
Endoscopic Ablation of Barrett's Esophagus Using Argon Plasma Coagulation

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Abstract

Barrett's esophagus (BE) is a complication of gastroesophageal reflux disease (GERD), and GERD symptoms, as well as fear of cancer, are the most disturbing concerns for BE patients. The vast majority of BE patients should be treated as ordinary GERD patients, except for periodical surveillance endoscopies. Ablation trials should not even be contemplated in BE patients without dysplasia. BE with low-grade dysplasia follows the same rules as for BE without dysplasia, but with more frequent surveillance esophagogastroduodenoscopies. These patients could be included in ablation trials. In BE with visible areas of high-grade intraepithelial neoplasia or intramucosal cancer, resection and adjuvant thermal ablation seems to be the most reasonable therapy. In BE with high-grade intraepithelial neoplasia without visible lesions, thermal ablation alone appears to demonstrate the best results.

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Barrett's esophagus (BE) is a premalignant complication of gastroesophageal reflux disease (GERD) and possesses a potential for neoplastic transformation ranging from 2 to 40%, according to several risk factors such as extension of the metaplastic tissue, grade of dysplasia, duration of disease and mutation-induced gene alterations [1, 2]. Esophageal adenocarcinoma arising in BE has one of the most rapidly increasing incidence rates of any malignancy over the last 30 years [2]. Since antireflux surgery and longstanding acid-reducing therapies by pharmacological means did not show a consistent fashion either to reduce the metaplastic epithelium extent or to halt the evolution to cancer in this population [3, 4], a myriad of endoscopic ablation techniques have been developed, although the vast majority of BE patients will never develop adenocarcinoma or die of this cancer [5].

BE patients with high-grade dysplasia (HGD) (high-grade intraepithelial neoplasia (HGIN)) or intramucosal adenocarcinoma are those with indications for endoscopic treatment in clinical practice. In the past, esophagectomy was the standard therapy for such patients. However, surgery carries high mortality and morbidity rates (about 5 and 30–40%, respectively), even when performed in referral centers [6]. Thus, as it occurs in the colon and stomach, surgery is no longer the treatment of choice for esophageal HGIN. Endoscopic methods that have been developed in the last decade include thermal ablation techniques: argon plasma coagulation (APC), photodynamic therapy (PDT), laser, multipolar electrocoagulation, heater probe, cryotherapy and radiofrequency ablation (RFA) [2, 7], and total or partial endoscopic resection or a combination of these methods [8, 9].

Technique of Endoscopic Ablation with APC

Each patient received supplementary medical therapy with high-dose proton pump inhibitors (60 mg omeprazole, 80 mg esomeprazole, 120 mg pantoprazole), commencing 2 days before the first APC session. This high-dose regimen is indicated until BE is considered ablated; thereafter, antireflux surgery or prolonged medical therapy is recommended according to the patient's life expectancy and wish.

APC is carried out using an argon beamer device (APC300; Erbe Medizintechnik, Tübingen, Germany) and 3.2-mm catheters with a monopolar electrode contained in a ceramic nozzle located close to the catheter distal tip. We do not employ catheters with a lateral opening. The use of a double-channel endoscope is preferable, although not obligatory, since during the procedure a large amount of gas in the upper gastrointestinal tract is insufflated, and with one-channel endoscopes, the APC probe has to be withdrawn many times in order to aspirate the argon gas. In our protocol, Barrett's mucosa is cauterized hemicircumferentially, beginning at its proximal end and continuing distally up to the cranial borders of the hiatal hernia folds or up to a maximum of 4 cm per session. Side effects (pain, fever, pleural effusion, stricture) are related to the extent of the cauterized area [10] (fig. 1, 2).

The operative distance between the probe tip and the tissue should be about 2–3 mm – the probe should not touch the tissue, otherwise high-pressure gas will be insufflated into the submucosa and/or deeper layers. Each application should be in a paintbrush manner in confluent areas and the probe should be maintained in the same area for about 8–10 s, or until the area is fully coagulated, and then advanced. Usually, 3–5 passes are necessary in each area to deeply coagulate Barrett's mucosa. Barrett's mucosa has a depth of about 1.5 mm [11] and APC can reach depths of 3 mm, according to power setting (at least 65 W – we use 69 W), gas flow (we employ 2 l/min) and contact time [12]. The worst mistake is to pinpoint Barrett's mucosa. With this technique, BE will be ablated until the submucosa, no Barrett's glands will be left underneath the necrotic tissue and the adjacent squamous epithelium will repopulate the area [10, 13].

