

# A retrospective comparative study of argon plasma versus polypectome snare tip coagulation: effect on recurrence rate after resection of large laterally spreading type lesions

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## Abstract

**Background** Endoscopic mucosal resection (EMR) is an established technique for treating large laterally spreading type (LST) lesions  $\geq 20$  mm. The aim of our study was to compare the use of argon plasma (APC) versus snare-tip coagulation on the recurrence rate of large LST lesions.

**Methods** All patients with large LST lesions resected by EMR between January 2006 and December 2014 were enrolled. After piecemeal resection, patients underwent either APC or snare-tip coagulation of the rim of the resection area and any residual adenomatous tissue. Follow up included colonoscopy and biopsies. Medical records, including characteristics of patients and polyps, complications and recurrence were retrieved and collected.

**Results** One hundred one patients were included in the final analysis. They were divided into the APC group (n=50) and the snare-tip coagulation group (n=51). The 2 groups were similar concerning patients' characteristics, size of polyps and histology. Post-polypectomy coagulation syndrome was observed in 8 patients (7.9%) (APC group: n=5 and snare tip group: n=3). EMR-related bleeding occurred in 9 patients (8.9%) (APC group: n=4 and snare tip group: n=5). Total recurrence rate was 14.85% (16% and 13.7% in APC and snare-tip groups, respectively, P=0.34).

**Conclusion** The effectiveness of snare-tip coagulation is comparable with that of APC with respect to recurrence rate after resection of large LST lesions. It thus represents a cost-effective alternative to APC.

**Keywords** Endoscopic mucosal resection, recurrence, argon plasma, snare tip coagulation

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## Introduction

The extensive adoption of colorectal cancer (CRC) screening, more rigorous colonoscopy techniques and advances

in endoscopic imaging have resulted in a greater awareness of complex polyps (level III-IV) [1]. Whereas surgery was once considered necessary for many large laterally spreading type (LST) lesions [2], the majority can now be removed endoscopically. Endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD), after adequate submucosal lifting of the lesion, are established techniques for treating large LST lesions ( $\geq 20$  mm). When performed by experts, EMR is highly effective and safe and can be completed in an outpatient or day-stay setting [3]. Nevertheless endoscopic resection of large LST lesions ( $\geq 20$  mm) remains challenging, because of morbidity, the possibility of incomplete endoscopic resection, the high possibility of a coexisting malignancy and the long-term recurrence rate [4-10]. Specifically, post-resection aggressive surveillance is justified because it has been shown that residual adenomatous tissue has a high growth rate and contributes to a higher subsequent incidence of CRC [11-13].

In addition, apart from the size, the recurrence rate after piecemeal EMR of large LST lesions is influenced by the use

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Conflict of Interest: None

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of argon plasma coagulation (APC) for cauterization of the resection margins of sessile polyps [12,14,15]. However, APC is expensive and not available in every endoscopic unit. In contrast, the polypectome snare is a cheap device available in conventional endoscopic units and can be used with safety by endoscopists; however, there are few reports in the literature regarding the use of the snare tip technique for cauterization of resection margins of large LST lesions.

The present retrospective study aimed to compare APC with snare tip coagulation of resection margins and residual adenomatous tissue after resection of large LST lesions, in terms of adenoma recurrence, post-procedure complications and long-term outcomes, in order to determine the best surveillance colonoscopy interval following EMR of large LST lesions.

## Patients and methods

A retrospective study was conducted in an academic tertiary referral endoscopic center where a total of >2000 colonoscopies and >800 polypectomies are performed yearly. The target population was consecutive patients with advanced mucosal neoplasia, i.e., large LST lesions (diameter  $\geq 20$  mm), who visited or were referred to our unit between January 2006 and December 2014. Data were collected prospectively and described in each endoscopic procedure report. They comprised a detailed description of the polyp by the endoscopist (Paris classification), size, the endoscopist's estimation whether a complete excision of the lesion was achieved, amount of injected submucosal solution, presence of a non-lifting sign [16], early and late complications, histology of the lesion, recurrence and success in resecting the residual/recurrent adenoma. The study protocol was approved by the Ethics Committee of our hospital and all study procedures were conducted in accordance with the Declaration of Helsinki.

