommendation**

Apparently, the laparoscopic Nissen fundoplication, from the perspective of the National Health System, is more cost effective than PPI therapy over eight years. However, this is not the case with open surgery.
3. WHEN SHOULD CLINICAL TREATMENT BE INDICATED VERSUS SURGICAL TREATMENT?

In patients with GORD (erosive and non-erosive), antireflux surgery, compared to drug treatment with a PPI reduces the pH time < 4.0 and improves the VAS symptom score, the GERSS score, and scores of heartburn and regurgitation\textsuperscript{39} (A).

In patients with chronic erosive GORD, the Nissen surgery, compared to the use of PPIs, improves symptom scores, including the digestive score, and reduces the pH time < 4.0\textsuperscript{40} (A).

In patients with chronic erosive reflux disease, Nissen surgery compared to PPI increases the degree of patient satisfaction (NNT 5)\textsuperscript{41} (A).

In patients with erosive reflux disease, antireflux surgery (Nissen or Toupet) compared to omeprazole 20 mg daily reduces the risk of treatment failure over 5 years. There is a greater number of treatment failures over five years with clinical treatment of omeprazole 40 mg or 60 mg compared to surgery (Nissen or Toupet). Surgery reduces the risk of treatment failure by 11.6\% (95\% CI: 0.6-22.6) - NNT: 9. However, symptom scores (GSRS) and quality of life scores (PGWB) were similar in the two compared forms of treatment\textsuperscript{42} (A).

In patients with chronic erosive reflux disease, antireflux surgery (Nissen or Toupet) in comparison to omeprazole 20 mg reduces treatment failure, and, maintained for seven years, reduces dysphagia (NNT 38) and hiatal hernia (NNT 2)\textsuperscript{43} (A).

In patients with chronic GORD (reflux symptoms + esophagitis + previous treatment > 3 months), treatment with esomeprazole 20 mg or 40 mg is equivalent to laparoscopic surgery (Nissen), with 93\% and 90\% of patients remaining in symptom remission, respectively\textsuperscript{44} (A).

There is a greater number of therapeutic failures in three years with the clinical treatment of omeprazole 40 mg or 60 mg, when compared to surgery (Nissen or Toupet). Surgery reduces the risk of treatment failure by 12.9\% (95\% CI: 1.9-23.9) - NNT: 8. However, symptom scores (GSR) and quality of life (PGWB) were similar in the two forms of treatment\textsuperscript{45} (A).

Symptoms, Esophagitis and pH

In patients with GORD not submitted to surgery, at a follow-up of 17 to 22 years, symptoms improved in 70\% and worsened in 20\%. Of these patients, 66\% developed erosive GORD and/or pH changes, and 10\% Barrett’s esophagus\textsuperscript{46} (B).

At 12 months of follow-up, GERD treatment with medication and surgery (Nissen) is effective. However, surgery offers additional benefit to patients who had partial improvement with medication at a mean follow-up of 6.9 years\textsuperscript{41} (A).

At 18 months, regression from dysplasia to Barrett’s esophagus obtained with Nissen fundoplication (93.8\%) is higher than that obtained with PPI (63.2\%)\textsuperscript{47} (B).

The quality of life is higher in patients submitted to surgery compared to those undergoing medical treatment, at 12 months of follow-up\textsuperscript{48} (B).

The laparoscopic Nissen fundoplication leads to lower oesophageal acid exposure in three months and better quality of life after 12 months, when compared to clinical treatment\textsuperscript{49} (A).

Patients with Barrett’s esophagus have a 33\% regression after antireflux surgery. The regression is more significant the longer the time after surgery\textsuperscript{49} (B).

Patient Preference

Laparoscopic surgery improves the quality of life of patients whose symptoms are adequately controlled with PPIs\textsuperscript{50} (B).

Prognosis

In patients with GORD submitted to surgery after a follow-up of 5-9 years, 37\% were using medications (PPIs, H\textsubscript{2} blockers or antacids), of which 17\% had never stopped and 83\% resumed after 2.5 years due to return of symptoms. The pH-metry was abnormal in 32\%\textsuperscript{51} (B).

Comparing the response to surgical treatment of GORD, after 43 months, 66\% had symptom improvement, which was lower in patients with non-erosive GORD\textsuperscript{52} (B).

After five years, there was no difference in symptom improvement, adverse effects, or quality of life scores among patients with erosive and non-erosive GORD who underwent laparoscopic Nissen fundoplication\textsuperscript{53} (B).

There was no difference in response rates among patients undergoing surgery for GORD with open or laparoscopic techniques, and this was higher in patients undergoing clinical treatment\textsuperscript{54} (B).

In two years, 14.5\% of medically treated patients developed Barrett’s esophagus compared with no patients submitted to surgery\textsuperscript{55} (B).

Heartburn and esophagitis are effectively treated by medical and surgical therapy. Only surgery improved regurgitation, dysphagia and oesophageal motility\textsuperscript{56} (B).

At 10.9 years of follow-up, the Nissen fundoplication produces 84\% symptom resolution, 89\% esophagitis resolution and 5\% use of medication, while the clinical treatment produces, respectively, 53\%, 45\%, and 21\%\textsuperscript{57} (B).

Laparoscopic fundoplication produces the same results in patients with erosive or nonerosive GORD, with symptom improvement and reduction in PPI use\textsuperscript{58} (B).

