Hot avulsion may be effective as salvage treatment for focal Barrett’s esophagus remaining after endoscopic therapy for dysplasia or early cancer: a preliminary study

Authors
Javier Aranda-Hernández, Yuto Shimamura, Andrea Grin, Yugo Iwaya, Maria Cirocco, Gabor Kandel, Gary May, Paul Kortan, Spiro Raftopoulos, Norman Marcon

Institution
Division of Gastroenterology, Department of Medicine, The Center of Advanced Therapeutic Endoscopy and Endoscopic Oncology, St. Michael’s Hospital, University of Toronto Faculty of Medicine, Toronto, Ontario, Canada

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Background and study aim
Both endoscopic mucosal resection (EMR) and radiofrequency ablation (RFA) are used to treat Barrett’s esophagus (BE) complicated by dysplasia and intramucosal cancer. However, focal areas of BE can remain after otherwise successful application of these techniques. We report the results of hot avulsion using a hot biopsy forceps to resect these residual focal areas.

Patients and methods
This was a retrospective study from a prospective database in a tertiary reference center from August 2013 to May 2015. All included patients had undergone hot avulsion for eradication of residual focal areas of BE that were ≤ 1 cm and not suspicious for dysplasia, following at least one previous endoscopic treatment for dysplasia or intramucosal cancer.

Results
35 patients harboring 124 residual areas of 1–7 mm were treated with hot avulsion. After a mean follow-up of 17.4 months, all patients achieved complete eradication of residual focal areas of BE. One of the patients required a second hot avulsion treatment. Hot avulsion provided samples in all cases but limited the assessment of dysplasia (cautery artifact) in 20.2% of them. The only complication was bleeding in two patients, which was easily stopped by soft coagulation.

Conclusions
Hot avulsion appears to be effective and safe in removing focal BE ≤ 1 cm at its greatest length remaining after endoscopic treatment for dysplasia or early cancer. Further studies are required before this technique can be considered the standard of care.

Introduction
Endoscopic treatment for Barrett’s esophagus (BE)-related neoplasia is a well-established, safe, and effective treatment. Endoscopic resection of all visible lesions followed by radiofrequency ablation (RFA) of the remaining BE (cylindrical) mucosa, to prevent the development of metachronous lesions is now considered the standard of care. Previous studies have shown that about one fourth to one fifth of the patients treated endoscopically are at risk of recurrent neoplasia if BE remains [1, 2].

To minimize this risk, most major society guidelines now recommend complete eradication of the BE mucosa [3–5]. However, this can be technically difficult, as persistent foci of BE can remain after otherwise successful endoscopic treatment. Resection, repeat ablation, application of snare-tip coagulation, and argon plasma coagulation have been proposed. There are no reports on using hot avulsion to eradicate BE mucosa. Since 2010, we have been eradicating small persistent BE areas ≤ 1 cm with hot avulsion using hot biopsy forceps, extrapolating from the success of this technique in removing nonlifting residual
colonic polyp tissue after failure by snare excision [6–8]. The aim of this study was to report the results of hot avulsion using a hot biopsy forceps to resect residual focal areas of BE.

Patients and methods

Study population

A retrospective analysis was performed using a prospectively maintained BE database of all cases involving endoscopic therapy at St. Michael’s Hospital, University of Toronto (Toronto, Canada) between August 2013 and May 2015. This prospective database was designed to collect all aspects of endoscopic procedures relating to endoscopic treatment of BE. The study period started in August 2013 because this was the first month that we started registering hot avulsion as a treatment for BE following approval of the prospective database by the St. Michael’s Hospital research ethics committee. Hot avulsion had been used before the prospective database was started, but the results were not prospectively recorded. All patients signed a consent form to be included in the prospective database, as well as before every endoscopic diagnostic and therapeutic procedure.

Inclusion criteria were: 1) at least one previous endoscopic treatment for BE-related dysplasia or early neoplasia; 2) presence of islands or tongues of persistent BE mucosa ≤1 cm not suspicious for dysplasia at follow-up endoscopy; 3) hot avulsion applied as the single treatment of these areas. The presence of dysplasia was suspected when vascular or mucosal irregularities were identified using white-light endoscopy and narrow-band imaging (NBI) with high resolution endoscopy as magnification was not available in all cases. Hot avulsion was accepted in combination with endoscopic mucosal resection (EMR) if EMR was at the gastroesophageal junction for a columnar area not meeting hot avulsion criteria and the distance from the EMR edge to the BE remnant was greater than 2 cm (estimated by the size of the snare: 15 × 25 mm).

