

## Treatment of Barrett's esophagus with low-grade dysplasia using Hibrid-APC

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### Keywords

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### Abstract

**Introduction:** Barrett's esophagus (BE) with low-grade dysplasia represents a risk of progression towards esophageal adenocarcinoma. Hybrid-APC turns out to be an effective, safe, easy to use and relatively low-cost technique to stop this progression. **Aims:** to describe the therapeutic response of Hybrid-APC in patients with low-grade dysplasia in Barrett's esophagus. **Method:** an observational, descriptive investigation of a series of cases was carried out at the National Center for Minimal Access Surgery between December 2018 and December 2020. Twenty patients with BE histologically classified with low-grade dysplasia were included. Ablation with Hybrid APC was applied, and endoscopy was performed three and six months after the end of the treatment. The therapeutic response was evaluated through histological remission and the presence of complications. The information was processed in the statistical program SPSS, version 21. **Results:** mean age 50.5 (range 27-81 years). 55% (11) are male. Eighty-five percent were asymptomatic and 90% had circumferential BE. 55% (11) required a Hybrid-APC session. With an average of 1.4 sessions, macroscopic and histological remission without dysplasia was achieved at three and six months in 90% (18/20) and 92.8% (13/14) of the patients respectively, without witnessing complications. **Conclusions:** endoscopic treatment with the Hybrid-APC has a good therapeutic response, with a good histological remission and without complications, in patients with low-grade dysplasia in BE.

### Introduction

Low-grade dysplasia in Barrett's esophagus (BE) represents a risk of progression to adenocarcinoma (1.6% per year). In recent years, esophageal adenocarcinoma (CEA) has been increasing in the West, and when it is diagnosed in advanced stages, 5-year survival is less than 15%. The application of safe and effective techniques is necessary to prevent the outcome towards malignant esophageal lesions. Multiple endoscopic techniques aimed at trying to reduce the risk of this progression have been developed [1-3].

Ablative therapies have been shown to have an impact on reducing the risk of developing adenocarcinoma in patients managed in the context of low-grade dysplasia [4].

Hybrid argon plasma coagulation (Hybrid-APC) is one of these techniques that allow stopping the natural history of BE in its initial stage, with the endoscopic eradication of dysplastic lesions confined to the mucosa, used in recent years. This technique, not yet endorsed in our setting, allows submucosal infiltration of fluids combined with argon

plasma ablation and the use of higher intensity without increasing complications. In addition, it allows the protection of the muscle layer, preserves the neighboring epithelium, is dynamic and applicable to large areas, and is cost effective (Hybrid-APC: 300-400 euros) vs (Radiofrequency: 2000 euros) [5,6].

The objective of this research is to describe the therapeutic response of Hybrid-APC in patients with low-grade dysplasia in Barrett's esophagus.

### Method

An observational, descriptive, case series study was conducted between December 2018 and December 2020. Twenty patients of both sexes, older than 18 years of age, with BE histologically classified as having low-grade dysplasia (confirmed by two biopsies with an interval of 6 months), with flat segment, treated at the National Center for Minimal Access Surgery. Patients who did not give their consent to participate in the project and pregnant women were excluded.

Demographic variables (age, sex), clinical (clinical symptoms), number of sessions were evaluated. The therapeutic response was

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evaluated through macroscopic and microscopic remission and the presence of complications. All patients underwent duodenogastrosocopy under anesthetic sedation. The Prague classification was used to measure BE length (C circumferential extension, M maximum length). Chromoendoscopy was performed with methylene blue, with previous cleaning with 2% acetic acid, and the NBI (narrow band image) was used to determine areas of dysplasia (these areas do not absorb methylene blue in a homogeneous way).

Ablation with the Hybrid-APC was applied in the dysplasia areas, in two quadrants per session (with an interval of 21 days per session). Ablation with 60 watt and effect 2 was applied, in the following sessions 50 watt and effect 2 were continued.

Treatment with Omeprazole (80 mg/day) was indicated for three months and was evaluated by outpatient gastroenterology consultation. They evolved clinically, endoscopically, and histologically three and six months after the last session (with taking a biopsy according to the Seattle protocol), which includes specific sampling of the visible lesions by endoscopy followed by random biopsies of the 4 quadrants every 1-2 cm, to assess macroscopic and histological remission (absence of intestinal metaplasia with dysplasia) and presence of complications (stenosis, bleeding, perforation).

The information was processed in the statistical program SPSS, version 21. The qualitative variables will be summarized using percentages and the quantitative variables using the mean and standard deviation.

