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Original article

Efficacy of standard and hybrid radiofrequency ablation and argon plasma coagulation in dysplastic Barrett's esophagus: A multicenter study with real-world evidence and inverse probability weighting analysis (IPTW)

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Abstract

Background: Endoscopic eradication of dysplastic Barrett's esophagus (DBE) using argon plasma coagulation (APC), hybrid APC (H-APC), or radiofrequency ablation (RFA) is the current standard. However, robust comparative evidence free from confounding bias remains scarce. The objective is to compare the efficacy (24-month recurrence) and safety (major adverse events) of APC, H-APC, and RFA in a real-world cohort using inverse probability of treatment weighting (IPTW). **Methodology:** Retrospective multicenter cohort study. The study included patients with DBE treated with the three modalities. The primary outcomes were dysplasia recurrence and a composite safety outcome (bleeding and stenosis). The study applied IPTW through multinomial logistic regression to balance covariates (age, body mass index [BMI], Prague classification, histology, and previous resection), evaluating balance with the standardized mean difference (SMD). **Results:** The analysis included 131 patients (APC = 48; H-APC = 41; RFA = 42). After IPTW adjustment, the study achieved optimal balance (SMD <0.1). Multivariate analysis showed no significant differences in 24-month recurrence (APC vs. RFA: OR: 0.62, 95% CI: 0.11-3.58; H-APC vs. RFA: OR: 1.18, 95% CI: 0.20-6.95) or adverse events (APC vs. RFA: OR: 0.58, 95% CI: 0.11-3.01; H-APC vs. RFA: OR: 0.38, 95% CI: 0.06-2.36). Barrett's extent (Prague M) was the only independent predictor of recurrence. **Conclusion:** After adjusting for confounding factors, APC, H-APC, and RFA demonstrated comparable efficacy and safety in the treatment of DBE. Clinicians should individualize therapeutic choice according to availability, costs, and technical expertise, as no modality showed intrinsic clinical superiority.

Keywords

Barrett's esophagus, argon plasma coagulation, radiofrequency ablation, statistical models.

INTRODUCTION

Barrett's esophagus (BE) is a metaplastic condition characterized by replacement of the normal esophageal squamous epithelium with columnar epithelium and is associated with a risk of progression along the dysplasia–carcinoma sequence[(1)]. Most esophageal cancers are diagnosed at an advanced stage, with a 5-year survival rate of 15% worldwide[(2)]. When early-stage cancer (T1) or high-grade dysplasia (HGD) is diagnosed, the prognosis is considerably more favorable. Endoscopic therapy is the treatment of choice for patients with BE-related dysplasia or early neoplasia (HGD or T1a adenocarcinoma),[(3)] given its favorable safety profile and comparable efficacy relative to esophagectomy.

Endoscopic thermal ablation has become the treatment of choice following endoscopic resection of esophageal neoplasia[(4)]. Argon plasma coagulation (APC) was one

of the first techniques used in this therapeutic setting and has been associated with low complication rates[5,6]. Studies comparing APC ablation with pharmacologic surveillance or postsurgical management have demonstrated a lower incidence of neoplasia with ablative therapy[7-10]. Complication rates following standard APC are comparatively low[11]. Stricture rates vary according to the amount of energy delivered and the size of the treated area. Hybrid argon plasma coagulation (hAPC) was developed to prevent post-treatment strictures. The technique involves injecting saline solution into the submucosal tissue to prevent thermal injury to the deeper layers and the *muscularis*. The first pilot study evaluating this technique demonstrated promising results,[12] while subsequent studies have reported complete macroscopic remission in 96% of cases and a stricture rate of 2%[13].

Radiofrequency ablation (RFA) has become the first-line ablative modality based on evidence from randomized controlled trials[14,15]. RFA involves the direct application of radiofrequency energy to the Barrett's epithelium, resulting in immediate coagulative necrosis. A meta-analysis reported pooled rates of complete eradication of metaplasia and dysplasia exceeding 80%[16]. Although RFA has an acceptable safety profile, strictures requiring dilation and postprocedural chest pain have been reported. Adverse events consist primarily of pain, acute bleeding, rare cases of perforation, and the development of post-treatment strictures[17]. A meta-analysis confirmed favorable eradication rates (88.4%), with a promisingly low complication rate (6.1%)[18].

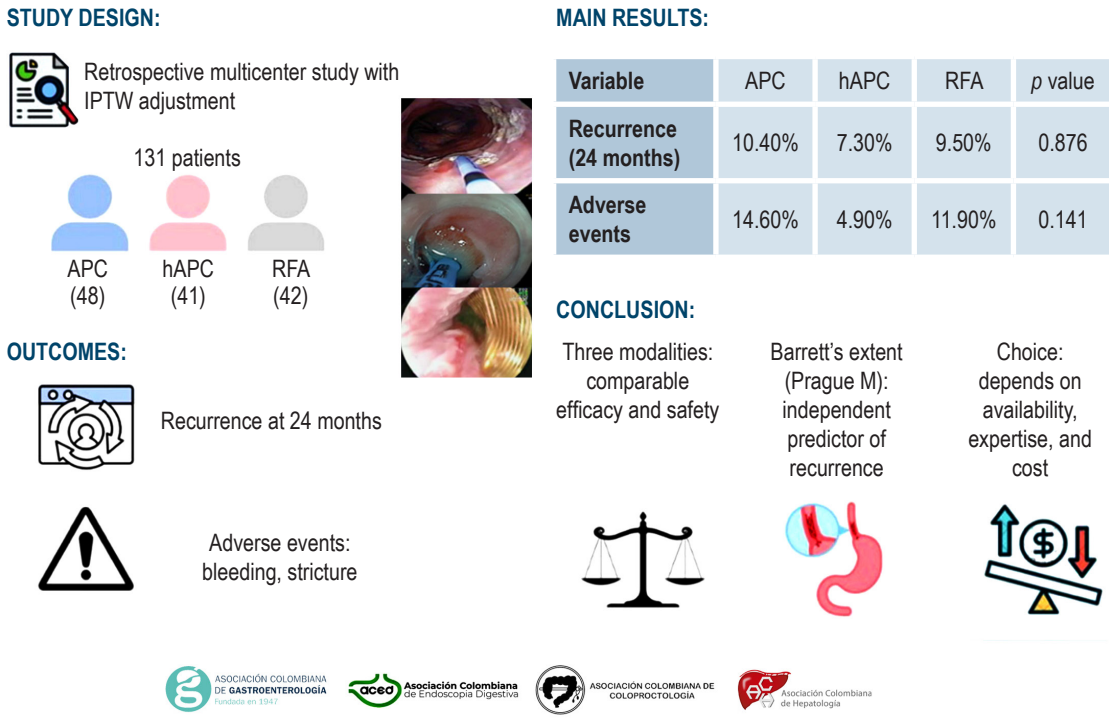
To date, most of the available literature has compared RFA with APC or hAPC separately; however, no studies have simultaneously evaluated all three techniques within the same cohort. This knowledge gap precludes robust conclusions regarding the relative efficacy and safety of these modalities in comparable clinical settings.

