

# Endoscopic Mucosal Resection of Superficial Colorectal Neoplasms: Review of 140 Procedures



## *Mucosectomia Endoscópica de Neoplasias Superficiais do Cólon e Recto: Análise de 140 Procedimentos*

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### ABSTRACT

**Introduction and Aims:** Endoscopic mucosal resection (EMR) has been shown to be useful in the removal of large colorectal sessile and flat lesions, avoiding the need for surgical resection. The aim of this study was to evaluate the efficacy and safety of EMR in colorectal lesions using the inject-and-cut technique.

**Material and Methods:** Based on the review of colonoscopy reports, performed from February 2007 and February 2010, resected lesions  $\geq 10$  mm in diameter were selected for the study. The endoscopic and histologic characteristics, complications, follow-up and surgical need were recorded.

**Results:** During the study period we performed 140 EMRs among 133 patients (82 men; mean age  $64.4 \pm 12.4$  years). The majority of lesions were located proximal to the hepatic flexure (47.8%). Lesions mean size was  $18.5 \pm 8.5$  mm. Morphologically lesions were classified as: Is-60; IIa-54; IIb-14; IIa+IIc-12. En-bloc resection was performed in 56.4% of cases. Lesions  $> 20$ mm in size were independently associated with a higher rate of piecemeal resection (OR: 13.7; 95% CI: 3.8-49.6;  $p < 0.0001$ ) and residual lesion (OR: 7.3; 95% CI: 1.6-34.2;  $p = 0.012$ ). A complete endoscopic clearance was achieved in 91.4% of cases. Histological classification: non-specific alterations-1; hyperplastic polyp-8; adenoma-124; adenocarcinoma-7. The complication rate was 5.7% (6 intra-procedural bleeding; 1 delayed bleeding; 1 perforation). Until now, 144 follow-up colonoscopies were performed in 90 patients. Local recurrence occurred in 17/90 (18.9%), 10 of whom were managed with a new EMR. The recurrence rate was not affected by the lesion's dimension, location, and resection type. Twenty-one patients (15%) were referred for surgery, mainly because of incomplete resection of the index lesion.

**Conclusion:** EMR was effective and safe in the treatment of colorectal sessile and flat lesions. Lesions larger than 20mm were frequently associated with piecemeal resections, which did not lead to a higher recurrence rate. EMR is feasible for managing local recurrence.

### RESUMO

**Introdução e Objectivos:** A mucosectomia endoscópica (ME) tem mostrado ser útil na ressecção de grandes lesões colorrectais sésseis e planas, evitando a necessidade de intervenção cirúrgica.

O objectivo deste estudo foi avaliar a eficácia e segurança da ME em lesões colorrectais usando a técnica de injeção e corte.

**Material e Métodos:** Com base na análise dos relatórios de colonoscopia, realizadas entre Fevereiro de 2007 e Fevereiro de 2010, seleccionaram-se as lesões ressecadas  $\geq 10$  mm de diâmetro, registando-se as suas características endoscópicas e histológicas, complicações, vigilância e necessidade cirúrgica.

**Resultados:** Durante o período em estudo foram realizados 140 MEs em 133 doentes (82 homens; idade média de  $64,4 \pm 12,4$  anos). A dimensão média das lesões ressecadas foi de  $18,5 \pm 8,5$  mm, tendo a maioria localização proximal ao ângulo hepático (47,8%). A classificação da sua morfologia endoscópica foi: Is-60; IIa-54; IIb-14; IIa+IIc-12. Em 56,4% dos casos a ressecção foi efectuada num fragmento. As lesões  $> 20$ mm foram ressecadas, mais frequentemente, em dois ou mais fragmentos (OR: 13,7; 95% CI: 3,8-49,6;  $p < 0,0001$ ). A ressecção endoscópica foi considerada completa em 91,4% dos casos. Histologicamente classificaram-se em: alterações inespecíficas-1; pólipó hiperplásico-8; adenoma-124, adenocarcinoma-7. Verificaram-se complicações em 5,7% dos casos (6 hemorragia intra-procedimento; 1 hemorragia tardia; 1 perfuração). Realizaram-se 144 colonoscopias de vigilância em 90 doentes. Verificou-se recorrência local em 17/90 (18,9%), 10 dos quais tratados com nova ME. A taxa de recorrência não foi afectada pela dimensão da lesão, localização e tipo de ressecção. Foram referenciados para cirurgia 21 doentes (15%), na maioria, por ressecção incompleta da lesão inicial.

