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Surgical Treatment of Gastro-Esophageal Reflux Disease: A Review of Concepts Misguiding the Indications for Surgery

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Abstract

Context: Clinical therapies and surgical interventions are the acceptable treatments for gastro-esophageal reflux disease (GERD). Referrals for surgery are yet limited, because of disadvantages associated to surgical treatment, including: (a) high rate of mortality; (b) high risk of side effects, especially dysphagia; (c) need for acid-reducing medications after surgery; (d) need for revision surgery; (e) unclear benefit of surgery on the risk of cancer; and (f) differences in the outcomes between a community setting and a tertiary care center. In contrast, surgeons report excellent outcomes after anti-reflux operation.

Evidence Acquisition: A thorough search in literature was performed with predefined keywords to identify relevant articles published from 1975 to January 2015, in order to analyze the complications from the aspect of current surgeon's perspective.

Results: Our review showed that: (a) the mortality rate of the surgical procedure is negligible and PPI therapy is also accompanied with mortality; (b) there is a 5% chance of severe dysphagia after anti-reflux operation; (c) postsurgical use of PPI is not an indication of surgical failure, but often represents misuse of the medication; (d) there is a 5% chance of re-operation after surgery, often because of severe dysphagia; (e) reduction in the risk of adenocarcinoma is probable but still controversial; and (f) good results can be achieved in a community setting.

Conclusions: A significant number of patients would benefit from surgical therapy to treat their GERD symptoms, but some incorrect beliefs still misguide the indications for the surgical procedure.

Keywords: Gastro-Esophageal Reflux, Surgery, Fundoplication, Mortality, Morbidity

1. Context

Gastro-esophageal reflux disease (GERD) is a prevalent disease. Populational studies have repeatedly demonstrated a significant proportion of adult individuals experiencing GERD symptoms with a certain frequency. Even though patients with these symptoms have a 50% - 65% chance of having GERD, as defined by 24-h esophageal pH studies (1), an estimated 240,000,000 people worldwide have reflux (Table 1).

Clinical therapies and surgical interventions are acceptable treatments for GERD. Referrals for surgery are yet limited, because of some disadvantages associated to this type of therapy. Recent review papers in top-ranked medical journals (based on the institute for scientific information-ISI list) claim that the benefits of surgery for GERD must be weighed against the following complications: (a) mortality (5-8); (b) high risk of side effects, especially dysphagia (6-8); (c) need for acid-reducing medications after surgery (5-8); (d) need for revision surgery (6); (e) unclear benefit of surgery on the risk of cancer (5, 6); and (f) differences in the outcomes between a community setting and a tertiary care center (5, 6, 8). In contrast to the statements published in medical journals, surgeons re-

Table 1. Prevalence of Gastro-esophageal Reflux Disease[a]

Region	Adult Population, Thousands[b]	% GERD Symptoms in the Community	Number of Patients With GERD, Thousands[c]
Europe, Oceania, Northern America	900,718	25	112,590
Latin America	393,199	12	23,591
Asia	2,819,430	7	98,680
Africa	530,357	2	5,303
World	4,463,705	-	240,164

Abbreviation: GERD, gastro-esophageal reflux disease.
[a]Population data according to the united nations, department of economic and social affairs, population division, 2005.
[b]Over 15 years.
[c]50% of those with GERD symptoms (2-4).

port excellent outcomes after anti-reflux operation. Since GERD-related literature is so vast that any statement can be supported by published studies, we reviewed the modern literature in order to demystify the current concepts that include wider use of anti-reflux operation from a surgeon's point of view.

2. Evidence Acquisition

A PubMed search was performed with predefined keywords to identify relevant articles published from 1975 to January 2015, in order to analyze the complications from the aspect of current surgeon's perspective. Search was limited to English language. "Gastro-esophageal reflux disease" and "surgery" or "operation" or "fundoplication" or "Nissen" were used as separate terms.

Due to the lack of a specific instrument for quality evaluation, methodologic quality appraisal of the reviewed articles was not carried out. Furthermore, we performed a systematic review without meta-analysis along with the objectives of the study, which was to clarify the current concepts from a surgeon's perspective.

3. Results

3.1. Mortality Rate

Surgical mortality rate of anti-reflux surgery (fundoplication) is classically reported between 0.5% - 2% (5, 7, 8). However, the growing experience towards development of minimally invasive surgery has reduced the mortality rate more than 50% over the past decade (9). Also, national-based studies from Finland, Germany, and the United States reported the surgical mortality of anti-reflux laparoscopic surgery less than 0.5% (10-12), which is comparable to the mortality rate of appendectomy (13-15). A point to be considered as well is the fact that para-esophageal hernias (intrathoracic stomach), treated by fundoplication that represent a different group of high-risk patients operated for a different disease (16) are also included in these statistics.