The inclusion criteria were large LST lesions ( $\geq 20$  mm in diameter), of benign appearance and resectable (Fig. 1),



**Figure 1** Endoscopic view of a large rectal sessile polyp

resected by piecemeal EMR. Exclusion criteria were the following: firm consistency, ulceration, converging folds (2 or more) towards the lesion predicting submucosal invasion by cancer cells even with negative biopsies; appearance of expansion of normal tissue immediately surrounding the lesion indicating the presence of cancer creeping into the surrounding submucosal space; the presence of a “non-lifting sign” after submucosal injection of solution [16]; biopsies raising suspicion of invasive cancer; incomplete polyp resection (endoscopist's estimation); patients or relatives unwilling to provide written informed consent; and lack of a follow-up colonoscopy.

Patients taking antiplatelet medication were instructed to consult with their treating cardiologist. Antiplatelet agents (clopidogrel, prasugrel, aspirin) were discontinued 7 days prior to the procedure and were replaced by low-molecular weight heparin while the resection of the large LST lesions was performed. Specifically, oral anticoagulants were replaced by subcutaneous low-molecular weight heparin 0.6 mg/day until normalization of the international normalized ratio (INR). After resection of the large LST lesions, the previous anticoagulation medication was restarted in combination with low-molecular weight heparin until achievement of the pre-resection INR [17].

All procedures were performed by a single experienced endoscopist (PK), using blended current (coag 30 W and cut 30 W) for lesions of the right colon and pure coagulation (30 W) for lesions of the left colon (ESGEg).

The EMR technique used in the present study has been previously described in detail [18]. In brief, the diameter of each large LST lesion was estimated at the time of resection by reference to an open polypectomy snare (diameter 20 mm) placed adjacent to the polyp. After the margins of the polyp had been confirmed, marking dots were placed by APC at a distance of 5 mm from the polyp margins. A 10-mL syringe with a 23-G disposable variceal injection needle, containing hydroxyl-ethyl starch (Voluven®) plus adrenaline in solution 1:10000, was used to perform submucosal injections at several sites all around the lesion, starting at the proximal portion and moving into the lesion until the polyp was bulging and blanched.

Once the polyp was lifted sufficiently from the *muscularis* layer, a 20 mm diameter spiral barbed snare (SD-230V-20, Olympus, Tokyo, Japan) was used for polyp resection. We prefer this type of snare, which is ideal for resection of large LST lesions after submucosal elevation because it is made from integrated spiral rings and spikes to grip mucosa and prevent slippage, and from braided wire for an improved coagulation effect. After the lesion had been fully resected, the resection area was carefully inspected to check for residual neoplastic tissue. The resection margins were then cauterized circumferentially as an adjuvant method to reduce local recurrence and any area suspicious for residual adenomatous tissue was ablated by APC (at a power of 50 W or 70 W in the right or left colon, respectively, and with gas flow at 1.5 L/min) or by snare tip with a 20 W soft coagulation current. The tip of the snare was advanced approximately

5 mm beyond the catheter tip and was targeted precisely to the resection's margin and residual adenomatous tissue; once the snare tip made contact with the adenomatous tissue the current was activated, creating the bubbling and blanching effect of cautery (Fig. 2). As the snare tip is relatively sharp, hard pressure on the colon wall was avoided. The site of polyp resection was marked by submucosal injection of a sterile carbon particle suspension into the adjacent normal mucosa. All resected specimens were retrieved with a Roth Net (US Endoscopy, Mentor, OH, USA) and pinned to a cork before fixation in formalin for histology assessment by a specialist gastrointestinal pathologist.

### Complications

Post-polypectomy coagulation syndrome was defined as transmural thermal injury with resultant serosal inflammation characterized by localized abdominal pain, leukocytosis and occasionally fever. Post-polypectomy bleeding was defined as intraprocedural, immediate (occurring in the first 24 h following the procedure), or delayed (passage of fresh blood per rectum within the following 2 weeks).

Macroperforation was readily recognized endoscopically. Microperforation was detected by the presence of free air on plain abdominal film and/or abdominal computed tomography scan with associated abdominal pain, leukocytosis and elevated C-reactive protein.

### Histopathology

Dysplasia was classified as low-, moderate- or high-grade, according to the modified Vienna classification. Infiltrating carcinoma was defined by the presence of tumor cells beyond the *muscularis* mucosa and a precise measurement of submucosal infiltration was made.