The research protocol was reviewed and approved by the Research Ethics Committee and the Scientific Council of the National Center for Minimal Access Surgery.

**Results**

A total of 20 patients were included, the median age of the patients was 50.5 years [SD 13.3; range 27-81]. Most of the patients were in the 40-50 age group (Figure 1).

The male sex predominated in our group of patients (11 patients, 55%) (Figure 2).

In the endoscopic findings, 90% of the patients presented circumferential BE, with a mean length of 2cm (C0M2). 55% of patients achieved macroscopic remission in BE in a single session of Hybrid APC. 35 hybrid-APC sessions were successfully performed (Figure 3).

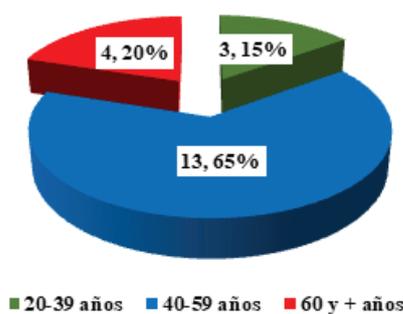


Figure 1. Distribution by ages group. Fuente: Database ProGastro v12.11.14.94. Dec 2018-2020.

recommended for its effectiveness (70-98%) [16].

The results obtained in the management of BE with Hybrid APC have shown a high rate of effectiveness. In a systematic review, the absence of BE was observed histopathologically in 39/50 patients (78%) [14]. While other studies by Rösch et al. [15] and Pech O et al. [17] showed a complete histological remission of BE in 92.50% (74/80). In an investigation that included 12 patients with BE with LGD, 100% achieved

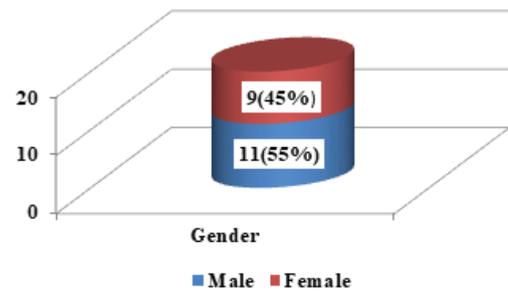


Figure 2. Distribution by gender. Fuente: Database ProGastro v12.11.14.94. Dec 2018-2020.

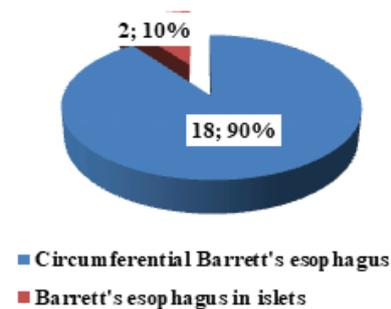


Figure 3. Distribution according to segment of Barrett's esophagus. Fuente: Database ProGastro v12.11.14.94. Dec 2018-2020.

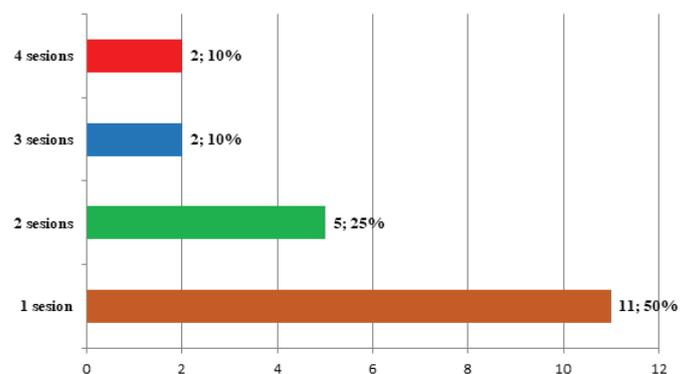


Figure 4. Therapeutic sessions with Hibrid-APC and number of patients. Fuente: Database ProGastro v12.11.14.94. Dec 2018-2020.

**Table 1.** Macroscopic and histological remission of the patients.  
Fuente: Database ProGastro v12.11.14.94. Dec 2018-2020..

Remission histological	3 months n=20 (%)		6 months n=14 (%)	
	Yes	No	Yes	No
Macroscopic	18 (90%)	2 (10%)	13 (92.8%)	1 (7.2%)
Microscopic	18 (90%)	2 (10%)	13 (92.8%)	1 (7.2%)

Of all the patients, macroscopic and histological remission was observed in 18/20 patients at three months, with eradication of dysplasia in 90% of cases. Of the 14 patients who were evaluated at six months, 13 remained without the presence of dysplasia, only one had recurrence of low-grade dysplasia (Figure 4), (Table 1).