**Conclusão:** A ME mostrou-se eficaz e segura no tratamento de lesões colorrectais sésseis e planas. Em lesões maiores que 20mm a técnica utilizada associou-se com frequência a ressecções em mais de um fragmento, que não determinaram uma taxa de recorrência mais elevada. A ME foi exequível na ressecção das recorrências locais.

### INTRODUCTION

Colorectal cancer (CRC) is the leading cause of death from cancer in Portugal.<sup>1</sup> The detection and removal of pre-cancerous adenomatous lesions and early CRC through colonoscopic polypectomy has been proven to reduce the incidence and mortality related to CRC.<sup>2</sup>

In fact, endoscopic resection is currently a standard treatment for superficial gastrointestinal premalignant and malignant lesions and is increasingly gaining acceptance.

The vast majority of polyps detected during colonoscopy is small or pedunculated and are easily removed by standard polypectomy.<sup>3</sup> However, large sessile and flat colonic lesions, found in 0.8-5.2%<sup>4</sup> of patients undergoing colonoscopy, are not amenable to standard endoscopic resection techniques. They represent a therapeutic challenge as they tend to more frequently contain high-grade dysplasia (HGD) and adenocarcinoma (ADC), and are associated with high-

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er recurrence and complication rates.<sup>5,6</sup> It is primarily in this group of lesions where endoscopic mucosal resection (EMR) is applicable.

EMR is currently a well-established technique for the treatment and staging of superficial colorectal neoplasia<sup>7</sup>. Among the various EMR techniques described, the inject-and-cut technique is the most widely used and most applicable in the colon and rectum.<sup>8</sup>

This minimally invasive technique allows the safe and effective removal of large colorectal sessile and flat lesions, thereby obviating the need for surgical intervention with its attendant morbidity, mortality and cost.<sup>9-11</sup> *En bloc* removal of lesions is preferable as it facilitates a thorough histological evaluation. There are limits to the size of lesions which can be removed in one fragment and those larger than 20mm in diameter are frequently resected by piecemeal EMR. Piecemeal resection has been associated with a high frequency of local recurrence, ranging from 10 to 23%.<sup>12-16</sup>

In the present study, we report our experience in the management of superficial colorectal neoplasia by EMR, evaluating the efficacy, safety and clinical outcome of this technique.

## MATERIAL AND METHODS

The data from all EMR performed at our institution, between February 2007 and February 2010, using the inject-and-cut technique in sessile or flat colorectal lesions measuring at least 10mm in size was retrospectively collected from the Endoscopy Unit Electronic Database Registry after reviewing all the colonoscopy reports performed during the studied period.

The endoscopic and histologic characteristics of the lesions, resection technique, *en bloc* resection vs. piecemeal resection (EMR), complications, follow-up and surgical need were recorded.

### Lesion Characteristics

The location, size and polyp morphology were collected from the endoscopy reports. In accordance with the Paris classification sessile (0-Is) and flat (0-II) lesions were defined as having no clear stalk and a height from the adjacent mucosa of  $\geq 2.5$ mm or  $\leq 2.5$ mm, respectively.<sup>17</sup> Flat lesions were further characterized as slightly elevated (0-IIa), completely flat (0-IIb), slightly depressed (0-IIc) or a combination of the previous.

### EMR technique

The performance of colorectal EMR is standardized in our Department as follows and is depicted in Fig. 1. The procedures are performed with a standard colonoscope or gastroscope (for lesions near the anal verge).