At the present time, we perform local endoscopic mucosal resection (EMR) for intramucosal cancer, dysplasia-associated lesions or masses (DALM) with the lift-and-cut technique and APC ablation of the rest of Barrett's epithelium (fig. 3–5).

Accessories

APC ablation is performed with a high-frequency monopolar electrosurgical generator source of argon gas, gas flow meter, APC delivery catheters, grounding pad and footswitch. Probes that deliver the energy either perpendicular or at the extremity of the catheter are available. EMR could be performed using band ligator – without submucosal saline injection – or with the lift-and-cut technique with submucosal saline injection (injection needle, grasping forceps or alligator forceps and a large snare).

Outcomes

Once BE is established (fig. 6), the possibility of malignant transformation does not depend on the elimination of acid reflux [1], thus the only mean of eliminating this higher risk of malignization

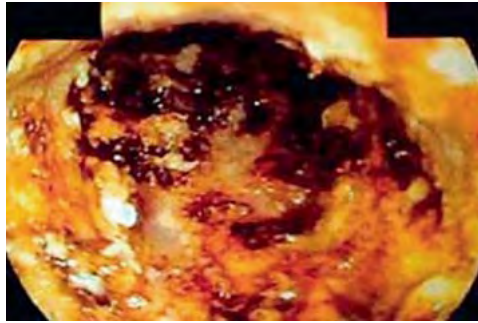
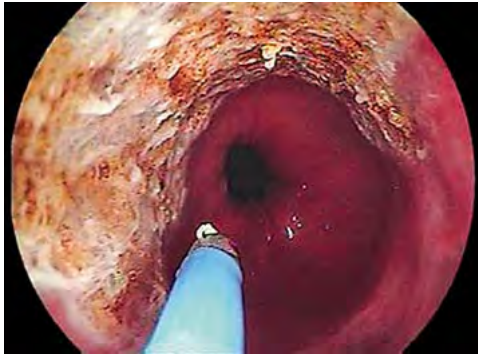


Fig. 1. Hemicircumferential cauterization of a BE with APC. **Fig. 2.** Circumferential ablation of a HGD BE with APC. Side effects are associated with the extent of the ablated area.

would be resection (endoscopic or surgical) or by endoscopic thermal ablation. Endoscopic ablation is based on the hypothesis that Barrett's epithelium is a healing process induced by multipotential stem cells from the basal layer of the squamous epithelium in response to acid injury [14]. Once the mucosa is destroyed by endoscopic techniques and reflux is effectively controlled, stem cells from the contiguous normal squamous epithelium repopulate this area and the distal esophagus turns again to become a squamous mucosa [13].

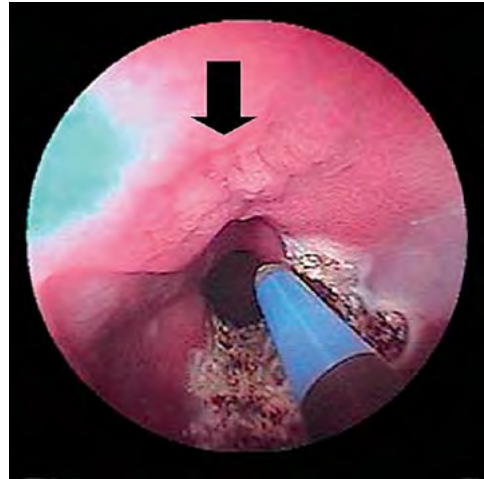
Endoscopic ablation is reported to reduce the incidence of Barrett's cancer in a study using weighted-average rates derived from pooled data taken from various studies [7]. The cancer incidence would be reduced from 5.98/1,000 patients-years to 1.63/1,000 in non-dysplastic BE; from 16.98/1,000 to 1.58/1,000 patient-years in low-grade dysplasia BE and from 65.8 to 16.76/1,000 patient-years in HGD patients.