**Figure 2** Complete resection of a sessile polyp with cauterization of resection margins and any residual adenomatous tissue using the snare tip

### Outcome

The primary endpoint of the study was to compare the effectiveness and safety of APC versus snare tip coagulation in the eradication of residual adenomatous tissue after polyp resection, in terms of long-term recurrence.

### Follow up

On discharge from the hospital, patients and their relatives were instructed to contact the endoscopic team in case of any adverse events. To monitor complications, the patients were contacted by telephone weekly for the first 3 weeks and were advised to undergo initial surveillance colonoscopy at 3, 6, 12 and 24 months. If no residual lesion was detected on inspection with standard white light, narrow band imaging (NBI) was used and biopsies from the center of the resection area were taken. If there was no recurrence by the 2-year follow up, the patients were considered cured and no further colonoscopy was scheduled. If recurrent adenomatous tissue was detected during follow up, it was resected with the mini-snare or ablated by APC. Specifically, the interval of surveillance colonoscopy was arranged according to previous guidelines and the recommendations of our referral center [18,19].

### Statistical analysis

Data were analyzed using the statistical program SPSS (version 21.0, Chicago, IL, USA). Continuous variables were compared using the non-parametric Mann-Whitney *U* test, while qualitative data were examined using the chi-square or Fisher's exact test, as appropriate. Statistical significance was set at  $P \leq 0.05$ .

### Results

A total of 140 patients with large LST lesions were treated between January 2006 and December 2014. Thirty-nine patients were excluded from the study: 3 underwent surgery because histological examination of resected polyps showed submucosal invasion by cancer cells; 25 patients were lost to follow up; and 11 patients had incomplete polyp resection (i.e., at the end of the procedure the endoscopist estimated that full resection could not be achieved even with the use of an adjunctive thermal method). Thus, 101 patients were included in the final analysis, 50 in the APC and 51 in the snare tip coagulation group.

There were no differences between the 2 studied groups in demographic data (Table 1) or in the histopathological analysis of the resected polyps (Table 2). Nine patients (8.9%) (4 in the APC and 5 in the snare tip group) presented post-resection bleeding (Fig. 3). All patients were successfully treated by injection of epinephrine solution (1:10000) plus the application of coagulation by Coagrasper or hemoclipping.

Five patients in APC group (10%) and 3 in the snare tip group (5.9%) developed post-polypectomy coagulation syndrome (Fig 3); all these patients were treated with hospitalization, bowel rest, crystalloid administration and antibiotics (ciprofloxacin plus metronidazole) for 5-7 days [20].

During the 3-month post-resection period, recurrence was observed in 9 patients (8.9%): 5 in the APC group (10%) and 4 in the snare tip group (7.8%) (Fig 3). The difference between the groups was non-significant ( $P=0.34$ ). At 6 months, 3 patients in the APC group and 2 in the snare tip group presented recurrence (Fig 3). At 1-year follow up, only 1 patient in snare-tip group presented recurrence, while no recurrence was observed at 2-year follow up (Fig 3). The overall recurrence rate was 14.85% (15 patients).

**Table 1** Patients' characteristics

Characteristics	APC group	Snare tip group	P
	N=50	N=51	
Age (years) (mean±SD)	64.27±12.41	64.11±21	0.934
Sex (M/F)	30/20	28/23	0.604
Associated comorbid diseases	32	28	0.503
Aspirin	6	8	0.721
Anticoagulants	3	2	0.429
Location of polyps			0.366
Rectum	34	32	
Sigmoid	7	10	
Descending	0	2	
Transverse	0	1	
Ascending	3	1	
Cecum	6	5	