In all cases the inject-and-cut EMR technique is used. A 0.9% saline solution or hypertonic dextrose solution, based on the endoscopist preference, is injected into the submucosal layer below the lesion using a 23 gauge needle. This elevates the mucosal layer containing the lesion on a submucosal fluid cushion, and provides a safety zone for snare resection. Epinephrine (1:100000) and/or a dye (indigo carmine or methylene blue) are added to the solution in some cases at the endoscopist discretion. The volume of injected fluid varied according to the site and size of the lesion. A standard polypectomy snare is then placed around the elevated lesion and resection carried out. After snare excision the resection area is inspected. If any residual adenomatous tissue is found it is resected in a similar fashion until judged endoscopically complete. Argon plasma coagulation (APC) is used to ablate any residual adenomatous tissue that is too small to be grasped by the snare and/or on

apparent clear margins in order to minimize recurrence at the endoscopist discretion. Patients are discharged on the same day of the procedure or, occasionally after an overnight stay.

Complete resection was defined as removal of the entire lesion at the first EMR. Endoscopic clearance was defined as the absence of residual polyp tissue after resection, regardless of the number of procedures needed to achieve it. Residual lesion was defined as the impossibility to attain an endoscopic clearance.

All EMR-induced complications were recorded through the review of patient medical chart and EMR report. Regarding complications, their treatment modality was classified as conservative, endoscopic or surgical.

### Histology

All specimens were sent for histopathological assessment and the results were collected from the pathology reports. Adenomas were defined according to the Vienna classification of gastrointestinal epithelial neoplasia.<sup>18</sup> Histological completeness was defined when lesions were resected *en-bloc* and no adenomatous tissue present at the resection margins.

### Follow up and recurrence

Surveillance colonoscopy was performed at 2 to 6 months, according to published guidelines,<sup>42</sup> or individualized based on the assistant physician judgment once endoscopic clearance had been established.

Recurrence was defined as the presence of a visible lesion, after endoscopic clearance, in the area of previous resection on a follow-up endoscopy with biopsies showing adenomatous tissue. The type of management applied to the recurrent lesion was also collected.

### Surgery

We collected the data regarding the need for surgery, the reason for referral, type of surgery and the histology of the surgical specimen.

### Statistical analysis

Descriptive statistics were calculated for the patients' data and EMR parameters, and are presented as means, and SD, as well as ranges (minimum-maximum) for continuous data, and as absolute and relative frequencies for categorical data.

A logistic regression analysis (Method: Enter) was performed to test the association of individual criteria from the lesions with the type of resection and the presence of residual or recurrent adenomatous tissue.

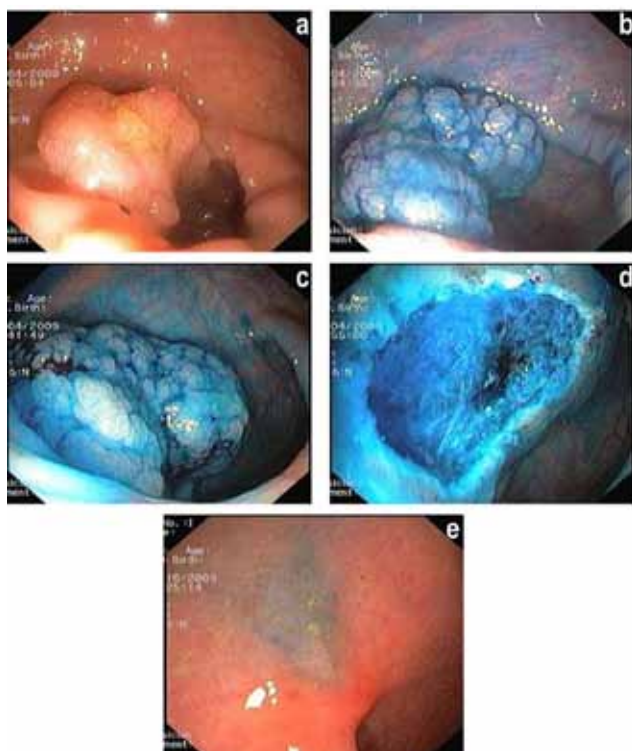
A *p* value  $< 0.05$  was considered statistically significant. Data handling and statistical analysis were performed with STATA/SE version 10.0 (StataCorp, College Station, TX).

## RESULTS

During the analysed period 140 EMRs, fulfilling the inclusion criteria, were performed in 133 patients (82 men and 52 women; mean age  $64.4 \pm 12.4$  years, range 24-87).