The greatest concerns with ablation therapy for BE are the lack of histologic specimens, and the risk of 'development' of Barrett's tissue underneath the new squamous epithelium. This 'new' BE tissue, with or without dysplasia, does not develop beneath the new squamous mucosa during repopulation of the distal esophagus after ablation. These Barrett's glands remained undestroyed during the thermal ablation due to an inadequate technique. This flaw is reported to occur with all thermal ablative modalities [15]. In the case of APC, it is reported in up to 40% of the cases [15]. Since the depth of tissue destruction depends on the gas flow rate, power setting, duration of application and the distance from the mucosa, inappropriate power setting or contact time would produce a shallow depth of tissue injury, and hence insufficient ablation of all Barrett's epithelium. Inappropriate power settings to reach the submucosa are reported in many studies [16–18] and even low doses of omeprazole, such as 10 mg, have been used by some groups [17, 18].

A high-power setting with a long contact time successfully ablates BE without intramucosal cancer [10, 19, 20]. After a follow-up of 5 years in 79 patients, there were no cases of buried glands in more than 5,000 biopsy specimens. There were 5 cases of BE recurrence. These patients developed BE after ablation had been confirmed, since they presented with normal squamous mucosa 6 months after ablation, erosive esophagitis in another follow-up endoscopy and finally a de novo BE. This was due to 4 surgical failures in controlling reflux and 1 case of medication non-compliance [20].

The most severe side effect of mucosal ablation with APC is not stenosis, fever, or chest pain that occurs in up to 20% of the patients, but the development of adenocarcinoma underneath the new squamous epithelium after inadequately performed ablation as reported by some authors

Fig. 3. Patient with long segment BE and DALM. Note the ablation of the metaplastic epithelium close to the DALM (arrow), which was submitted to EMR in the same procedure.



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Fig. 4. An intramucosal adenocarcinoma in a patient with a long segment BE with previous anti-reflux surgery.

Fig. 5. Same case as in figure 4. The muscularis propria is visible after EMR. This patient underwent APC ablation in a following procedure.



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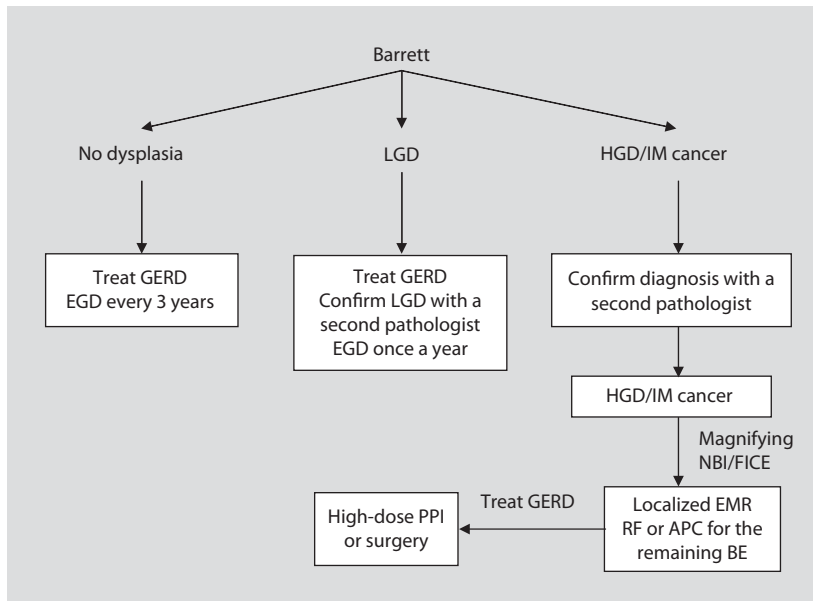


Fig. 6. Algorithm for Barrett's esophagus.

[21, 22]. Direct contact techniques (heat probe, multipolar electrocoagulation) have the drawback of not being particularly suitable for large areas of mucosa and also have difficulty in regulating the depth of tissue damage [15]. PDT is reported to have plenty of major side effects, such as strictures (one-third of patients) and photosensitivity for up to 3 months, and HGD ablation occurs in 78–95%, with a 15% cancer occurrence being reported over a 5-year follow-up period [15, 23]. In one study, PDT was as effective as APC, but the latter is cheaper and safer [24].

RFA is the newest of endoscopic ablative techniques and offers as its greatest advantage (in opposite to APC) uniformity of results in all the targeted mucosa at a given power setting. At the present time, RFA is the thermal technique that should be propagated throughout the world (especially in non-referral centers), despite its costs. RFA enables similar results by all operators in contrast to APC and EMR. In fact, RFA could be compared to the results of fast-food chains sandwiches – they are all the same thing around the globe and APC is like French cooking. RFA alone or combined with EMR for focal lesions achieved excellent results, with 98% of BE eradication (with HGD or intramucosal cancer) [8, 25].