The present retrospective, multicenter study addresses this limitation by providing the first direct comparative analysis of APC, hAPC, and RFA in patients with dysplastic Barrett's esophagus (DBE), while also employing an inverse probability of treatment weighting (IPTW) statistical model. This methodological approach minimizes the biases inherent to retrospective studies and more closely emulates the conditions of a real-world clinical trial, thereby providing a more robust and balanced estimate of outcomes (**Figure 1**).

METHODS

Patient selection

A retrospectively analyzed, prospectively maintained (ambispective) database of patients who underwent endoscopic



Variable	APC	hAPC	RFA	*p* value
Recurrence (24 months)	10.40%	7.30%	9.50%	0.876
Adverse events	14.60%	4.90%	11.90%	0.141

Figure 1. Infographic comparing APC, hAPC, and RFA for the management of dysplastic Barrett's esophagus. Image courtesy of the authors.

ablation for the treatment of DBE and intramucosal carcinoma between July 2007 and May 2023 at three tertiary referral centers in Medellín, Colombia, was reviewed.

Patients were included if they underwent RFA or APC as the primary ablative modality for the management of DBE or intramucosal carcinoma following the initial endoscopic evaluation. Patients were excluded if they had incomplete clinical records, duplicate cases, indeterminate dysplasia, or previous treatment with APC or RFA, or if APC or RFA had been used as salvage therapy following failure of the initial ablative modality. The data collected included basic demographic characteristics, DBE segment characteristics, treatment details, histologic findings, adverse events (perforation, clinically significant intra- or postprocedural bleeding, or stricture formation requiring dilation), and the date of the last follow-up.

Endoscopic ablation methods

All procedures performed during the study period were carried out by experienced endoscopists with expertise in endoscopic ablation therapies using standard endoscopic equipment. Patients received general anesthesia, propofol sedation, or conscious sedation, as clinically indicated. The DBE mucosa was carefully evaluated during all procedures using high-definition white-light endoscopy, in addition to narrow-band imaging (including near-focus imaging) or flexible spectral imaging color enhancement (FICE). All visible lesions were endoscopically resected using snare resection or cap-assisted endoscopic submucosal dissection, at the discretion of the treating endoscopists. Ablation was performed after all abnormalities had been resected. The techniques are briefly described below.

Argon plasma coagulation therapy

Ablation was performed using an axial APC catheter (ERBE, Tübingen, Germany), with an argon flow rate of 1–1.5 L/min and a power setting of 50 W in forced mode (ICC 200) or pulsed mode (VIO), depending on the equipment available. A "brushing" technique was used from distal to proximal, with the probe extended 1 cm beyond the working channel. During each session, up to 60% of the esophageal circumference was treated, with rotation of the endoscope to cover the radial sectors. Residual Barrett's islands or tongues were treated using the same parameters. At 12 months, high-definition endoscopy was performed with targeted biopsies and four-quadrant biopsies every 2 cm, including the gastroesophageal junction.

Following the initial treatment, patients underwent repeat high-definition endoscopic evaluation at 12 months, including targeted biopsies of suspicious areas and four-quadrant biopsies every 2 cm, covering both the neosquamous epithelium and persistent Barrett's segments.

Hybrid argon plasma coagulation therapy

hAPC treatment was performed using the HybridAPC® system (ERBE, Tübingen, Germany), which combines pressurized submucosal saline injection through an integrated retractable needle with subsequent application of argon energy. Following submucosal hydrodissection, ablation was performed at a flow rate of 1–1.5 L/min and a power setting of 60 W in pulsed mode, achieving controlled superficial coagulation and a lower risk of transmural injury. The same partial circumferential "brushing" pattern was used (<60% per session), with focal retreatment of persistent islands or tongues during subsequent sessions.

Radiofrequency ablation

RFA was performed using the HALO® system (Medtronic, Sunnyvale, California). For circumferential segments, the HALO360 Express catheter was used, with balloon diameter calibrated to the esophageal diameter. For focal lesions, HALO90 catheters mounted on the tip of the endoscope were used. Standard doses of 12 J/cm^2 per application were delivered using a double-pass technique (initial application followed by repeat application after removal of the debris). Follow-up evaluations were performed at 3- to 6-month intervals, with retreatment of residual areas until complete eradication was achieved.