All patients evolved without complications related to the application of the procedure.

## Discussion

The management of Barrett's esophagus (BE) and its associated dysplastic changes have been modified with the advent of safe and effective endoscopic techniques that are able to eradicate dysplasia, with few complications [7].

With the aim of reducing the risk of progression (12%) towards high-grade dysplasia (HGD) or esophageal adenocarcinoma (CEA), the use of endoscopic therapy with ablative techniques is recommended for patients with a confirmed diagnosis of low-grade dysplasia (LGD) [8,9].

The median age of the patients was 50 years and predominantly male, which corresponds to the reviewed literature. Some research suggest that BE with dysplasia most frequently in male patients over 50 years of age [10]. In a research conducted by Alnasser S et al. (3) the median age of the patients was 58 years, where 79% were men.

EB can be detected in 15-20% of patients with chronic symptoms of gastroesophageal reflux disease (GERD) [11]. In our casuistry there was a predominance of asymptomatic patients, only 10% had digestive symptoms of GERD, since they have been controlled with medications.

The most frequent distribution of the BE segment was circumferential with a mean length of C0M2. Kashin et al. [12] in their study reported a similar mean length (C1M2). In another review, Han et al. [13] described a mean of C = 0.7 M = 2.1.

The Hybrid-APC ablation technique is dynamic and applicable to large areas. Various authors require several sessions to achieve macroscopic remission. In our research, similar to previous investigations, this remission was achieved after a mean of 1.5 [SD 1.02; range 1- 4]. However, Manner et al. [14] achieved macroscopically complete remission after a median of 3.5 sessions [SD 2.4; range 1-10]. However, other authors only applied a median of 2.5 sessions, [range 1-5] [12,15]. Thus, it is clearly shown that a good therapeutic response is achieved with a few sessions.

Ablative endoscopic eradication techniques have shown good, albeit variable, results in the treatment of dysplastic lesions confined to the mucosa. RFA is the technique

histological remission 3 months after completing the ablation with Hybrid-APC [18].

In correspondence with the literature reviewed, ablation with Hybrid-APC was effective in our research, since 90% (18/20) of the included patients achieved histological remission at 3 months and 92.8% (13/14) maintained it at the 6-month follow-up. Dysplasia recurrence was only observed in 7.2% (1/14) of the patients, values lower than those reported in the literature, which can occur at 8% - 10% per year. These results help to reduce the risk of progression to HGD or ACE [19].

Hybrid-APC has been used as rescue therapy after the failure of other endoscopic techniques, such as RFA and cryotherapy, complete eradication of BE with low- and high-grade dysplasia, mainly in nodular lesions. Nieto et al. [20] used this variant, achieved the eradication of 100% (6/6) of the patients, without showing recurrence of dysplasia at 6 months of follow-up. They thus demonstrated that the Hybrid-APC is a highly effective technique, with histological remission.

Other ablation methods such as radiofrequency (RFA) and argon-plasma coagulation (APC) show stricture formation in 5-15% of patients, being the most frequent complication. Therefore, it would be desirable to use new ablation techniques that can overcome this disadvantage. Using the Hybrid-APC, the coagulation depth is reduced by half compared to standard APC, without thermal damage to the muscle layer. Therefore, it can lead to a lower rate of stricture formation during clinical application. (21)

Hybrid APC is considered a safe technique. In our casuistry, all the patients did not present complications related to the procedure. Kashin et al. [12] did not detect perforation or uncontrollable bleeding. He observed stricture formation in one patient after combination therapy with Hybrid-APC and EMR in one session and was treated by balloon dilation. Similar to the result, Han et al. [13] reported stenosis in 4.2%. Authors such as Manner et al. [14] in addition to stricture (2%) and observed minor adverse events in 11 patients (22%). Among the other complications described are fever (9/80; 11.25%), bleeding (2/80; 2.50%), and perforation (1/80; 1.25%). The Hybrid-APC has a lower risk of stricture formation than the conventional APC [17].

The present investigation obtained a good therapeutic response, results that coincide with the latest reviews about the effectiveness and safety of Hybrid-APC, where they found a histological remission in 92.5-100% of cases, without the presence of related complications with proceeding [17,18,20,21].

## Conclusions

Endoscopic treatment with the Hybrid-APC has a good therapeutic response, with a good histological remission and without complications, in patients with low-grade dysplasia in BE.

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