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Regression of Barrett's Esophagus: Is There a Difference between Clinical and Surgical Treatment?

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Abstract: Objective: To evaluate the response to clinical and surgical treatment of Walter Cantídio University Hospital patients who were diagnosed with Barrett's esophagus between 2012 and 2016. Methodology: From the database analysis of Walter Cantídio University Hospital's pathology service, we identified all patients with a diagnosis of Barrett's esophagus between 2012 and 2016. We analyzed the patients' medical records and collected epidemiological and clinical data. Results: 22 patients were included in the study, 13 of whom were surgically treated and 9 were clinically treated. The regression was 33.3% in the clinical group and 30.7% in the surgical group, with no statistical difference between these two groups. Conclusions: The results show synchrony with data from the medical literature regarding the response of Barrett's esophagus to clinical and surgical treatment.

Key words: Barrett's esophagus, treatment, regression.

1. Introduction

In 1950 Norman Barrett described a condition he believed to be a short congenital esophagus associated with an intrathoracic stomach. Subsequently, in 1953, Allison and Johnstone, after investigating 70 esophagectomy products, realized that this condition was in fact an esophagus with the presence of columnar epithelium.

BE (Barrett's Esophagus) is now defined as the presence of intestinal metaplasia in the esophagus and it is a condition related to GERD (gastroesophageal reflux disease) which may progress to esophageal adenocarcinoma, and it is therefore a pre-malignant condition.

The prevalence of BE diagnosed from high levels gastrointestinal endoscopies for any reason is from 1% to 2%, while in patients with GERD it varies from 5% to 15%. The risk factors for BE are high age, male gender, white race, GERD symptoms (especially when initiated in youth), central obesity and smoking.

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Patients with BE have 30 to 125 times higher risk of developing esophageal adenocarcinoma when it compared to the general population. However, the absolute risk of a patient with non-dysplastic BE evolved to esophageal adenocarcinoma is from 0.1% to 0.5% per year. On the other hand, when there is an association with low-grade dysplasia, the risk becomes 1% per year, and when there is high-grade dysplasia the risk goes up 7% to 19%.

The BE can still be divided into short and long Barrett, having a cut point of 3 cm. This division is important because there is a direct implication in the response to treatment. Gurski et al. [[1]] recently reviewed pre- and post-treatment endoscopic biopsy samples from 77 patients with Barrett esophagus treated surgically and 14 treated with PPIs (proton pump inhibitors). Histopathologic regression occurred in 28 of 77 (36.4%) patients after anti-reflux surgery and in 1 of 14 (7.1%) treated with PPIs alone. Babic et al. [[2]] showed that regeneration of the squamous epithel was the same for all PPIs but not good enough to stop the progression BE after stopped a invasive therapeutic approach.

Oelschlager and contributors [[3]] showed that 55% of the patients with short BE had regression of the disease after video laparoscopic anti-reflux surgery. However, no patient with long BE achieved this result. There are other studies showing that anti-reflux surgery in patients with non-dysplastic BE decreases the risk of disease progression to high-grade dysplasia.

On the other hand, a systematic review performed by Chang and contributors [[4]] showed no significant difference in progression to dysplasia between the surgically and clinically treated groups.

Therefore, anti-reflux surgery is not indicated to prevent progression of BE to adenocarcinoma, but it is indicated to control GERD. Sharma [[5]] concluded in a review that anti-reflux surgery is better than medical management for heartburn-free days. Other therapeutic options have been studied, such as endoscopic techniques and evaluations with biomarkers [[6]].

In this study, we reviewed the medical records of patients with a diagnosis of BE and evaluated the relationship with risk factors, surgical or clinical treatment, and the behavior of the disease.

2. Methods

The work was submitted to the Brazil platform and approved by the Ethics Committee of Walter Cantídio University Hospital. This is a retrospective study in which all patients had a diagnosis of BE confirmed by histopathology between 2012 and 2016 had their medical records reviewed.

The data searched were related to the risk factors for BE: disease duration, age, sex, obesity and smoking. Prognostic data searched were long or short BE. The form of treatment and the response to it were also investigated.

The evolution of BE to cancer was considered to be progression of the disease. Regarding the response to clinical treatment, the patients who had complete control of symptoms even after discontinuation of treatment were considered as a complete response. Those who controlled the symptoms, but had them returned with discontinuation of treatment, were considered to be chronic dependents of PPIs and, finally, those patients who maintained partial control of symptoms even with treatment were considered as low response.

Other data such as indications for surgical treatment were also collected at first follow-up consultation, with the intention of having a detailed epidemiological design.