Primary and secondary endpoints

The primary endpoint was the rate of complete eradication of BE and DBE, defined as the absence of intestinal metaplasia and dysplasia in biopsy specimens obtained from the tubular esophagus and gastroesophageal junction during two consecutive surveillance endoscopies. As a secondary endpoint, adverse-event rates were assessed, including perforation; clinically significant bleeding requiring endoscopic management, hospitalization, or red blood cell transfusion within 30 days; and strictures requiring dilation.

Follow-up at 6, 12, and 24 months

All patients returned for endoscopic follow-up at 6, 12, and 24 months for endoscopic reassessment and retreatment of residual neoplasia or BE. During each follow-up endoscopy, the BE segment was carefully inspected. Residual flat columnar mucosa was retreated with hAPC or RFA, depending on the initial treatment modality. If there was no endoscopic evidence of BE, surveillance endoscopic biopsy specimens were obtained from the gastroesophageal

junction and neosquamous mucosa. All histologic specimens were reviewed by general pathologists at each participating center.

The presence of metaplasia or dysplasia detected during the 6-month follow-up endoscopy was interpreted as indicative of technical failure of the initial endoscopic procedure (technical success). In contrast, detection of metaplasia or dysplasia during subsequent follow-up evaluations was considered recurrence of the lesion, reflecting the pathological reappearance or persistence of the dysplastic process (clinical failure).

Statistical analysis

Continuous variables are presented as median (interquartile range [IQR]), and categorical variables as frequency (%). Comparisons among the treatment groups (APC, hAPC, and RFA) were performed using the Kruskal–Wallis test for continuous variables and the χ^2 test for categorical variables.

To account for confounding bias inherent to the retrospective study design, a multivariable analysis was performed using inverse probability of treatment weighting (IPTW). Propensity scores were estimated using a multinomial logistic regression model that included the following baseline covariates: age, sex, body mass index (BMI), presence of hiatal hernia (≥3 cm), Prague C and M lengths, histology (high-grade dysplasia and *carcinoma in situ* versus low-grade dysplasia), and prior endoscopic resection. A pseudo-randomized cohort was generated by assigning each patient a weight corresponding to the inverse probability of receiving the observed treatment. Covariate balance after weighting was confirmed, with a standardized mean difference (SMD) <0.1 considered indicative of adequate balance.

Finally, the association between treatment modality and outcomes (recurrence at 12 and 24 months and a composite adverse-event endpoint [bleeding or stricture]) was assessed using IPTW-weighted binomial logistic regression models, with RFA as the reference group. Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) were reported. A p value <0.05 was considered statistically significant.

RESULTS

Between January 2004 and December 2023, 131 patients treated for dysplastic Barrett's esophagus at three medical centers in Medellín, Colombia, were identified. Patients underwent ablation therapy with argon plasma coagulation (APC, n = 48), hybrid argon plasma coagulation (hAPC, n = 41), or radiofrequency ablation (RFA, n = 42) (**Figure 2**).

The temporal distribution of ablative therapies from 2004 to 2023 shows that the series began with APC therapy in 2004, followed by the introduction of RFA in 2011; hAPC therapy was implemented beginning in 2017 (**Figure 3**).

Univariate analysis

Baseline demographic characteristics were similar across all groups, with no significant differences in age (median,

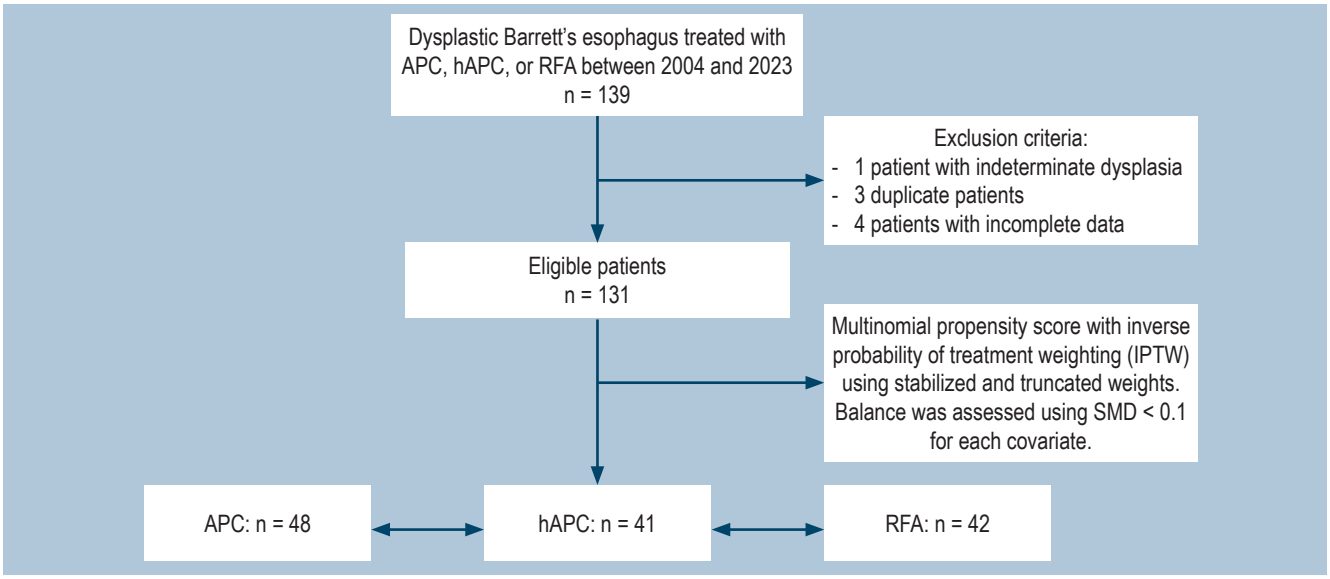


Figure 2. STROBE-type flow diagram depicting the patient selection process, including exclusions and cohort formation before and after propensity score matching (PSM). APC: argon plasma coagulation; hAPC: hybrid argon plasma coagulation; IPTW: inverse probability of treatment weighting; RFA: radiofrequency ablation; SMD: standardized mean difference. Image courtesy of the authors.