### Lesion Characteristics

The endoscopic characteristics of the resected lesions are presented in Table 1. Eighty percent of the lesions measured from 10 to 20mm. The mean size of the resected lesions was  $18.5 \pm 8.5$ mm (range 10 – 55mm). The most common location was the cecum/ascending colon with 67 lesions (47.9%) followed by the descending/sigmoid colon with 32 cases (22.8%). According to the Paris classification sessile polyps (0-Is) accounted for the majority of lesions



**Fig. 1** - Endoscopic mucosal resection inject-and-cut technique. (a) A 30-mm sized Paris 0-Is lesion of the rectum at conventional white light colonoscopy. (b) Chromoendoscopy with methylene blue spray dye to enhance lesion margins. (c) The lesion was lifted by injecting a solution of normal saline and methylene blue into the submucosal plane. (d) The tumor was entirely resected by EPMP with a total of 3 pieces, resulting in a wide and clean mucosal defect leaving the *muscularis propria* as the base; histology: tubulovillous adenoma with low-grade dysplasia. (e) At six-month follow-up a scar is visible without any sign of recurrence.

encountered in our series (42.8%). The mean size of the sessile and flat lesions was  $22.4 \pm 8.9$  and  $15.6 \pm 6.8$ mm respectively. More than one third of the circumference was involved in 12% of the cases and two or more haustral folds in 6.4%.

### EMR technique

The characteristics of the lesions and EMR technique and results are summarized in Table 2. *En-bloc* resection was feasible in 79 cases (56.4%) while the remaining 61 lesions were submitted to EPMP (43.6%).

The excision was judged endoscopically complete in 123 cases (87.9%) after a single session. The reasons for incomplete resection were partial lifting (10 cases) and difficult endoscopic access (7 cases). Five lesions were successfully managed with a new EMR session, making a total endoscopic clearance success rate of 91.4%. Residual lesion was present in 12 cases (8.6%).

Post-EMR APC was applied in 25 (17.8%) of the 140 lesions, including 2 incomplete resections and 23 cases on clear margins in order to minimize recurrence.

All lesions larger than 30 mm were submitted to EPMP. The logistic regression analysis performed to identify individual lesion criteria independently associated with EPMP determined that the only significant association was with lesions larger than 20mm (OR: 13.7; 95% CI: 3.8-49.6;  $p < 0.0001$ ).

The presence of residual adenomatous tissue was

**Table 1:** Endoscopic characteristics of the resected lesions

	No. of cases (%)
<b>Size (mm)</b>	
10 – 20	112 (80)
21 – 30	18 (12.9)
> 30	10 (7.1)
<b>Location</b>	
Cecum / ascending	67 (47.9)
Transverse	17 (12.1)
Descending / sigmoid	32 (22.9)
Rectum	24 (17.1)
<b>Morphology [17]</b>	
0 – Is	60 (42.9)
0 – Ila	54 (38.5)
0 – I Ib	14 (10)
0 – I Ia + I Ic	12 (8.6)

significantly associated with lesions >20mm (OR: 7.3; 95% CI: 1.6-34.2;  $p = 0.012$ ), regardless of the resection technique used ( $p = 0.14$ ).

### Histology

The histopathological examination results are described in Table 3. Neoplastic proliferation was observed in 131/140 lesions (90.7%), including 124 adenomas (32 with high grade dysplasia) and 7 invasive adenocarcinomas (3 in adenomas containing invasive carcinoma).

### Complications

Complications occurred in 8 of the 140 procedures (5.7%). There were 6 intraprocedure minor bleeding (4.3%) and 1 delayed bleeding (0.7%). Delayed bleeding occurred 3 days after the procedure, presented with hemodynamic instability and required packed red blood cell transfusion. The bleeding was controlled endoscopically, by epinephrine (solution 1:10000) injection (3 cases), use of hemostatic clips (2 cases) or both (2 cases).

Perforation occurred in one (0.7%) case following the EMR of a 15mm 0–I Ia lesion in the sigmoid colon. The complication was recognized during the recovery period after the procedure and led to an exploratory laparotomy; a microperforation in the anterior wall of the rectum was found, which was judged to be a colonoscopy-related rather than an EMR-induced complication.