Patients with incomplete data in their medical records or who had not performed digestive endoscopy with biopsy for control were excluded from the study.

3. Results

After performing a search in the database of the Pathology Department, 61 blades with biopsies were identified, confirming BE. Out of these, 15 were biopsies from the same patients, making a total of 46 diagnoses of BE between 2012 and 2016.

The 13 out of these 46 patients were excluded from the study due to incomplete or conflicting data: 01 was not present in the system, 03 were not localized, 02 presented gastric and non-esophageal intestinal metaplasia, 01 presented gastric neoplasia with esophageal invasion and 05 had no complete data in their medical records. At the end, we were left with 33 patients, of whom 11 were excluded due to absence of upper digestive endoscopy with biopsy to control the disease.

And 76.9% of patients in the surgical arm were men, while 33.3% were men in the clinical arm. The mean age in the surgical group was 58.8 years and in the clinical group 56.2 years.

All patients had esophageal GERD symptoms, had clear risk factors for GERD and had an initial treatment of acid suppression with proton pump inhibitors or H2 inhibitors.

The mean time for evolving between the beginning of symptoms and BE was 33.5 months in the surgical group and 31.7 months in the clinical group. In the clinical group, 06 patients had short BE, 02 had long

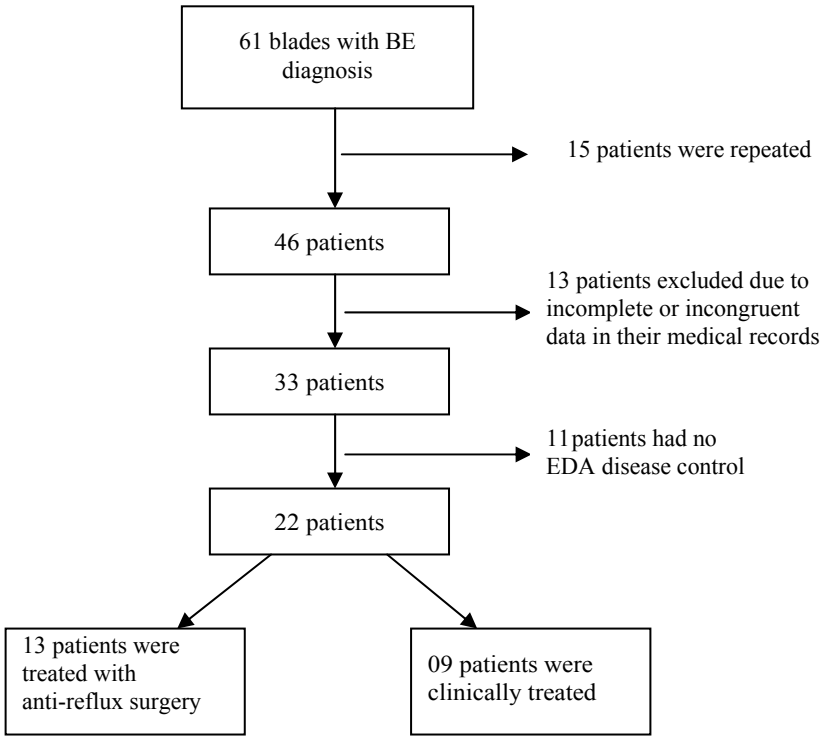

Fig. 1 General design of study groups.

Table 1 Comparative groups analysis.

	Clinical	Surgical
Gender	33.3% ♂ 66.3% ♀	76.9% ♂ 23.1% ♀
Age	42-74 years old (mean of 56.2 years old)	27-75 years old (mean of 58.8 years old)
Risk factors for GERD	1-4 factors (mean of 1.8 factors per patient)	1-4 factors (mean of 2.3 factors per patient)
Time until diagnosis of BE	2-84 months (mean of 31.7 months)	6-240 months (mean of 33.5 months)
Regression of BE	33.3%	30.7%
Evolution for adenocarcinoma	0 patient	1 patient

BE and one had not been described. In the surgical group, 08 were short BE, 03 were long BE and 02 were not described.

In the clinical group, only 2 patients presented dysplasia in the first biopsy, one of which was low grade and the other one high grade. In the surgical group, 4 presented dysplasia in the first biopsy, two of which were low grade and two were high grade.

And 85.6% of patients in the surgical arm had their first consultation related to GERD at Walter Cantidio University Hospital already with the surgical team, after being referred from other health units. In the clinical patients, 77.7% had a classic indication of anti-reflux surgery, under the same indication: dependence on PPIs to control symptoms. However, only 33% of the total patients had the surgical treatment offered.