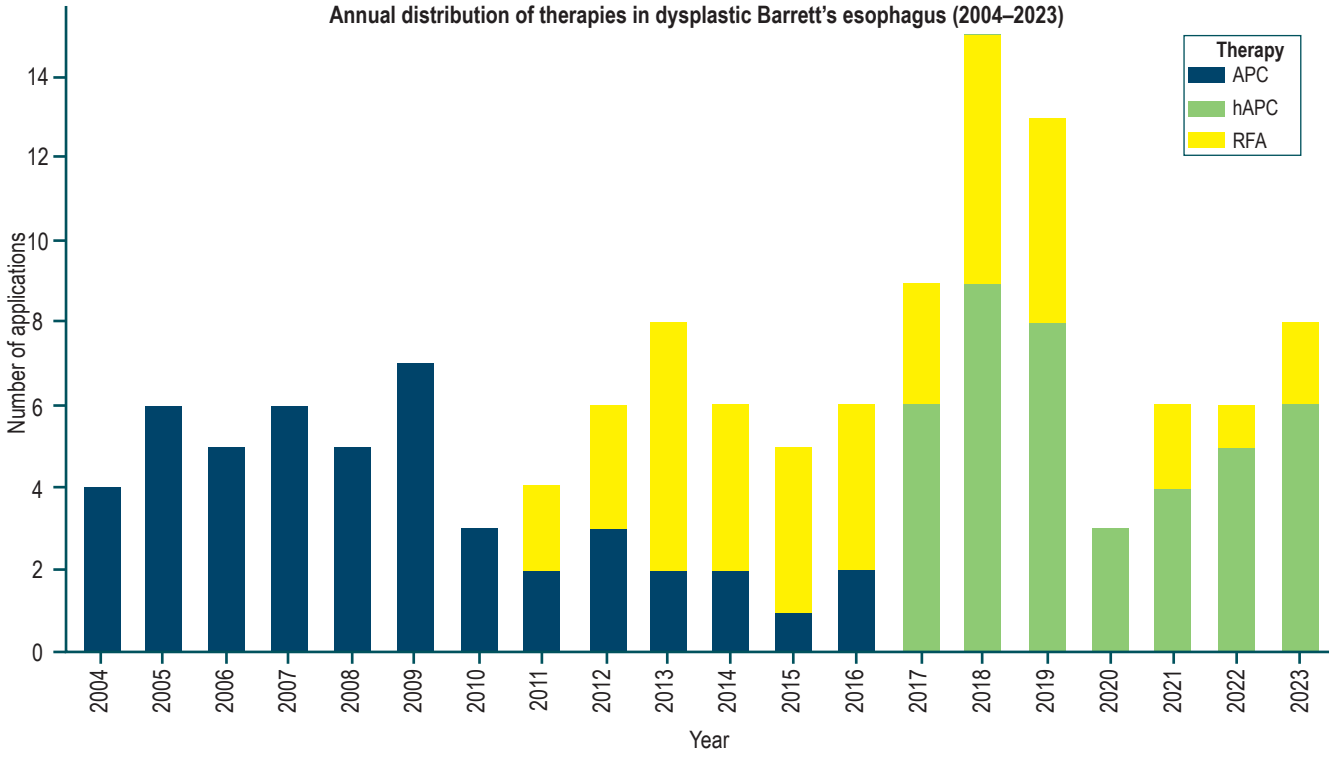


Figure 3. Annual evolution of APC, hAPC, and RFA use in dysplastic Barrett's esophagus (2004–2023). APC: argon plasma coagulation; hAPC: hybrid argon plasma coagulation; RFA: radiofrequency ablation. Image courtesy of the authors.

61 years [IQR, 52–72] for APC vs. 62 [IQR, 56–69] for hAPC vs. 61 [IQR, 56–70] for RFA; $p = 0.923$) or BMI ($p = 0.579$). However, significant imbalances were observed in Prague M length (median, 4 cm [IQR, 3–5] for APC vs. 5 cm [IQR: 4–7] for hAPC vs. 5 cm [IQR: 4–7] for RFA; $p = 0.004$) and histology, with a higher proportion of low-grade dysplasia in the APC group (65% vs. 39% for hAPC vs. 31% for RFA; $p = 0.018$). Rates of prior endoscopic resection were comparable ($p = 0.986$). Overall, unadjusted outcome rates were low, with no significant differences in recurrence at 12 months (14.6% for APC vs. 9.8% for hAPC vs. 11.9% for RFA; $p = 0.784$) or at 24 months (10.4% for APC vs. 7.3% for hAPC vs. 9.5% for RFA; $p = 0.876$). Adverse events (bleeding or stricture) occurred in 16.7% of patients treated with APC, 4.9% of those treated with hAPC, and 11.9% of those treated with RFA ($p = 0.141$), suggesting a numerical trend toward fewer events with hAPC. However, because these were unadjusted comparisons, the findings may have been influenced by bias or confounding factors. This provided the rationale for applying an inverse probability of treatment weighting (IPTW) model in the multivariable analysis to obtain more robust and comparable estimates. Baseline characteristics and outcomes are summarized in **Table 1**.

Multivariable analysis adjusted by inverse probability of treatment weighting

Inverse probability of treatment weighting (IPTW) was applied to achieve balance across baseline covariates, resulting in excellent covariate balance, with all standardized mean differences (SMDs) <0.1 after weighting (**Figure 4**).

Pre-weighting standardized mean differences (SMDs) were elevated for Prague M (0.567 for APC vs. RFA; 0.136 for hAPC vs. RFA) and histology (0.468 for APC vs. RFA; 0.290 for hAPC vs. RFA), but were substantially reduced after weighting (e.g., Prague M: 0.071 for APC vs. RFA; 0.050 for hAPC vs. RFA) (**Table 2**).

