Complementation by argon plasma coagulation after endoscopic piecemeal resection of large colorectal adenomas

Complementação por coagulação com plasma de argônio após a ressecção endoscópica completa pela técnica de fatiamento para grandes adenomas colorretais

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A B S T R A C T

Objective: To evaluate the efficacy of complement by argon plasma coagulation to reduce the rate of residual or recurrent tumor after complete endoscopic piecemeal resection of large sessile colorectal adenomas. **Methods**: Inclusion criteria: patients with large sessile colorectal adenomas (> 20mm), without morphological signs of deep infiltration, submitted to complete endoscopic piecemeal resection studied with chromoendoscopy and magnification of images. Patients were randomized into two groups: group 1 - no additional procedure, and group 2 - complementation by argon plasma coagulation. follow-up colonoscopy was performed at three, six and 12 months postoperatively. We evaluated the rate of local recurrence or residual malignancy. **Results**: The study included 21 patients, eleven in group 1 and ten in group 2. There were two local recurrences or residual tumors in each group, detected at three months follow-up. **Conclusion**: Complementation by argon plasma coagulation after apparent complete endoscopic piecemeal resection of large sessile colorectal adenomas does not seem to reduce the occurrence of residual adenomatous lesions or local recurrence.

Key words: Adenoma. Colorectal neoplasms. Endoscopy. Coagulation agents. Argon plasma coagulation.

INTRODUCTION

Large sessile colorectal adenomas (> 20 mm) are an important clinical problem due to an increased risk of malignant transformation[1]. These lesions are often endoscopically resected into several fragments, a technique called endoscopic piecemeal mucosal resection (EPMR). The disadvantage of this approach is the high rate of local recurrence or residual adenoma, present in up to 55% of cases[2-16]. Soon after the EPMR, particularly when small foci of residual lesions at the site of resection are identified, the additional application of argon plasma coagulation (APC) appears to reduce local recurrence[5,11]. However, after the considered complete EPMR, the actual value of the routine APC in terms of improvement of outcomes is yet to be demonstrated.

The aim of our study was to evaluate the effectiveness of complementation by argon plasma coagulation to reduce the rate of residual or recurrent tumor after complete endoscopic piecemeal resection of large sessile colorectal adenomas

METHODS

Patients aged over 18 years with sessile colorectal adenomas > 20mm were referred for endoscopic treatment. Those who agreed to participate signed an informed consent and were included in the investigation. Lesions with malignant aspect at morphology and chromoendoscopy with images magnification (firm, ulcerated, friable, pit pattern – Vi or Vn) or considered technically impossible to be completely resected due to size or difficult position, were excluded. The flowchart of the patients studied is shown in figure 1.

The study was approved by the Ethics in Research Committee and of the institution (ETIC No. 019 / 04).

Endoscopic technique

Endoscopic procedures were performed with the same colonoscope by two experienced operators. The following protocol was used in all cases: after the identification of the lesion and removal of mucus with water

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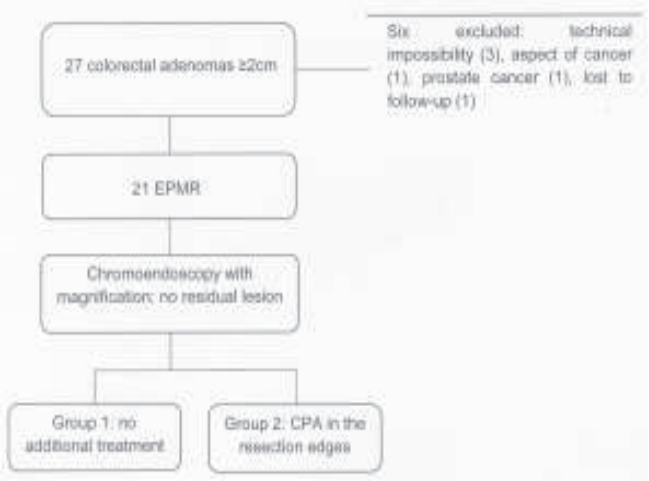

Figure 1 - *Flowchart of the patients studied.*

and washing with N-acetylcysteine application, a detailed examination was carried out with white light followed by instillation of 0.4% indigo carmine for chromoendoscopy and magnification of images. Tumors were classified according to their morphology (Classification of Paris)[17] and to the pit pattern (Kudo classification)[18]. Small coagulation marks were made around the lesion with two millimeters apart. Submucosal injection of 0.4% hydroxypropyl methylcellulose was performed to provide an adequate and prolonged elevation of the lesion[19]. Initially, we used hexagonal or oval, wide polypectomy loops, with application of a pure cut current (35 Watts), seizing large fragments, followed by resection of any small residual areas with miniloops until all adenomatous lesions were completely removed. We then repeated chromoendoscopy with magnification of images to check for residual lesions and, if present, had them totally removed.