The size of the BE remnant was estimated using the height of the closed cups of a biopsy forceps (2.2–2.8 mm), which is analogous to the Paris classification recommendations. In all endoscopies, the mucosa was examined with both white-light endoscopy and NBI using high resolution endoscopes. Hot avulsion was never used as the primary treatment during the first endoscopic treatment for eradicating BE dysplasia/cancer – it was used solely as salvage treatment and only after the previous therapeutic endoscopy according to guidelines. After the first endoscopic treatment, all patients were placed on oral double-dose proton pump inhibitor therapy.

The surveillance protocols included: 1) follow-up every 2–3 months at least for the first year after treating intramucosal cancer (IMC) or high grade dysplasia (HGD), and until two endoscopies had been negative for dysplasia; follow-up endoscopies were then done every 6 months in the second year, and yearly thereafter; 2) follow-up every 6 months after treatment for low grade dysplasia and yearly after two negative endoscopies had been achieved; 3) follow-up endoscopy after RFA treatment every 2–3 months until the entire segment of Barrett’s had been eradicated; 4) in a few cases, these schedules may have been slightly different depending on patient context and circumstances (admissions for other reasons, travel, etc.). At follow-up endoscopy after hot avulsion, a search was made for persisting intestinal metaplasia with both white-light endoscopy and NBI with high resolution endoscopes. In all cases, the same endoscopist who performed the treatment endoscopies also did the follow-up examinations.

Primary outcomes were the success rate of eradication of BE residual mucosa and the histopathological diagnostic yield of the hot avulsion procedure, defined as the proportion of patients for whom the pathologist could provide a diagnosis and interpretation of dysplasia based on the specimen provided. Successful eradication of BE mucosa was defined as the absence of macroscopic and/or microscopic intestinal metaplasia at the hot avulsion site (our records included distance from the mouth and clock position of the avulsed islands, and images of the vast majority of procedures). A secondary outcome was the procedural adverse events, such as immediate and delayed bleeding or perforation.
Hot avulsion technique

The hot avulsion technique consisted of “lifting” the columnar mucosa by injecting saline with methylene blue into the submucosa and then grasping the lesion with the hot biopsy forceps (▶Fig. 1, ▶Fig. 2, ▶Video 1). This was immediately followed by application of short bursts of current (0.5 to 1 second) as the mucosa was gently pulled off, either with the forceps or with the shaft of the scope, until that “bite” had been stripped off. If required, side-by-side samples were taken to complete the avulsion of the lesion. The procedure was performed using standard blended electrocautery (Endocut 3, 150 W, ICC 200; ERBE Elektromedizin, Tübingen, Germany). We utilized serrated and nonspiked hot biopsy forceps (Radial Jaw 4 – Boston Scientific Co., Marlborough, Massachusetts, USA; and Captura – Wilson-Cook Medical, Winston-Salem, North Carolina, USA). Specimens were taken one by one to minimize cautery artifact.

At follow-up endoscopy, biopsies were taken of all previous hot avulsion-treated areas, as well as routine random biopsies from the gastroesophageal junction and/or re-epithelialized segments, according to the Seattle protocol. High resolution gastroscopes (GIF H/HQ 190; Olympus America, Center Valley, Pennsylvania, USA) including NBI mode were used in all cases.

Results

▶Table 1 summarizes patient baseline characteristics. A total of 35 patients underwent 38 hot avulsion procedures, with a total of 124 residual BE areas treated during the study period with a mean follow-up of 17.4 months. The median age was 65 years (range 47 – 87 years) and 85.7 % (30/35) were male. The mean of initial Barrett’s dimensions were C segment 3.1 cm and M segment 5.6 cm. Previous treatments were EMR in 91.4% (32/35) and RFA alone in 8.6% (3/35). Of the patients with initial EMR, 65.6 % (21/32) had subsequent therapies (RFA, photodynamic therapy or thermal ablation).