These findings indicate that treatment modality, age, and the variables reflecting the extent of metaplasia (C and M) were statistically significant predictors of the outcome after IPTW adjustment, whereas BMI and hiatal hernia were associated with the outcome but did not reach statistical significance in this model.

Adverse events

For adverse events, the multivariable analysis revealed a similar pattern. The APC group exhibited a markedly higher

Table 1. Univariate analysis of baseline characteristics and outcomes in unadjusted data

Variables		APC n = 48	hAPC n = 41	RFA n = 42	*p*
Age		61.0 (52.0-72.0)	62.0 (56.0-69.0)	61.0 (56.2-69.8)	0.923
Sex (%)	Male	34 (70.8%)	30 (73.2%)	30 (71.4%)	0.969
	Female	14 (29.2%)	11 (26.8%)	12 (28.6%)	
BMI, kg/m², mean ± SD		27.9 ± 2.7	28.4 ± 3.1	27.8 ± 3.4	0.579
Hiatal hernia (%)	<3 cm	16 (33.3%)	14 (34.1%)	12 (28.6%)	0.838
	≥3 cm	32 (66.7%)	27 (65.9%)	30 (71.4%)	
Prague classification	C, cm	3.0 (2.0-4.0)	3.0 (2.0-4.0)	3.0 (3.0-4.0)	0.190
	M, cm	4.0 (3.0-5.0)	5.0 (4.0-7.0)	5.0 (4.2-7.0)	**0.004**
Histology (%)	LGD	31 (65)	16 (39)	13 (31)	0.72
	HGD	15 (31)	21 (51)	23 (55)	
	Intramucosal carcinoma	2 (4)	4 (10)	6 (14)	
Prior therapies (%)	None	42 (88)	32 (79)	31 (74)	0.668
	Band ligation	1 (2)	1 (2)	3 (7)	
	EMR	3 (6)	3 (7)	3 (7)	
	ESD	2 (4)	5 (12)	5 (12)	
Sessions (%)	1	7 (15)	3 (7)	5 (12)	**0.003**
	2	15 (31)	11 (27)	16 (38)	
	3	13 (27)	12 (29)	21 (50)	
	≥4	13 (27)	15 (37)	0 (0)	
Pain (%)	Mild	12 (25)	17 (41)	12 (29)	0.22
	Moderate	21 (44)	17 (41)	19 (45)	
	Severe	15 (31)	7 (18)	11 (26)	
Days with pain, mean ± SD		4.1 ± 1.3	3.2 ± 1.3	6.8 ± 1.9	**<0.01**
Fever (%)	Yes	6 (13)	2 (5)	6 (14)	0.335
	No	42 (87)	39 (95)	36 (86)	
Bleeding (%)	Yes	4 (8)	2 (5)	0 (0)	0.141
	No	44 (92)	39 (95)	42 (100)	
Dilation (%)	Yes	7 (15)	1 (2)	7 (17)	0.141
	No	41 (85)	40 (98)	35 (83)	
Recurrence at 6 months (%)		5 (10)	2 (5)	2 (5)	0.543
Recurrence at 12 months (%)		7 (15)	4 (10)	5 (12)	0.784
Recurrence at 24 months (%)		5 (10)	3 (7)	4 (10)	0.876
Residual Barrett's esophagus (%)		11 (23)	7 (10)	8 (17)	0.779
Follow-up, months, median ± SD		39.0 (36.0-43.0)	39.0 (33.0-43.0)	39.5 (35.0-44.8)	0.524

APC: argon plasma coagulation; hAPC: hybrid argon plasma coagulation; IMC: intramucosal carcinoma; HGD: high-grade dysplasia; LGD: low-grade dysplasia; SD: standard deviation; ESD: endoscopic submucosal dissection; BMI: body mass index; EMR: endoscopic mucosal resection; RFA: radiofrequency ablation. Table prepared by the authors.