After agreement by two expert examiners that the entire lesion had been removed, we removed four fragments of tissue from the specimen's resection margin, one from each quadrant. Patients were randomized into two groups: Group 1 - no additional procedure beyond mucosectomy; and Group 2 - application of APC on all surrounding edges, with coagulation effect of 60 Watts and output flow of 2.0L/min. Coagulation was considered sufficient when the tissue acquired a white color, proper of the coagulated area. The specimens' fragments were fixed in 10% formalin and embedded in paraffin. The slides were evaluated by an expert gastrointestinal pathologist and the results presented in accordance with the Vienna Classification[20]. If the histological examination revealed adenocarcinoma invading the submucosa, patients would be referred for surgical evaluation. Follow-up colonoscopies were performed at three, six and 12 months postoperatively. The site of resection was evaluated with chromoendoscopy with 0.4% indigo carmine and magnification of images, followed by biopsy of the scars. Should residual or recurrent lesions be detected, a new endoscopic treatment was performed.

RESULTS

During the study period, a total of 25 patients with 27 large sessile colorectal adenomas were referred to our center for endoscopic treatment. Five patients were excluded because of: overly large size of the lesion (n=3), aspect of deep infiltration (n=1) and association with prostate cancer infiltrating the rectum (n=1). Tables 1 and 2 describe the demographic characteristics and morphological classification of lesions in groups 1 and 2, respectively. There was no difference between the groups with regards to age, gender distribution, average size of tumors and their location.

Among the included patients, there were ten in group 1 (3 males and 7 females, total of 11 lesions), with a mean age of 67.1 years (range 54-77) and ten in group 2 (4 males and 6 females, total of ten lesions), with a mean age of 66.2 years (range 36-80). One patient had two lesions and therefore was randomized twice, both to Group 1. The results of the histological examination of the resection margins taken after the EPMR were all negative for adenomas. Two patients in group 2 had bleeding during the procedures, successfully treated by injection of adrenaline or hemostasis with metallic clips, without operation or blood transfusion. There were no other adverse events.

Residual/recurrent lesions

Two residual/recurrent lesions were detected in each group at three-months follow-up colonoscopy. In group 1 (without APC), the lesion occurred in a patient having a 30mm, 0-Is + 0-IIa lesion located in the descending colon and the other in an individual with a previous 40mm, 0-IIa lesion in the cecum. In group 2 (APC), the resected lesion was 60mm, 0-IIa, located in the rectum and the other was a 50mm, 0-Is +0-IIa adenoma in the ascending colon. In all cases, the number of resected fragments was > 4.

Among these four patients with residual/recurrent lesions, two in each group, three underwent new endoscopic resection with complementation with APC. They all remained tumor-free at six and 12 months follow-up. A lesion in group 1, located in the descending colon, with 30mm size, morphology 0-Is + 0-IIa, pits IIIL, of villous component, removed in four fragments, was referred for surgical resection because adenocarcinoma invading the submucosa was detected by histopathology.

DISCUSSION

The endoscopic management of large superficial sessile colorectal neoplasms recently evolved to *en bloc* resection by endoscopic submucosal dissection (ESD). The reported benefits of ESD over EPMR are the lower rate of residual or recurrent lesions and a better quality of the specimen for appropriate histological evaluation[21].

Table 1 - Demographic characteristics, endoscopic and histological aspects of residual / recurrent lesions, Group 1.

Patients Age/gender	Localization	Size (mm)	Morphology	Pits* Pattern	Number of Fragments	Histology	Residual lesion
72/F	Descending	30	0-Is+IIa	IIIL	4	VA/HGD	Yes
67/M	Cecum	20	0-Is	IV	3	TA/HGD	No
70/M	Rectum	20	0-Is	IIIL	2	TA/LGD	No
73/M	Rectum	40	0-Is	N/A	>5	TVA/HGD	No
77/F	Rectum	30	0-Is+IIa	IV	3	VA/LGD	No
54/F	Transverse	35	0-Is+IIa	N/A	4	TVA/HGD	No
75/F	Sigmoid	20	0-IIa	IIIL+IV	2	TVA/HGD	No
74/F	Cecum	40	0-IIa	IV	>5	VA/HGD	Yes
54/F	CecumAscending	3030	0-Is+IIa0-Is+IIa	IIILIIIL	>5>5	TVA/LGD TA/LGD	NoNo
68/F	Ascending	30	0-Is+IIa	IIIL	>5	TA/LGD	No

Source: Medical charts of patients of the Clinic Hospital, UFMG.
**Pattern of opening of the glands; VA: villous adenoma, HGD: dysplasia high-grade, TA: tubular adenoma, LGD: low-grade dysplasia, TVA: tubulovillous adenoma.*

Table 2 - Demographic characteristics, endoscopic and histological aspects of residual / recurrent lesions, Grupo 2.