The most advanced neoplasia was IMC in 48.6 % (17/35), HGD in 37.1 % (13/35), and low grade dysplasia in 14.3% (5/35). Savary bougie dilations for previous procedure-related stricture immediately preceded hot avulsion in 31.4% (11/35). Previous treatments were EMR in 91.4 % (32/35) and RFA alone in 8.6% (3/35). Of the patients with initial EMR, 65.6 % (21/32) had subsequent therapies (RFA, photodynamic therapy or thermal ablation).

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▶Table 2 lists the results. All patients meeting the inclusion criteria had at least one follow-up endoscopy after hot avulsion. The mean number of areas avulsed was 3.3 per patient, and the size of the avulsed tissue ranged from 1 mm to 7mm. Cautery limited the histological assessment in 20.2% (25/124) of the avulsed tissues. Histological examination of avulsed tissue revealed IMC in one patient, HGD in one patient, and indefinite dysplasia (due to cautery) in six patients.

The patient with IMC underwent diagnostic and therapeutic EMR of the hot avulsion area 8 weeks after the initial hot avulsion procedure. Histology did not reveal any neoplastic lesion or remnant intestinal metaplasia, and follow-up endoscopies for up to 18 months later showed persisting absence of dysplasia and neoplasia. The patient with HGD had no residual lesion or intestinal metaplasia at follow-up endoscopy 10 weeks after hot avulsion, and is currently being followed at another institution.
Hot avulsion specimens also revealed intestinal metaplasia in 63.2% (24/38) and gastric metaplasia in 36.8% (14/38). Buried glands were found in 34.3% of patients (12/35 [13/38 samples]); 10 with intestinal metaplasia and 2 with gastric metaplasia.

First follow-up endoscopy after hot avulsion was at a mean of 6.5 months. Endoscopic resolution of the BE was achieved in 91.4% (32/35) and partially achieved (fewer or smaller islands) in 8.6% (3/35). Of these partially achieved patients, one patient had intestinal metaplasia and underwent repeat hot avulsion, which showed complete eradication at follow-up 5 months after this second hot avulsion treatment, and two patients had no intestinal metaplasia and were just followed with surveillance biopsies. Thus, intestinal metaplasia was eradicated in 95.8% (23/24) after an initial treatment and in 100% (24/24) after a second treatment. Of the 35 patients, 30 (85.7%) had a second follow-up during the study period at a mean of 14.8 months with no recurrence endoscopically or histologically.

We encountered two patients with minor intraprocedural bleeding, which was easily controlled with the hot biopsy forceps using soft coagulation. No other adverse event was encountered that was related to the hot avulsion procedure.

Discussion

In patients with BE-related dysplasia or neoplasia, eradication of the entire segment of metaplastic columnar mucosa is recommended given the known risk of metachronous dysplasia [1–5]. Therefore, the standard endoscopic therapy is endoscopic resection of all visible lesions followed by ablation of the remaining BE. Complete eradication of intestinal metaplasia after endoscopic treatment has been reported in up to 95% in several series [1–5, 9–11]. In our cohort, we achieved complete eradication of intestinal metaplasia in all patients by using hot avulsion, pointing toward the high efficacy of this technique. Limiting hot avulsion to small residual areas (<1 cm in largest diameter) with no obvious endoscopic findings suspicious for deep invasion may have contributed to this high eradication rate with no major adverse event.

In standard algorithms [3–5], these patients would have been treated with either EMR or other ablative therapy such as RFA, argon plasma coagulation or cryotherapy. These treatments are associated with higher costs and/or risk of adverse outcomes. The major benefits of the hot avulsion technique are its ease of use, low cost, and wide availability. Another advantage is that, hot avulsion could be conducted in all cases, even for patients with scarring or strictureting, problems that can be challenging with other therapies. Moreover, hot avulsion not only successfully treated residual BE areas but also yielded a histological diagnosis in most cases.