### Follow up and Recurrence

Until this analysis, 144 follow-up colonoscopies were performed in 90 patients (Table 4). The mean follow up time was  $15.9 \pm 8.9$  months, ranging from 2 to 38 months. Recurrence occurred in 17 (18.9%) of the 90 patients submitted to surveillance (12 within the first twelve months at the first colonoscopy and 5 during the second year of follow-up at subsequent exams). Ten were successfully managed with a new EMR, 2 with a standard polypectomy and 5 were referred for surgery because the recurrence was considered not amenable to endoscopic treatment. The recurrence rate was not affected by the size, location, morphology and his-

**Table 2:** Lesions characteristics stratified by the resection technique

	Resection technique	
	En-bloc	EPMR
Number of lesions (%)	79 (56.4)	61 (43.6)
Residual lesion (%)		
No	78 (98.7)	50 (81.9)
Yes	1 (1.3)	11 (18.1)
Size in mm (%)		
Mean $\pm$ SD	14.7 $\pm$ 4.5	23.5 $\pm$ 9.8
10–20	76 (96.2)	36 (59)
21–30 *	3 (3.8)	15 (24.6)
>30 *	0 (0)	10 (16.4)
Location (%)		
Cecum / ascending	39 (49.4)	28 (45.9)
Transverse	14 (17.7)	3 (4.9)
Descending / sigmoid / rectum	26 (32.9)	30 (49.2)
Morphology (%) <sup>17</sup>		
0 – Is	25 (31.6)	35 (57.4)
0 – IIa	38 (48.1)	16 (26.2)
0 – IIb	12 (15.2)	2 (3.3)
0 – IIa + IIc	4 (5.1)	8 (13.1)
APC (%)		
No	73 (92.4)	42 (68.9)
Yes	6 (7.6)	19 (31.1)

\*EPMR was more frequent in lesions > 20mm, regardless of lesion location ( $p = 0.3$ ) and morphology ( $p = 0.09$ ).

**Table 3:** Histological characteristics of the resected lesions<sup>18</sup>

Histology	No. of cases (%)
LGD	87 (62.1)
HGD	32 (22.8)
Invasive ADC	7 (5)
Sessile serrated adenoma	5 (3.7)
Hyperplastic polyp	8 (5.7)
Non specific alterations	1 (0.7)

LGD – low grade dysplasia; HGD – high grade dysplasia; ADC – adenocarcinoma

topathology of lesions, resection type and APC application.

### Surgery

Twenty-one patients (15%) were referred for surgery. In 8 cases due to residual lesion. In 3 cases the surgical

indication was related to adenoma with invasive carcinoma that did not met criteria to consider endoscopic resection as safe. Surgery was also performed in 4 cases of deep invasive adenocarcinoma (all with residual lesion), in 1 perforation and in 5 patients who showed recurrence during

Table 4: Characterization of the lesion, resection technique and APC usage stratified by local recurrence

	Local recurrence	
	No	Yes
Number of lesions (%)	73 (81.1)	17 (18.9)
Size in mm (%) *		
Mean ± SD	17.6 ± 7.5	20.4 ± 6.7
10 – 20	62 (84.9)	12 (70.6)
21 – 30	7 (9.6)	4 (23.5)
> 30	4 (5.5)	1 (5.9)
Location (%) *		
Cecum / ascending	38 (52.1)	12 (70.6)
Transverse	9 (12.3)	0 (0)
Descending / sigmoid / rectum	26 (36.6)	5 (29.4)
Morphology (%) *		
0 – Is	27 (37)	9 (52.9)
0 – IIa	32 (43.8)	8 (47.1)
0 – IIb	5 (6.8)	0 (0)
0 – IIa + IIc	9 (12.4)	0 (0)
Dysplasia (%) *		
LGD	58 (79.5)	10 (58.8)
HGD	15 (20.5)	7 (41.2)
Resection technique (%) *		
En-bloc	43 (58.9)	9 (52.9)
Piecemeal	30 (40.1)	8 (47.1)
APC (%) *		
No	59 (80.8)	13 (76.5)
Yes	14 (19.2)	4 (23.5)

LGD – low grade dysplasia; HGD – high grade dysplasia;

\* The recurrence rate was not affected by the size, location, morphology and histopathology of lesions, resection type and APC application ( $p = ns$ ).

surveillance, not suitable for a new EMR (mean follow up time of 17.2 months).