In the group of patients treated with surgery, only one, 7.6%, had complete response to clinical treatment, 69.2% had a low response and 23% were chronic dependents of PPIs. And 22.2% of patients in the clinical arm had a complete response to clinical treatment, 11.1% had a low response and 66.6% were chronic treatment dependents.

In the surgical group, 04 patients had a regression of BE, 04 had appearance of dysplasia, 01 had appearance of adenocarcinoma and 04 had kept the disease stable. In the clinical group, 03 patients presented regression

of the disease and 06 patients maintained the disease stable. The disease regression occurred in 33.3% of patients in the clinical treatment arm and in 30.7% of patients undergoing surgical treatment, with no statistical significance, with P of 0.89.

4. Discussion

Several studies have already shown that the regression of short BE can occur with both surgical and clinical treatment, a fact that our statistics show. The regression was 33.3% in the clinical group and 30.7% in the surgical group, with no statistical difference between these two groups.

It is also known that surgical treatment is not able to change the natural history of BE and, therefore, the surgical indication for anti-reflux surgery is due to the patient's symptoms. However, Fernández et al. [[7]] compared clinical and surgical treatment for patients with BE. Treatment results were significantly worse with medical treatment than with anti-reflux surgery and should be optimized to improve acid reflux control in BE.

In this aspect, we have an important fact: in the clinical group, 77.7% had a clear indication of surgical treatment for GERD according to the Brazilian consensus of GERD [[8], [9]]. Despite this, only 28.5% of these patients had, at some point of their follow-up, the suggestions of a surgical treatment.

Maintaining the indication of surgical treatment only in reference to the response to clinical treatment, in the surgical group, only one patient had a complete response to the clinical treatment, and the surgery was indicated in other causes.

Considering that all patients in the clinical group were followed up at Walter Cantidio University Hospital Specialties Ambulatory, we evaluated that, for this group, there was a mismatch between the course followed and the indications in the medical literature.

This finding is important, as we already have bibliographical references that show a weak synergism between clinicians and surgeons. Herbella et al. [[10]] showed that clinicians make significantly lower referrals to surgical journals than surgeons do for clinical journals.

Therefore, one of the challenges is to improve communication between the clinical and surgical groups, with the intention of not delaying the surgical treatment when it is indicated.

This challenge increases after recent studies showing an increased incidence of gastric cancer in patients with H. pylori and chronic use of proton pump inhibitors. Although the results of Cheung et al. [[11]] and Brusselaers et al. [[12]][12] are linked to specific ethnic groups, they are relevant findings. These results put us in question: in patients with H. pylori and BE that would not the surgical treatment be indicated immediately, independently of other factors?

Another controversial aspect is the indication of surgical treatment as prevention for BE evolution for adenocarcinoma. In this paper, the surgical group had one patient who progressed to adenocarcinoma and in the clinical group, no patient. There is no statistical significance between the groups. It is important remember: clinical or surgical treatment does not suspend the obligatory surveillance for the transformation of BE into adenocarcinoma with endoscopy [[13], [14]]. This surveillance is valid only for patients diagnosed with BE, patients with GERD have no indication of endoscopic surveillance unless there are other warning signs or risk factors for Barrett's esophagus [[15], 16].

Despite this finding of our study and the controversy of this topic, there are peppers showing advantages in surgical management. De Haro and colleagues [[17]] compared the presence of malignant biomarkers (Ki 67, p53 and apoptosis) in patients with BE. Patients were randomized into two groups: Barrett's epithelium remains more stable after a long-term follow-up in patients with BE treated surgically than in those under PPIs even in the absence of abnormal rates of acid reflux.

Therefore, there are relevant indications that the

surgical treatment is better indicated, despite indications of fundoplication related to GERD. Obviously, we need multicenter studies, with greater sampling and prolonged follow-up to have more reliable answers on which are the best treatments for BE.

5. Conclusions

The results of the present study show a synchronicity with data from the medical literature regarding the response of BE to clinical and surgical treatment. An important secondary investigation of the study weighs the indication of the surgical treatment for GERD by the clinical specialties, since only 28.5% of the patients with a precise indication for the anti-reflux surgery had this therapy presented.

It is relevant to identify this mismatch in the indication of surgical treatment for GERD, especially since we have new studies showing complications, although rare, of the prolonged use of proton pump inhibitors. Multi-professional meetings are necessary to better manage patients with BE.

Another aspect to be evaluated is the importance of a detailed report of the clinical history and the patients' exams in their medical records, both for their adequate follow-up and for the best performance of clinical studies.

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