EMR offers significant advantages over thermal ablation in the treatment of BE. EMR supplies histological specimens which provide accurate pathologic analysis in terms of disease differentiation and invasion. Localized resection of HGIN/intramucosal carcinoma in BE leaving the rest of Barrett's mucosa untouched counts with a rate of metachronous lesions of 21.5–31% in a German series, according to the length of BE and follow-up [26]. It seems logical that a BE that contains chromosomal abnormalities (that had already produced a cancer) cannot be left untreated, otherwise new cancers will develop in this metaplastic segment. In total, Barrett's EMR, both the HGIN/intramucosal cancer and all underlying Barrett's segments are theoretically completely removed. This technique would resect all at-risk zones, addressing the pitfalls of missing synchronic lesions, as well as possible future metachronic tumors. However, total BE-EMR is performed in a piecemeal fashion and can leave ridges of Barrett's epithelium within the resected zones. In a large French series, Lopes et al. [27] reported a 12% recurrence rate at 32 months. Soehendra et al. [28] analyzed 10 patients who underwent total BE-EMR with a ligator device. These authors reported the development of stricture in 7 (70%) with 1 perforation and 1 death. Larghi et al. [29] reported 1 (4%) intramucosal cancer and 2 cases of BE underneath the new squamous epithelium at a 2-year follow-up. Endoscopic submucosal dissection (ESD) offers en bloc resection of the diseased area. Yoshinaga et al. [30] described 15 cases (14 of them with short-segment BE) of ESD due to Barrett's cancer. Specimen sizes ranged from 2.5 to 6 cm. Of these 15 cases, 4 invaded the submucosa. No recurrence was observed in the 11 cases of intramucosal cancer during a mean follow-up of 2.5 years. ESD might be the best endoscopic treatment for BE, however it should only be performed by endoscopists experienced in this field. Do they exist outside of Japan?

References

- 1 Sharma P, McQuaid K, Dent J, et al: A critical review of the diagnosis and management of Barrett's esophagus: the AGA Chicago Workshop. *Gastroenterology* 2004; 127:310–330.
- 2 Fennerty MB: Endoscopic ablation of Barrett's-related neoplasia: what is the evidence supporting its use? *Gastrointest Endosc* 2003;58:246–249.
- 3 Gurski RR, Peters JH, Hagen JA, et al: Barrett's esophagus can and does regress after antireflux surgery: a study of prevalence and predictive features. *J Am Coll Surg* 2003;196:706–713.
- 4 Corey KE, Schmitz SM, Shaheen NT: Does a surgical antireflux procedure decrease the incidence of esophageal adenocarcinoma in Barrett's esophagus? A meta-analysis. *Am J Gastroenterol* 2003;98:2390–2394.