Histologic assessment of the surgical specimen (Table 5) revealed advanced adenoma in 10 cases (50%) and invasive ADC in 6 (30%). In the remaining four cases there was no evidence of neoplastic tissue (20%).

## DISCUSSION

The introduction of CRC screening programs and open access colonoscopy led to an increase in the detection of polyps with different sizes and morphology.<sup>19</sup> Endoscopic polypectomy therapy is the primary and standard treatment for colon polyps. As reported earlier in Japan, neoplastic lesions morphology is also changing in Europe. In a recent study by Hurlstone, *et al.*,<sup>20</sup> the nonpolypoid colorectal lesions accounted for 38% of all adenomas detected in the United Kingdom. EMR is indicated for the treatment of adenomas and superficial adenocarcinomas. It is considered curative for intramucosal or submucosal superficial adenocarcinomas, due to their negligible lymph node me-

tastasis risk<sup>21</sup> and excellent clinical outcome.<sup>9-11</sup> EMR also allows complete pathologic staging of the lesion, which is critical because it allows stratification and refinement of further treatment.<sup>22</sup> When performing EMR it is important the evaluation of tumor invasion depth. This can be estimated based on the morphologic appearance (firm consistency, adherence, fold convergence, depression and ulceration) and evaluated through the non-lifting sign after submucosal injection, which indicates deep invasive carcinoma (sensitivity 61.5 – 100%; specificity 95.5 – 99%) and precludes the procedure.<sup>23-26</sup>

The goals of this study were to analyze our experience regarding the efficacy, safety and outcome of EMR in the treatment of colorectal sessile and non-polypoid lesions larger than 10mm.

Several EMR techniques have been described, namely the, inject and cut method, cap-assisted EMR, EMR with ligation and the inject, lift and cut method (strip biopsy). In our series all lesions were resected using the inject and cut method because it is simple, safe and the most applicable



**Table 5:** Patients submitted to surgery: Characterization of the lesions, reasons for referral, type of surgery and histology of the surgical specimen

Case no.	Reason for surgery	Size (mm)	Morphology	Preoperative histology	Type of surgery	Histology of the surgical specimen
1	Incomplete resection	40	0 – Is	TVA HGD	Right hemicolectomy	ADC pT3N0
2	Incomplete resection	30	0 – Is	TVA HGD	Right hemicolectomy	TA LGD
3	Incomplete resection	20	0 – IIa + IIc	TA LGD	Transanal excision	TA LGD
4	Incomplete resection	30	0 – Is	TVA HGD	Right hemicolectomy	Ø residual lesion
5	Incomplete resection	18	0 – Is	TVA LGD	Left hemicolectomy	Ø residual lesion
6	Incomplete resection	25	0 – Is	TA HGD	Transverse colectomy	ADC pT1N0
7	Incomplete resection	45	0 – Is	TVA HGD	Left hemicolectomy	TVA LGD
8	Incomplete resection	15	0 – Is	TA HGD	Rectal resection	ADC pT2N1
9	Recurrence	20	0 – IIa	VA LGD	Right hemicolectomy	TVA LGD
10	Recurrence	20	0 – Is	TVA LGD	Right hemicolectomy	TA LGD
11	Recurrence	25	0 – IIa	TA LGD	Right hemicolectomy	TA LGD
12	Recurrence	30	0 – Is	TVA HGD	Transanal excision	TVA HGD
13	Recurrence	13	0 – IIa	TA HGD	Right hemicolectomy	TA HGD
14	Adenoma with invasive carcinoma	35	0 – Is	Invasive ADC	Left hemicolectomy	TA LGD
15	Adenoma with invasive carcinoma	20	0 – Is	Invasive ADC	Right hemicolectomy	Ø residual lesion
16	Adenoma with invasive carcinoma	20	0 – Is	Invasive ADC	Transanal excision	Ø residual lesion
17	Deep invasive ADC	30	0 – Is	Invasive ADC	Left hemicolectomy	ADC pT1N0
18	Deep invasive ADC	30	0 – Is	Invasive ADC	Sigmoidectomy	ADC pT2N0
19	Deep invasive ADC	55	0 – Is	Invasive ADC	Rectal resection	TVA HGD
20	Deep invasive ADC	22	0 – IIa + IIc	Invasive ADC	Sigmoidectomy	ADC pT2N1