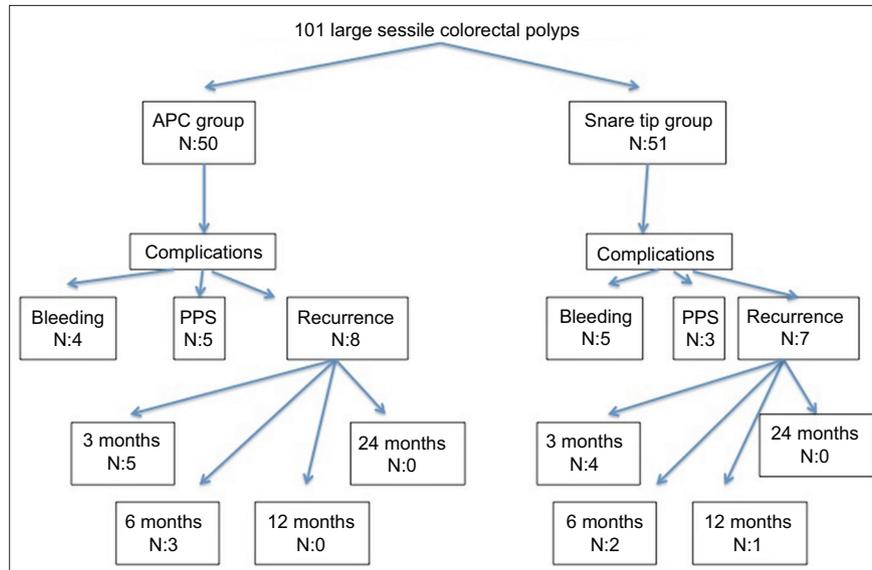
**Table 2** Results of the endoscopic resection of large colorectal sessile polyps

Results	APC group	Snare tip group	P
	N=50	N=51	
Size (cm) (mean±SD)	4.27±1.25	3.86±1.26	0.07
Amount of injected solution (mL) (mean±SD)	17.31±6.32	16.41±5.94	0.687
Complications	10	9	0.408
Bleeding	4	5	0.643
Perforation	3	4	0.527
Post-polypectomy syndrome	5	3	0.344
Histology			0.702
Villus	18	15	
Tubulovillous	20	26	
Tubular	10	9	
<i>In situ</i> carcinoma	2	1	

## Discussion

Achieving clear resection margins without neoplasm tissue in the specimen margins is the most desirable goal of curative procedures. In the present series, the use of APC and snare-tip coagulation techniques achieved low short-term recurrence after resection of large LST lesions (10% and 7.8%, respectively), while no difference in recurrence rate was observed between the APC and snare-tip coagulation groups during the 2-year follow up (Fig. 3). Therefore, the polypectome snare, a cheap device used widely and with safety by endoscopists, can be introduced as a cost-effective alternative to APC; the latter is the traditional standard ablation technique, but is expensive and not widely available. In this regard, an Australian group with remarkable experience in the endoscopic treatment of large LST lesions showed recently that the snare tip soft coagulation technique is also a simple and efficient first-line treatment for achieving hemostasis of intraprocedural bleeding during wide-field EMR of large LST lesions [20]. Although there are studies that have shown the beneficial effect of APC use for ablation of residual adenoma tissue after resection of large LST lesions, a recent meta-analysis did not demonstrate a relative benefit [12,21,22]. The observed low rate of recurrence in both groups of our series is related to our policy to include 2-3 mm margins of normal tissue around the polyp during the excision and to the use of NBI, which distinguishes the presence of residual adenomatous tissue from normal or cauterized tissue.

Recently, in 2014, the technique called avulsion demonstrated promising results in clearing remnant neoplastic tissue from the polypectomy bed and margins. In this technique, a biopsy forceps is used to grasp and to avulse small islands of neoplastic mucosa off the colon wall. A high-frequency cutting current is used, generated by a microprocessor-controlled electro-surgical unit [23]. The hot avulsion technique has been shown to be superior to APC [24], demonstrating a dramatic reduction in recurrence rates after piecemeal EMR from 59.3% to 10.3%, without



**Figure 3** Flow chart showing patients' recurrence during the 24-month follow up  
PPS, post-polypectomy coagulation syndrome

significantly affecting the procedure's safety profile. However, few studies reporting data on hot avulsion have been published and most of them were retrospective [24]; furthermore, there are no reported data from a head-to-head comparison between the hot avulsion technique and snare tip cauterization.