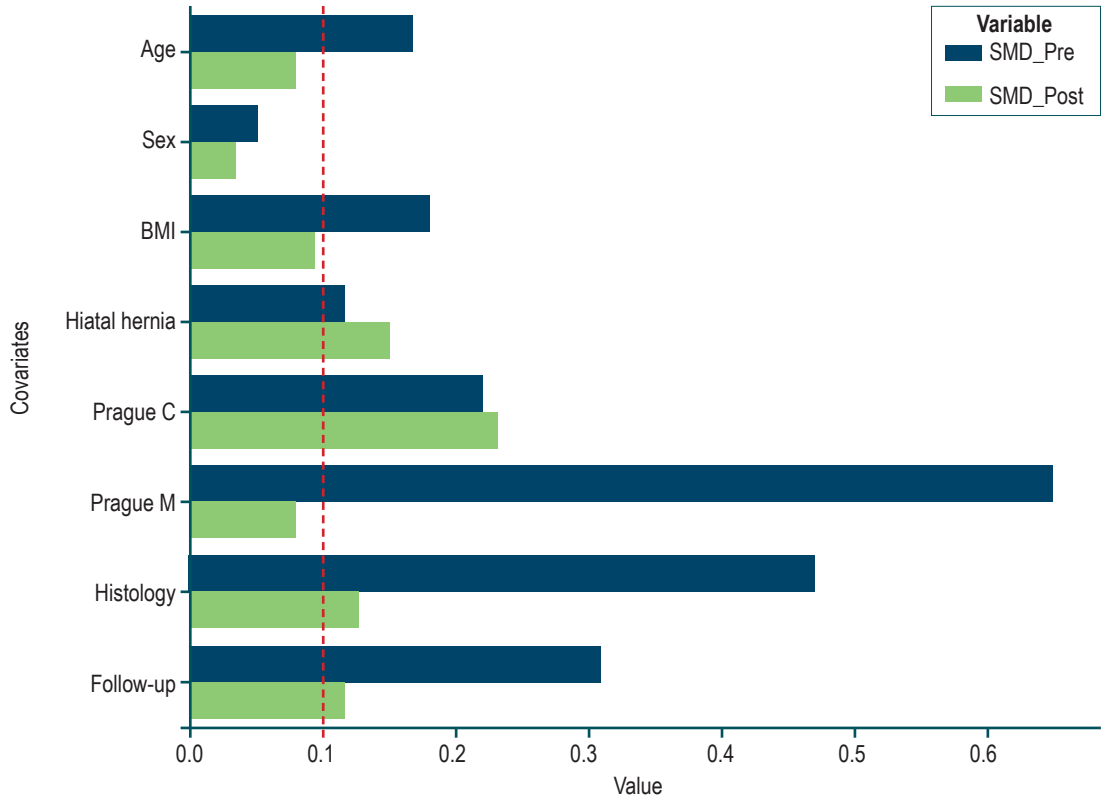


Figure 4. Love plot illustrating the assessment of baseline covariate balance before and after inverse probability of treatment weighting (IPTW). Image courtesy of the authors.

risk compared with RFA, with an adjusted OR of 4.76 (95% CI, 2.26–10.03; p <0.001), suggesting that patients treated with APC had nearly fivefold higher odds of experiencing post-treatment bleeding or stricture. This finding highlights an inferior safety profile for APC relative to RFA, even after adjustment for confounding factors. In contrast, hAPC did not differ significantly from RFA, with an adjusted OR of 1.01 (95% CI, 0.41–2.52; p = 0.976), indicating a comparable risk of complications. The wide confidence intervals reflect the low event rates and the moderate sample size.

Six-month follow-up (technical success)

At 6-month follow-up, lesion persistence was more frequent among patients treated with APC (5/48; 10%) than among those treated with hAPC (2/41; 5%) or RFA (2/42; 5%). However, the difference in persistence rates among the three groups did not reach statistical significance (p = 0.78, χ^2 test). These findings indicate that, although a higher proportion of persistent disease was observed in the APC group, a definitive difference in initial treatment effectiveness among the techniques cannot be established in this cohort.

Table 2. Multivariable analysis of the IPTW-adjusted clinical outcome in patients with Barrett's esophagus treated with APC, hAPC, or RFA ablation

Variable	Coefficient	Standard error	*z* value	*p* value
Intercept	-2145	765	-2805	0.005
Treatment	972	452	2149	0.031
Age	27	12	2250	0.024
BMI	13	10	1300	0.194
Hiatal hernia	134	78	1718	0.086
C	738	265	2783	0.005
M	512	210	2438	0.015

APC: argon plasma coagulation; hAPC: hybrid argon plasma coagulation; C: circumferential extent of Barrett's esophagus according to the Prague classification; BMI: body mass index; IPTW: inverse probability of treatment weighting; M: maximal extent of Barrett's esophagus according to the Prague classification; RFA: radiofrequency ablation. Table prepared by the authors.

Twelve-month follow-up

In the adjusted model for 12-month recurrence, the standard APC group demonstrated a significantly higher risk compared with RFA, with an adjusted OR of 3.04 (95% CI, 1.48–6.23; p = 0.002). This indicates that patients treated with APC had approximately threefold higher odds of developing dysplastic or metaplastic recurrence at 12 months after adjustment for baseline covariates. In contrast, the hybrid APC (hAPC) group did not differ significantly from RFA, with an adjusted OR of 1.06 (95% CI, 0.46–2.43; p = 0.885), suggesting comparable efficacy in preventing recurrence over the intermediate term. Age showed a trend toward an association but did not reach statistical significance, whereas BMI and hiatal hernia had no statistically significant effect.

Twenty-four-month follow-up (clinical success)

For 24-month recurrence, the findings likewise demonstrated a statistically significant association between treatment modality and the extent of metaplasia and recurrence, with minor changes in the magnitude of the coefficients, whereas the remaining variables showed no statistically significant effects (**Table 3**).

Table 3. Recurrence of dysplasia or Barrett's esophagus at 12 and 24 months based on IPTW-adjusted logistic regression models

Variable	OR, 12 months	95% CI, 12 months	OR, 24 months	95% CI, 24 months
Treatment	2.65	1.09-6.45	2.38	1.08-5.24
Age	1.03	1.00-1.06	1.02	1.00-1.05
BMI	1.01	0.99-1.03	1.01	0.99-1.02
Hiatal hernia	1.14	0.97-1.34	1.13	0.99-1.29
C	2.09	1.21-3.63	1.97	1.23-3.17
M	1.67	1.13-2.48	1.54	1.13-2.10

C: circumferential extent of Barrett's esophagus according to the Prague classification; BE: Barrett's esophagus; 95% CI: 95% confidence interval; BMI: body mass index; IPTW: inverse probability of treatment weighting; M: maximum extent of Barrett's esophagus according to the Prague classification; OR: odds ratio. Table prepared by the authors.

The recurrence-free survival analysis showed that, although all three techniques exhibited a favorable recurrence-free survival profile, the APC curve demonstrated a more pronounced decline toward the end of the follow-up period, suggesting a higher cumulative recurrence rate compared with hAPC and RFA.

Taken together, these adjusted findings confirm that, although APC is associated with higher rates of recurrence and adverse events compared with RFA, the hybrid modality (hAPC) provides an efficacy and safety profile comparable to that of RFA (**Figure 5**).