Patients Age/gender	Localization	Size (mm)	Morphology	Pits* Pattern	Number of Fragments	Histology	Residual lesion
80/M	Rectum	25mm	0-Is	IIIs+IIIL	>5	TVA/HGD	No
61/F	Descending	20mm	0-IIa	II+IIIL	3	AS/LGD	No
78/F	Rectum	35mm	0-IIa	IV	>5	VA/HGD	No
36/F	Rectum	60mm	0-IIa	IIIL+IV	>5	TVA/HGD	Yes
68/F	Ascending	20mm	0-Is	IIIs	4	TVA/HGD	No
50/F	Rectum	40mm	0-Is+IIa	IV	4	AS/HGD	No
73/M	Cecum	50mm	0-Is+IIa	IV	4	TVA/LGD	No
75/M	Ascending	50mm	0-Is+IIa	IV	>5	AS/HGD	Yes
61/F	Rectum	25mm	0Is+IIa	IIIL+IV	3	VA/HGD	No
80/M	Descending	60mm	0-Is	IIIL+IV	>5	TVA/HGD	No

Source: Medical charts of patients of the Clinic Hospital, UFMG.
**Pattern of opening of the glands; VA: villous adenoma, HGD: dysplasia high-grade, LGD: low-grade dysplasia, TVA: tubulovillous adenoma.*

The ESD is technically difficult and time consuming and requires a long learning curve, in particular for resection of large colonic adenomas. Therefore, EPMR is still widely practiced, at least in Western institutions. The addition of APC application in the site the EPMR is an attractive tool for the treatment of visible residual adenoma due to its simplicity, safety and efficacy[5,6,11,22].

Only one randomized controlled study has addressed the role of the APC after the EPMR of large sessile colorectal adenomas, when the resection site presented with an aspect "clean" of neoplastic lesions. This study showed a decrease of residual or recurrent adenomas in the group treated with APC[23].

In this study, complete resection was considered when there was no visible residual lesions, both in the margins and in the central area of resection, as assessed by chromoendoscopy with indigo carmine and magnification of images, as proposed by Hurlstone *et al.*[24]. Among the 20 patients included in this study, four had in residual / recurrent lesions, two in each group, indicating that in this population the use of complementary APC did not affect the rate of residual adenomas after EPMR.

A complete analysis of the patients with residual / recurrent lesions showed that the tumor size was 30 and 40mm in group 1 and 50 and 60mm in group 2, and in all of them the amount of resected fragments was greater than four with histology of high-grade dysplasia. Our data suggest that in patients with these characteristics treated with EPMR, with or without additional APC, the expected rate of residual / recurrent lesion is at least 20%.

It is possible that some area of diminutive adenomatous lesion has not been recognized by chromoendoscopy with magnification image due to clotting

artifacts and therefore APC was not properly applied. Another possibility is that, due to a small number of cases, our study lacked statistical power to detect a difference in the recurrence rate of adenomas treated with EPMR with or without APC.

In conclusion, in patients with sessile colorectal adenomas > 20mm, the routine application of additional APC after complete resection of the lesion by EPMR does not appear to decrease the rate of local residual or recurrent lesions. Our results suggest that lesions larger than 30 mm, resected in over four fragments with high-grade dysplasia, have a recurrence rate of 20% after EPMR. Further studies with a larger number of patients should be made for a more definitive conclusion.

R E S U M O

Objetivo: *avaliar a eficácia da complementação por coagulação com plasma de argônio para reduzir a taxa de neoplasia residual ou recorrente após ressecção endoscópica completa fragmentada de grandes adenomas sésseis colorretais.* ***Métodos:*** *critérios de inclusão: pacientes com grandes adenomas colorretais sésseis, > 20mm, sem sinais morfológicos de infiltração profunda, submetidos à ressecção endoscópica completa fragmentada estudada com cromoendoscopia e magnificação de imagens. Os pacientes foram randomizados em dois grupos: grupo 1 – nenhum procedimento adicional e, grupo 2 – complementação por coagulação com plasma de argônio. O seguimento por colonoscopia foi realizado em três, seis e 12 meses de pós-operatório. Foi avaliada a taxa de neoplasia residual ou recidiva local.* ***Resultados:*** *foram incluídos no estudo um total de 21 lesões. Onze lesões no grupo 1 e dez no grupo 2. Ocorreram duas neoplasias residuais ou recorrências locais em cada grupo, detectadas em três meses de acompanhamento.* ***Conclusão:*** *a complementação por coagulação com plasma de argônio após uma aparente ressecção endoscópica completa em fragmentos de grandes adenomas sésseis colorretais não parece reduzir a ocorrência de lesão adenomatosa residual ou recidiva local.*

Descritores: *Adenoma. Neoplasias colorretais. Endoscopia. Agentes de coagulação. Coagulação com plasma de argônio.*

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