In the current study, specimens retrieved with hot avulsion revealed IMC in one patient and HGD in another patient, which prompted further aggressive observation with additional intervention. The endoscopic images of these lesions prior to hot avulsion are shown in Fig. 3. These lesions were observed carefully with white light and NBI imaging; however, we were unable to predict the histological results prior to avulsion. This shows the difficulty of predicting advanced HGD and IMC in this scenario, and the importance of histological evaluation. At first follow-up in less than 12 weeks in both patients, no dysplastic lesions were seen. The site of hot avulsion that revealed IMC was re-treated with EMR and the histology confirmed the absence of dysplasia. This observation suggests the possibility that hot avulsion may be an appropriate technique to treat...
small areas of dysplasia or to assist EMR resections that may be difficult owing to anatomy or scarring, as has been described for difficult colonic polyps [6–8]. However, further study is required before this can be used as standard practice.

Buried glands – columnar metaplasia seen on biopsy underneath what is visualized as neosquamous epithelium endoscopically – have been most frequently found after photodynamic therapy but have also been reported after other endoscopic treatments, and even before treatment. Buried glands were seen in 34.3% of our cases, a far higher number than in other series of EMR/RFA [12–14]. For example, in the Netherlands trials, buried glands were reported in 0.08% of patients [13], but overall in 0.9% according to a review [12] written before the outcome of the Netherlands trials was reported. The presence of neoplasia in buried glands is possible but uncommon [12]. The 12 patients in whom buried glands were identified in the current study had undergone previous EMR (n = 1), RFA (n = 2), EMR and RFA (n = 5), EMR and photodynamic therapy (n = 3), and EMR with thermal ablation (n = 1). The three patients who had undergone previous photodynamic therapy inflate the buried gland prevalence in this study, but even without these three patients the proportion of patients with buried glands is high. This high prevalence may reflect the increased depth of the samples obtained by hot avulsion, as suggested in a recent review [14], or buried glands may be more common in small residual islands. Another possibility is that what we label as buried glands may be pseudo-buried Barrett’s mucosa [15]. Closer attention to orienting the biopsy specimen may have determined the prevalence of such pseudo-buried Barrett’s, but this was not included in our protocol.

Hot avulsion involves the use of a hot biopsy forceps, which has previously been reported as a cause of delayed perforation and bleeding. However, the current method of hot avulsion differs from the previous technique in three ways: 1) applying predominantly cutting electrocautery (Endocut mode with short burst of current) rather than a forced coagulation current; 2) injecting saline into the submucosal layer; and 3) using the mechanical traction away from its base to avulse the tissue. All these maneuvers protect the esophageal wall from transmural injury. In our series, only two minor bleedings occurred (5.7%), which were easily treated with the same device; no other significant complications were encountered.

Other authors have described using soft coagulation for hot avulsion. This could have been used as an alternative technique in our patients [6]. Cold biopsy forceps with or without a follow-up ablative coagulation technique such as argon may be another option to salvage foci of residual intestinal metaplasia. However, hot avulsion facilitates larger and deeper specimens as there is less slippage of the cups during biopsy, plus it provides cautery to increase the likelihood that the offending tissue has been successfully obliterated. On the other hand, at least conceptually, cold biopsy might be safer than hot avulsion. Further studies comparing these two techniques and including histological parameters would be of interest.

One strength of our study is that none of the patients were lost to follow-up. We believe that this is due chiefly to our center being the only site where Barrett’s dysplasia is treated endoscopically in our catchment area, but scheduling patients for follow-up endoscopy immediately after hot avulsion, and phone reminders about appointments may have also contributed.

This study has a number of limitations. First, this was not a randomized study and the sample size was small. Second, although the study used a prospective database, the primary purpose of the database was not the assessment of hot avulsion and therefore variables such as the number of avulsions required for island eradication, and the time required for hot avulsion were not recorded. Third, the follow-up period in our study was shorter than other reported series for the assessment of complete eradication of intestinal metaplasia, so longer follow-up observation is needed to convincingly demonstrate the efficacy and safety of hot avulsion in the long term [10]. Fourth, no comparisons were made with the current standard treatment approaches. These limitations need to be addressed by more rigorous studies before hot avulsion can become an established tool in the armamentarium of endoscopic treatment for BE.
Conclusions

Hot avulsion is a promising technique to safely diagnose and treat persisting residual focal BE (< 1 cm) after initial endoscopic treatment. Larger studies, focusing on this technique in comparison with other methodologies and with longer follow-up, are required to determine its ultimate role.

Competing interests

None.

References