Proton pump inhibitors (PPI) are associated with a 4.5 times increased risk of hip fracture after 7 or more years (17). It has been estimated that 8% of men and 3% of women over 50 years pass away whilst hospitalized for hip fracture. These mortality rates continue to rise over the subsequent months, and reach 36% for men and 21% for women at one year (18). Furthermore, mortality or life-threatening conditions related to PPI usage has been reported to be due to: (a) interaction with other medications, such as clopidogrel (19), (b) toxic epidermal necrolysis and neutropaenia (20) and (c) enteric infections (21).

The well-known study by Spechler et al. (22) called attention for late mortality in patients with GERD. The authors reported lower long-term survival for surgically treated patients in comparison to medically treated patients due to higher rate of cardiac-related death, although no explanation was given for this finding. Interestingly the causes of death that can be linked to GERD had a higher incidence in the medical group, although no statistical significance was found. For instance, pneumonia was almost 4 times more frequent, and lung failure 3 times more frequent in the medical group and esophageal cancer only occurred in the medical group. Rantanen et al. (23) reported more common mortality due to GERD in medically treated patients in a population-based study.

In summary, these data showed that surgical mortality rate is negligible and that the risk of death after surgical therapy is no higher than in medically treated patients.

3.2. Morbidity

Some criticisms to the surgical therapy for GERD are based on the onset of new symptoms after the operation, particularly dysphagia and gas symptoms (flatulence, inability to belch, gas bloating).

Early postoperative and transient dysphagia is common in patients after laparoscopic fundoplication. This symptom could be explained by postoperative edema and by the time it takes for the esophageal peristalsis to be restored after laparoscopic fundoplication (24). Dysphagia occurs in different degrees ranging from 5% to 20% (25-28). In most patients, however, swallowing usually improves progressively with time. Severe and persistent dysphagia occurs in about 5% of patients (29, 30).

Gas symptoms are very common in patients treated surgically or medically. In the aforementioned work by Spechler et al. (22), the Authors found no significant between-groups difference in the frequency of gas symptoms, including increased abdominal girth (36% of medical and 34% of surgical group), abdominal fullness (41% of medical and 42% of surgical group), inability to belch (20% of medical and 29% of surgical group), and inability to vomit (20% of medical and 32% of surgical group).

Although anti-reflux operations may create some postoperative symptoms, several studies showed that quality of life is not impaired and patients' satisfaction with the operation is sustained (29, 31-35). Regurgitation is also a bothersome symptom, not treated by medical therapy (36).

3.3. Postsurgical Medication Usage

Surgical therapy is considered an alternative to chronic medical treatment. In fact, the majority of the

patients are operated nowadays with this premise. However, Spechler et al. (22) reported in their famed study that 62% of the patients in the surgical treatment group took anti-reflux medications regularly after the operation. This finding is still used as a strong argument against surgery. However, it is important to clarify and define the indications for PPI usage.

The first point to be considered is that many studies have confirmed the poor correlation between postoperative reflux symptoms and actual reflux, when objectively measured by ambulatory pH-monitoring (37-40). Unfortunately, the majority of patients on PPI therapy after fundoplication are either not tested for reflux or have a normal pH-monitoring (32, 34, 39, 40). Besides, a minority of patients receiving PPI complain of GERD symptoms and medication is often prescribed for the treatment of their symptoms such as nasal and abdominal symptoms (40, 41). Other unjustifiable indications for the use of medication include: (a) primary-care physicians or gastroenterologists uncomfortable to discontinue the medications due to the presence of Barrett's esophagus (32, 41); or (b) patients with normal ambulatory pH-monitoring restart their medications either by themselves or on the advice of their medical physicians (32).

These data showed that a minority of patients need PPI therapy after fundoplication due to GERD recurrence.

3.4. Need for Revision Surgery

Clinical reviews often quote rates of re-operation due to fundoplication disruption or complications as high as 7% within the first 1 to 3 years (6). The rate of redo surgery in populational studies ranges from 2 to 5 % (10, 42, 43). In single institution series, the statistics are very similar, ranging from 1 to 5% (30-32, 34, 44). The re-operation rates do not reflect a low durability, since several well conducted studies have shown that good results are maintained after more than 10 years of the operation (44-47).