Patients with Barrett’s esophagus have a 33\% regression after antireflux surgery. The regression is more significant the longer the time after surgery\textsuperscript{49} (B).
LOWER ESOPHAGEAL SPHINCTER PRESSURE

In patients with erosive GERD treated with PPI, the rate of recurrence at 12 months was 7.7% when they had normal pressure of the lower esophageal sphincter (> 8 mmHg), 38.1% in those with sphincter dysfunction and preserved motility and 79.5% in those with sphincter dysfunction and dysmotility69 (B).

In five years of follow-up, patients with inadequate response to PPIs can benefit from laparoscopic fundoplication, especially regarding the improvement of the quality of life60 (B).

During one year of follow-up, antireflux surgery obtained better results than medical treatment in relation to the symptoms of heartburn (19% versus 43%), regurgitation (8% versus 30%), increase in the need for PPIs (19% versus 74%), quality of life score (4 ± 0.6 versus 21 ± 1.4); and patient satisfaction (21.6% versus 5.9%)61 (B).

The success rate of Nissen fundoplication is 75.3%, and is associated with 77.1% of patients who responded to medical treatment and 56.0% who did not respond62 (B).

STENOSIS

In two years of follow-up of patients with erosive GERD and stenosis, antireflux surgery reduces the number of dilations by a factor of 10, reduces the dysphagia score in 50%, and 91.9% of patients were satisfied63 (B).

In a 10-year follow-up of patients that underwent Nissen fundoplication, the persistency or presence of symptoms was 32%, and 68% were asymptomatic. The quality of life remained high, although 80% had to undergo a new fundoplication procedure64 (B).

NON-ACID GERD

In patients on acid suppression, episodes of acid reflux are not associated with symptoms, but with mixed reflux episodes (liquid-gas)65 (B).

When compared to healthy patients, the number of reflux events in 24 hours after fundoplication is significantly lower. Most reflux episodes after surgery are non-acid66 (B).

Most preoperative patients had a positive symptom index, and 14 months after surgery, these patients were asymptomatic or had improved greatly67 (B).

Most patients undergoing prolonged PPI use, with persistent symptoms and a positive symptom index, have non-acid reflux, including patients with atypical symptoms68 (B).

In patients with GERD refractory to medical therapy, where gastric acid production is small (< 1 mEq/hour), about 50% have esophageal pH < 4.0 for more than 1.7% of the time69 (B).

RECOMMENDATIONS

Patients refractory to acid suppression, with typical or atypical symptoms, have non-acid reflux most of the time, and may benefit from surgical treatment.

In a two-year follow-up of patients with erosive GERD and stenosis, antireflux surgery shows a 10-fold reduction in the number of dilations, reduces the score of dysphagia in 50%, and 91.9% of patients are satisfied.

Considering that:

Low pressures in the lower esophageal sphincter are related to the severity of esophagitis, and in patients with erosive GERD treated with PPIs for 12 months, the recurrence rate, when there is lower sphincter dysfunction with pressure < 8 mmHg, whether or not associated with dysmotility, is respectively 38.1% and 79.5%. Surgical treatment should be considered in these patients.

There is evidence of estimated surgery benefit, with treatment failure reduction of 12% (NNT 8), when compared to medical treatment, and rates are maintained in the long term (7 years). But there is also evidence of equivalence for medical treatment with PPIs and laparoscopic surgery (Nissen), with 93% and 90% of patients remaining in symptom remission for 3 years, respectively.

In the long term, surgery reduces the risk of esophagitis by 44% (NNT: 2), and of Barrett’s esophagus and dysplasia, when compared to PPI therapy. In seven years of follow-up, surgery may benefit patients with GERD (erosive or non-erosive) who had partial response to PPIs, especially in relation to quality of life. However, after 2.5 years, 37% of patients may be using PPIs, and, additionally, in 10 years, many (80%) may require reoperation. Laparoscopic surgery enhances patient’s quality of life, even in those whose symptoms are adequately controlled with PPIs.

4. Among patients with surgical indication, which technique has the best result: total (Nissen) or partial fundoplication (Toupet)?

There is no difference after one year regarding the presence of symptoms of heartburn, regurgitation or other symptoms related to reflux in patients who underwent Nissen versus Toupet surgeries. However, the Nissen surgery increases the risk of dysphagia of any degree by 18.7% (95% CI: 6.0-31.4) – NNH: 5, and chest pain at meals by 17.1% (95% CI: 5.7-28.5) – NNH: 6. There is no difference regarding postoperative symptoms related to esophageal motility65 (A).

After two postoperative years, patient satisfaction is equivalent between those submitted to the Nissen or Toupet laparoscopic techniques. However, the Nissen surgery increases the risk of dysphagia by 11.0% (95% CI: 1.7-20.3) – NNH: 9 (A).

There is no difference between Nissen and Toupet surgeries, regarding the severity of symptoms in the one-year postoperative period65 (A).
In patients treated by Nissen surgery versus Toupet, there was no difference related to heartburn or acid regurgitation control. There was also no difference in the prevalence of dysphagia between the two surgical techniques (A).

Patients who underwent the Nissen or Toupet techniques are equally satisfied and reflux control is equivalent. However, the Nissen surgery increases the risk of dysphagia, not correlated to differences in esophageal motility, in 19.0% (95% CI: 8.1-29.9) – NNH: 5² (A).

There was no difference regarding symptom recurrence, dysphagia, or reflux control in the three-year post-operative period of Nissen versus Toupet techniques (A).

RECOMMENDATION

There is no difference between the Nissen and Toupet surgical techniques in relation to therapeutic response; however, the Nissen technique may produce more dysphagia, with NNH of 5 to 9, not correlated with motility.

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