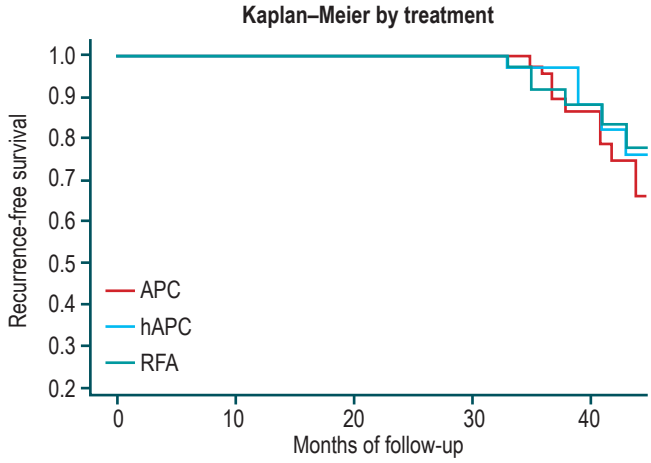


Figure 5. Kaplan–Meier recurrence-free survival curves according to the therapeutic modality used for ablation of dysplastic Barrett's esophagus. Comparison using the log-rank test revealed no significant differences (p = 0.35). Image courtesy of the authors.

DISCUSSION

In this real-world cohort study, the efficacy and safety of three ablative therapy modalities (APC, hAPC, and RFA) were compared for the treatment of dysplastic Barrett's esophagus. The principal finding, after robust adjustment for confounding using IPTW, was that all three therapies demonstrated comparable efficacy in eradicating dysplasia at 24 months. However, clinically relevant differences emerged in their safety profiles, with hAPC associated with a significantly lower rate of esophageal stricture compared with APC and RFA. This finding suggests that, although eradication of dysplasia can be achieved with multiple technologies, the choice of modality may have a substantial impact on patient morbidity.

Radiofrequency ablation has become established as the standard of care for the eradication of dysplastic BE, supported by high-quality evidence from randomized controlled trials such as the SURF study, which demonstrated a complete eradication rate of dysplasia and intestinal metaplasia exceeding 90%[15]. Our efficacy results for RFA are consistent with those reported in this and other large registries, including the UK RFA Registry, supporting the effectiveness of this technique in our cohort[19]. In this context, any alternative therapeutic modality should demonstrate, at a minimum, noninferior efficacy and, preferably, advantages in safety, accessibility, or cost.

Historically, conventional APC has been an attractive alternative because of its widespread availability and lower

cost. However, its use for extensive Barrett's segments has been questioned because of unpredictable tissue penetration, which may result in incomplete eradication or an increased risk of complications such as stricture and perforation,[20] as reflected in the literature review. The findings of our study, even after adjustment, place APC in a position of potentially lower efficacy and a safety profile that is not superior to that of RFA, supporting the current view that conventional APC should not be considered a first-line therapy for eradication of dysplastic Barrett's epithelium, but rather a complementary or salvage treatment.

The most recent innovation evaluated in our study was hAPC. This technique was specifically developed to overcome the limitations of conventional APC by combining argon ablation with the creation of a protective submucosal cushion. The underlying rationale is that this cushion permits more uniform and safer ablation while minimizing thermal injury to the muscularis propria[13]. Our finding of a significantly lower stricture rate with hAPC compared with RFA and APC (1 case in the hAPC group vs. 7 cases in the other two groups, in both the raw and post-IPTW data) provides strong clinical evidence supporting this mechanistic hypothesis. Whereas RFA induces controlled-depth coagulative necrosis (approximately 500–1,000 μm), hAPC may provide a superior safety profile by thermally isolating the deeper layers of the esophageal wall, a particularly relevant advantage when treating long or circumferential Barrett's segments[21-24].

From a clinical perspective, our findings have important implications. They suggest that multiple effective tools are available for the eradication of dysplastic Barrett's esophagus[25]. Accordingly, therapeutic decision-making may be more nuanced. Although RFA remains the benchmark modality, with an extensive evidence base, hAPC emerges as a promising alternative, particularly in patients at high risk for stricture (e.g., those with long Barrett's segments, preexisting stricturing disease, or post-endoscopic resection treatment). Patient counseling should therefore address not only the likelihood of successful dysplasia eradication but also the risk of adverse events such as stricture, which may require multiple interventions and substantially affect quality of life[21].

In addition to the modalities evaluated in our study, cryotherapy has emerged as an important alternative within the therapeutic armamentarium for eradication of dysplastic Barrett's epithelium[26] and even for recurrent dysplastic Barrett's esophagus after chemoradiotherapy[27]. This technique induces cellular necrosis through the application of extreme cold, either via a liquid nitrogen spray at −196 °C or through a nitrous oxide balloon system (balloon cryoablation). Its mechanism of action, which induces cell death through intracellular ice crystal formation, vascular ischemia, and apoptosis, fundamentally differs from the coagulative necrosis induced by thermal therapies such as RFA and APC[28]. Beyond its use as a primary therapy, cryotherapy has established a crucial role as salvage therapy for the small but clinically significant proportion of patients with persistent dysplasia who do not respond to RFA. In this setting of "treatment failure," cryotherapy has been shown to achieve complete eradication of dysplasia in more than 75% of cases, making it an indispensable tool for the management of the most refractory cases[28]. Therefore, any discussion of the treatment algorithm for dysplastic Barrett's esophagus should consider cryotherapy not only as a first-line alternative but also as a key second-line strategy.

It is important to place these findings in context. Although IPTW adjustment successfully balanced the measurable covariates, our study is not without limitations. Its retrospective nature entails reliance on the quality of clinical documentation and the potential for unmeasured confounding. For example, endoscopist experience with each technique is a potentially influential variable that was not quantified and may have affected both efficacy and safety. In addition, the moderate sample size and differences in group size (with a larger APC group) may affect the precision of estimates for the smaller groups (hAPC and RFA), as may follow-up limited to 24 months, the absence of central histopathologic review by expert pathologists, and heterogeneity in endoscopic technique.