- 5 Rastogi A, Puli S, El-Serag HB, et al: Incidence of esophageal adenocarcinoma in patients with Barrett's esophagus and high-grade dysplasia: a meta-analysis. *Gastrointest Endosc* 2008;67:394–398.
- 6 Hulscher JB, van Sandick JW, de Boer AG, et al: Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med* 2002;347:1662–1669.
- 7 Wani S, Puli SR, Shaheen NJ, et al: Esophageal adenocarcinoma in Barrett's esophagus after endoscopic ablative therapy: a meta-analysis and systematic review. *Am J Gastroenterol* 2009;104:502–513.
- 8 Pouw RE, Gondrie JJ, Sondermeijer CM, et al: Eradication of Barrett's esophagus with early neoplasia by radiofrequency ablation, with or without endoscopic resection. *J Gastrointest Surg* 2008;12: 1627–1636.
- 9 Seewald S, Ang TL, Gotoda T, et al: Total endoscopic resection of Barrett esophagus. *Endoscopy* 2008;40:1016–1020.
- 10 Pereira-Lima JC, Busnelo JV, Saul C, et al: High power setting argon plasma coagulation for the eradication of Barrett's esophagus. *Am J Gastroenterol* 2000;95:1661–1668.
- 11 Sampliner RE: Ablative therapies for the columnar-lined esophagus. *Gastroenterol Clin North Am* 1997; 26:685–694.
- 12 Johans W, Luis W, Jansen J, et al: Argon plasma coagulation in gastroenterology: experimental and clinical experiences. *Eur J Gastroenterol Hepatol* 1997;9:581–587.
- 13 Lopes CV, Pereira-Lima J, Hartmann AA: p53 immunohistochemical expression in Barrett's esophagus before and after endoscopic ablation by argon plasma coagulation. *Scand J Gastroenterol* 2005;40:259–263.
- 14 Bright T, Watson D, Tam W, et al: Randomized trial of argon plasma coagulation versus endoscopic surveillance for Barrett's esophagus after antireflux surgery: late results. *Ann Surg* 2007;246:1016–1020.
- 15 Rodriguez SA, Adler DG, Chand B, et al: Mucosal ablation devices. *Gastrointest Endosc* 2008;68:1031–1042.
- 16 Martin WR, Jakobs R, Spiethoff A, et al: Treatment of Barrett's esophagus with argon plasma coagulation with acid suppression – a prospective study. *Z Gastroenterol* 1999;37:779–784.
- 17 Byrne J, Armstrong G, Atwood S: Restoration of the normal squamous lining in Barrett's esophagus by argon beam plasma coagulation. *Am J Gastroenterol* 1998;93: 1810–1815.
- 18 Van Laethem J, Cremer M, Peny MO, et al: Eradication of Barrett's mucosa with argon plasma coagulation and acid suppression: immediate and mid term results. *Gut* 1998;43:747–751.
- 19 Schulz H, Miehle S, Antos D, et al: Ablation of Barrett's epithelium by endoscopic argon plasma coagulation in combination with high-dose omeprazole. *Gastrointest Endosc* 2000;51:659–663.
- 20 Pereira-Lima JC, Hornos AP, Lopes CV, et al: Tratamento Endoscópico do Esôfago de Barrett por Ablação (Plasma de Argônio); in Parada AA et al (eds): *Esôfago de Barrett*, ed 1. Ribeirão Preto, Tecmed Editora, 2006, pp 202–211.
- 21 Maas S, Martin WR, Spiethoff A, et al: Barrett's esophagus with severe dysplasia in argon beam therapy. *Z Gastroenterol* 1998;36:301–306.
- 22 Van Laethem JL, Jagodzinski R, Peny MO, et al: Argon plasma coagulation in the treatment of Barrett's high-grade dysplasia and in situ adenocarcinoma. *Endoscopy* 2001;33:257–261.
- 23 Overholt B, Wang K, Burdick S, et al: Five-year efficacy and safety of photodynamic therapy with Photofrin in Barrett's high-grade dysplasia. *Gastrointest Endosc* 2007;66:460–468.
- 24 Kely CJ, Ackroyd R, Brown NJ, et al: Endoscopic ablation of Barrett's esophagus: a randomized-controlled trial of photodynamic therapy vs. argon plasma coagulation. *Aliment Pharmacol Ther* 2004; 20:1289–1296.
- 25 Ganz RA, Overholt BF, Sharma VK, et al: Circumferential ablation of Barrett's esophagus that contains high-grade dysplasia: a US multicenter registry. *Gastrointest Endosc* 2008;68:35–40.
- 26 Pech O, Behrens A, May A, et al: Long-term results and risk factor analysis for recurrence after curative endoscopic therapy in 349 patients with high-grade intraepithelial neoplasia and mucosal adenocarcinoma in Barrett's esophagus. *Gut* 2008;57:1200–1206.
- 27 Lopes CV, Hela M, Pesenti C, et al: Circumferential endoscopic resection of Barrett's esophagus with high-grade dysplasia or early adenocarcinoma. *Surg Endosc* 2007;21:820–824.
- 28 Soehendra N, Seewald S, Grath S, et al: Use of modified multiband ligator facilitates circumferential endoscopic mucosal resection in Barrett's esophagus. *Gastrointest Endosc* 2006;63:847–852.
- 29 Larghi A, Lightgale CJ, Ross AS, et al: Long-term follow-up of complete Barrett's eradication endoscopic mucosal resection for the treatment of high-grade dysplasia and intramucosal carcinoma. *Endoscopy* 2007;39:1086–1091.
- 30 Yoshinaga S, Gotoda T, Kusano C, et al: Clinical impact of endoscopic submucosal dissection for superficial adenocarcinoma located at the esophagogastric junction. *Gastrointest Endosc* 2008;67: 202–209.

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