3.5. Cancer Prevention

Whether fundoplication reduces the risk of esophageal adenocarcinoma is debatable. Intuitive thinking favors an acceptance of risk reduction for the following reasons: (I) it is common knowledge that Barrett's esophagus is the precursor of esophageal adenocarcinoma and that GERD is the precursor of Barrett's esophagus (48); (II) the progression to esophageal adenocarcinoma follows the classic sequence of carcinogenesis: metaplasia - dysplasia - neoplasia; (III) bile reflux is associated to this sequence not treatable by PPIs; (IV) in a percentage of patients this sequence can be reversed after surgical anti-reflux treatment (49, 50), while Barrett's regression is rare with pharmacological therapy; and (V) the risk of cancer development usually decreases after ceasing exposure to risk factors, such as tobacco and esophageal cancer (51), tobacco and lung cancer (52), etc. Thus, an aggressive reflux control should intuitively prevent cancer.

Two different systematic reviews focused on this topic, which showed conflicting results. Very interestingly, a review conducted by a surgical team showed a reduction in the risk of adenocarcinoma after surgical treatment, compared to medical therapy (53), while a similar review conducted by a clinical team did not show any advantage for the surgical group (54). Generally, several studies show a trend towards efficacy of anti-reflux surgery over PPI therapy in reducing the development of adenocarcinoma (19, 55). If only successful operations are considered, a greater improvement is noticed in the outcome of surgery (56, 57).

3.6. Results in the Community Setting

Patients' dissatisfaction with surgical outcomes in community practice is used as a denial for surgery referral (6). The relationship between volume/outcomes is debatable. High-volume hospitals may deliver poor care while low-volume hospitals can deliver good care (58).

Regarding GERD, some studies report a higher incidence of complications in low-volume centers (9, 10); however, good outcomes, similar to academic centers, have been reported by different community centers (31, 59-62). It must be remembered that this operation is relatively easy to be performed; however, it is also relatively easy to be performed wrong. Different studies showed a learning curve close to 20 cases and that the experienced supervision should be accompanied for surgeons beginning laparoscopic fundoplication during their initial experience (63).

Obviously, more complex operations must be referred to specialized centers, such as the treatment of para-esophageal hernias or re-operations. Pham et al. (64) showed that increased institutional case volume reduces inpatient morbidity and mortality after para-esophageal hernia repair.

3.7. Nissen's Procedure

The Nissen fundoplication is the most commonly performed procedure. Before 1956, GERD and hiatal hernia (almost synonyms by that time) were surgically managed with reduction of the herniated stomach and some kind of gastropexy. Not surprisingly, results were disappointing. Nissen, when operating a case suffering from GERD in Switzerland performed an operation where the anastomosis of a cardia resection was protected by the stomach, like a Witzel gastrostomy and the patient did not develop

esophagitis. He tried to wrap the distal esophagus with the gastric fundus in patients with GERD. Two cases describing this new operation were published in 1956 for the first time. Nissen called the procedure 'fundoplication'. He later reported clinical and radiological resolution of hiatal hernia and reflux in 88% of the cases undergoing this operation. Nissen's technique was quickly accepted after a short period (65). An escalation in the number of procedures occurred after the advent of laparoscopic surgery; however, the procedure underused. Probably there is still a significant number of people who would benefit from surgical therapy for their reflux symptoms.

We believe that Nissen fundoplication, after more than 50 years of age, can be considered a very successful creation. It treats a high proportion of cases; brings excellent results in more than 80% of the patients; improves patients' quality of life and seems to prevent the progression of Barrett's esophagus to adenocarcinoma. Unfortunately, patients are still not offered surgical therapy based on some untrue concepts that still misguide indications for surgery.

4. Conclusions

This review shows that anti-reflux surgery is an effective and durable treatment for GERD. Among different alternatives, fundoplication is by far the most frequently used anti-reflux operation. It also shows that: (a) surgical mortality rate is negligible and PPI therapy is also accompanied with mortality rate; (b) there is a 5% chance of severe dysphagia after anti-reflux operation, gas symptoms are as common after surgical therapy as after PPI therapy; (c) post-surgical medication is not an indication for surgical failure, but rather a misuse of medication; (d) there is a maximum of 5% chance of re-operation after anti-reflux surgery, but most of these patients encompass those with severe dysphagia; (e) reduction in the risk of adenocarcinoma is probable but still controversial; and (f) good results can be achieved in a community setting with well-trained surgeons.

In conclusion, surgical therapy is an appropriate option for treatment of GERD and most prejudiced concepts linked to this operation must be abandoned.

Footnote

Authors' Contribution: Priscila Rodrigues Armijo: acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published; Fernando Augusto Mardiros Herbella: conception and design, acquisition of data, analysis and interpretation of data, drafting the article, final approval of the version to be published; Marco G. Patti: analysis and interpretation of data, review for intellectual content, final approval of the version to be published.

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