The principal strength of our study lies in the use of an advanced analytical methodology (IPTW) in a large and heterogeneous real-world clinical cohort, which enhances the external validity and generalizability of the findings beyond the highly selected populations enrolled in clinical trials. It also identifies Prague C/M as key predictors and provides evidence applicable to settings with cost constraints, in keeping with the contemporary literature[11,17,29,30].

Although an economic analysis was not a primary objective of the study, the difference in costs between the therapies is noteworthy: radiofrequency ablation is more than tenfold more expensive than argon plasma coagulation, despite providing equivalent clinical outcomes. This finding reinforces the observations reported by Ragunath et al.,[31] who demonstrated that more complex and costly thermal techniques, such as photodynamic therapy, do not provide significant additional benefits over argon plasma coagulation for the eradication of dysplastic Barrett's esophagus, despite requiring an additional investment of approximately £266 for each percentage-point reduction in Barrett's extent and £146 for each percentage point of dysplasia eradication. From a pragmatic perspective, these differences suggest that argon plasma coagulation, particularly in its hybrid form, represents a more cost-effective

alternative in geographic settings where technological availability or financial resources are limited, without compromising short- or intermediate-term clinical outcomes.

Future research should focus on confirming these findings through randomized controlled trials directly comparing RFA and hAPC. Such studies should assess not only long-term endoscopic and histologic outcomes but also cost-effectiveness and patient-reported outcomes, including postprocedural dysphagia and quality of life (**Table 4**).

CONCLUSION

Our study provides robust real-world evidence supporting hAPC as a safe and effective alternative to RFA for the eradication of dysplastic BE. Although long-term efficacy appears to be comparable among modern ablative therapies, the superior safety profile of hAPC, particularly its low risk of stricture, makes it a highly attractive therapeutic option that warrants further consideration in clinical practice and future research.

Ethical considerations

The study was conducted in accordance with the principles of the Declaration of Helsinki and in compliance with the guidelines of the International Conference on Harmonisation–Good Clinical Practice (ICH-GCP). According to the ethical risk classification established by Colombian Resolution 8430 of 1993, this study was considered research involving no more than minimal risk, as it involved retrospective documentary research techniques and methods without any intentional intervention or modification of the biological, physiological, psychological, or social variables of the individuals included in the study. The

Table 4. Summary of randomized controlled trials of Barrett's esophagus treatment

Study	Country	n	Male	Age	Therapy	Histología	Terapia
Kahaleh, 2002[32]	Belgium	39	76.9%	63.7 ± 8.7	12	NDBE + LGD	APC
Ackroyd, 2004[33]	United Kingdom	40	80.0%	48.9 ± 5.1	12	NDBE + LGD	APC, surveillance
Hage, 2004[34]	Netherlands	40	77.5%	59.6 ± 6.3	12	NDBE + LGD	PDT, APC
Kelty, 2004[35]	United Kingdom	72	80.1%	59.0 ± 11.9	12	NDBE	PDT, APC
Ragunath K, 2005[31]	United Kingdom	26	80.8%	61.2 ± 13.2	12	LGD + HGD	APC, PDT
Sharma P, 2006[36]	United States	35	97.1%	61.1 ± 12.4	24	NDBE + LGD	APC, MPEC
Bright, 2007[10]	Australia	40	80.0%	58.0 ± 9.6	60	NDBE + LGD	APC, surveillance
Bright T, 2009[9]	Australia	54	70.4%	59.1 ± 7.6	12	NDBE + LGD	APC, surveillance
Shaheen NJ, 2009[14]	United States	127	86.6%	66.0 ± 1.7	12	LGD + HGD	RFA, placebo
Zhang, 2009[37]	China	35	62.9%	53.3 ± 10.7	12	NDBE + LGD	APC, PPI
van Vilsteren, 2011[38]	Netherlands	47	85.1%	67.6 ± 8.5	24	HGD + EC	SRER, RFA
Sie C, 2013[7]	Australia	129	-	61.5 ± 9.3	12	NDBE + LGD	APC, surveillance
Manner H, 2014[12]	Germany	63	90.5%	63.0 ± 9.9	36	HGD + EC	APC, surveillance
Phoa KN, 2014[15]	Europe	136	85.3%	63 ± 9.5	36	LGD	RFA, surveillance
Peearally MF, 2019[39]	United Kingdom	76	84.2%	70.0 ± 9.2	12	HGD + EC	RFA, APC
Wronska E, 2021[40]	Poland	71	76.1%	61.1 ± 4.2	1.5	LGD	APC
Barret M, 2021[41]	France	82	92.7%	62.3 ± 10.0	36	LGD	RFA, surveillance
Knabe M, 2023[22]	Germany	101	-	64.6	21	LGD, HGD, IMC	RFA, APC
Current series	Colombia	131	71	61.3 ± 5.39	39	LGD, HGD, IMC	RFA, APC, hAPC

APC: argon plasma coagulation; RFA: radiofrequency ablation; HGD: high-grade dysplasia; LGD: low-grade dysplasia; NDBE: nondysplastic Barrett's esophagus; PPI: proton pump inhibitors; PDT: photodynamic therapy; MPEC: multipolar electrocoagulation; SRER: stepwise radical endoscopic resection. Table prepared by the authors.

study consisted of reviewing medical records, conducting interviews, administering questionnaires, and other procedures in which participants were neither identified nor subjected to the disclosure or treatment of sensitive aspects of their behavior.

Conflicts of interest

The authors declare no conflicts of interest.

Use of artificial intelligence

Artificial intelligence tools (ChatGPT, OpenAI) were used in an auxiliary capacity during the drafting and editing of the manuscript, particularly to improve the English-language writing and to generate structured abstracts. All sections were reviewed, validated, and approved by the authors, who assume full responsibility for the scientific content and conclusions of the study.

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Author contributions

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