It is important to note that only 1 patient (snare-tip group) presented recurrence at 1-year follow up. Inspection of the post-resection scar with NBI during the early follow up (3 and 6 months) helped evaluate the scar for the presence of adenoma recurrence. The post-resection scar has a characteristic appearance as a pale area with disruption of the usual vascular pattern, often with convergence of surrounding colonic folds. When recurrent adenomatous tissue was identified, we avoided submucosal injection because the recurrent adenoma is prevented from elevating by underlying submucosal fibrosis from the initial resection. It is well known that, if injection is performed, the surrounding normal mucosa is elevated, resulting in a "canyon effect" that makes resection very difficult or even impossible. We prefer the use of high power APC (100 W, flow 2 L/min) in short sequential bursts of forced coagulation until there is no visible adenomatous tissue. It is known that tissue injury during application of a thermal technique is divided into 4 zones (desiccation, coagulation, devitalization, and hyperthermia); when the tissue is coagulated by APC, it becomes desiccated and loses its electrical conductivity, leading the plasma arch to jump to adjacent non-desiccated tissue. This mode of APC action decreases the depth of penetration and the tissue destruction [25]. Therefore, APC is ideal for ablation of small residual adenomatous tissue after resection of large LST lesions, especially in the thin-walled right colon [13,26]. In contrast, in snare tip coagulation, which uses monopolar current, injury may be extended to all 4 zones, leading to post-polypectomy syndrome or perforation. Therefore, because the snare tip is relatively sharp, hard pressure on the colon must be avoided, especially in the cecum and ascending colon.

In our study, no difference in the incidence of post-polypectomy syndrome or perforation was observed between the 2 groups. We believe that this finding is related to the adequate submucosal cushion before polyp resection, which protected against transmural injury, and to the endoscopist's experience. Studies performed in porcine models have shown that a submucosal injection of normal saline solution prevents *muscularis propria* damage after thermal injury to mucosal lesions [27].

Generally, the recommended interval for sufficient surveillance colonoscopy is based on the risk of metachronous neoplasms, as predicted by the clinical and histological findings of the index colonoscopy. However, for large LST lesions, the surveillance colonoscopy interval is decided upon according to the risk of tumor remnants or recurrence. The local recurrence rate after EMR has been reported to range from 5-50% [19,28]. This variation is explained by the wide variation in polyp size, polyp location and length of follow up [5,14,19,29,30]. Specifically, the risk of neoplasm remnants or recurrence is strongly related to technical factors, such as *en bloc* resection, the therapeutic procedure and the endoscopist's experience [31-33].

The absence of recurrent adenoma at 2-year follow up in our study confirms most experts' opinion that a surveillance colonoscopy with NBI plus biopsies 3 and 6 months after initial EMR allows a clearer view of the polypectomy site for proper treatment, thus possibly making extended follow up for 1 and 2 years redundant and expensive [10,13].

The limitations of our study include its retrospective design. In addition, all EMRs, plus ablation of residual and recurrent adenomatous tissue by APC and snare tip coagulation, were performed by a single experienced endoscopist; thus, this study does not reflect everyday endoscopic activity. Moreover, the relatively small number of resected large LST lesions made it difficult to obtain statistically significant differences in the success of eradication of residual adenomatous tissue

## Summary Box

### What is already known:

- Whereas surgery was once considered necessary for large laterally spreading type (LST) lesions, the majority can now be removed endoscopically
- Endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) after adequate submucosal lifting of the lesion, are established techniques for treatment of large LST lesions ( $\geq 20$  mm)
- Nevertheless endoscopic resection of large LST lesions ( $\geq 20$  mm) remains challenging, because of morbidity, the possibility of incomplete endoscopic resection, the high possibility of a coexisting malignancy and the long-term recurrence rate

### What the new findings are:

- In the present series, the use of argon plasma coagulation (APC) and snare-tip coagulation techniques achieved low short-term recurrence after resection of large LST lesions (10% and 7.8%, respectively)
- No difference in recurrence rate was observed between the APC and snare-tip coagulation groups during the 2-year follow up
- The polypectome snare, a cheap device used widely and with safety by endoscopists, can be introduced as a cost-effective alternative to APC, the traditional standard ablation technique for eradication of residual adenomatous tissue after EMR of large LST lesions

by APC and snare tip coagulation and in the post-procedure complications. The strength of the study is the long-term follow up.

In conclusion, our study shows that the use of a very cheap and easily available polypectome snare device can effectively be introduced for eradication of residual adenomatous tissue after EMR of large LST lesions. However, large-scale prospective studies are warranted to confirm our results and to define a sufficient interval of surveillance colonoscopy.

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