TA – tubular adenoma; TVA - tubulovillous adenoma; TV – villous adenoma; LGD – low grade dysplasia; HGD – high grade dysplasia; ADC – adenocarcinoma.

in the colon.<sup>8</sup>

Dealing with large sessile or flat neoplasias is technically demanding and complete ablation may require more than one EMR session. However, when feasible, removal of

all neoplastic tissue in a single session is recommended, as future attempts at lesion lifting will be hampered by submucosal fibrosis, leading to an increase risk of complications and incomplete resection.<sup>27</sup>

Regarding our study, technical success was achieved in 87.9% of cases if only the first EMR was considered, but the total endoscopic clearance rate ascended to 91.4% if a new EMR session was taken into account. In our experience lesions > 20mm in size were independently associated with a higher rate of EPMR and residual lesion. In the literature the clearance rate ranges from 50% to 100%,<sup>27-33</sup> with a trend towards better results in the last decade. This wide variation in the clearance rate represents the heterogeneity of the studies regarding the differences in lesions size and morphology and the EMR technique used. In order to improve current success rate it is important to refine patient selection, following the actual indications and limits of EMR.<sup>7,6,34</sup>

The most frequent complications of colonic EMR are bleeding (average frequency of 8.5%), perforation (0.7 – 4%) and post-polypectomy syndrome (0 – 7.6%).<sup>27-33</sup> The majority of bleeding episodes occur during the first 24 hours, but a few cases present as delayed bleeding.<sup>26</sup> Complications in our series included a bleeding rate of 5% and just one case of perforation (0.7%). Endoscopic hemostasis was successfully achieved in all cases as is similarly reported in the literature. According to published evidence both bleeding and perforation may be potentially controlled with endoscopic treatment rarely requiring surgical intervention.<sup>27-33</sup> In order to reduce bleeding episodes many authors have added epinephrine to the injected solution, but the clinical evidence of its efficacy is limited.<sup>35</sup> In this study epinephrine was added to the saline solution at the discretion of the endoscopist and was not subject to evaluation, though we feel that its added value pertains to a clearer field of work rather than to prevent major bleeding.

One of the major concerns when performing EMR is the high frequency of local recurrence, reported as ranging from 0% to 23.5%.<sup>12-16</sup> This wide range of results is surely related to heterogeneity of study designs and endoscopic follow-up. It has been reported that recurrence occurred more frequently in lesions > 20mm in diameter<sup>27,36</sup> and with EPMR compared to en-bloc resection (10 – 23.5% vs. 0 – 9.1%).<sup>12-16</sup> However in a recent study by Ferrara, et al. no relation was found between recurrence rate and lesion size or resection technique.<sup>26</sup> In order to reduce recurrence rates some centers use APC in the edge and/or base of the mucosectomy ulcer, but the results are controversial. Combined EMR and APC was shown to reduce the recurrence rate by 50% in comparison to EMR alone in two studies.<sup>37,38</sup> However other three studies failed to show this effect in the recurrence rate.<sup>26,28,39</sup> Our 18.9% observed recurrence rate, during a mean follow up of 15.9 months, is similar to that reported in the literature. Curiously, in our experience local recurrence was not affected by the size, location, morphology and histopathology of lesions, resection technique and APC application, although the impact of each of these factors cannot be discarded due to the low power of this study. Also, as previously reported,<sup>40,41</sup> most recurrences were successfully dealt with new EMR or standard polypectomy thereby underlying the importance of an early schedule for endoscopic review of the scar.

Surveillance colonoscopy plays an essential role following EMR. However the appropriate interval time remains controversial. According to the most recent published guidelines follow-up colonoscopy should be performed in 2 to 6 months<sup>42</sup> or within 9 months<sup>43</sup> after piecemeal removal of large sessile adenomas to check for recurrence. There are no further recommendations on subsequent surveillance and it should be individualized based on the endoscopist's judgment, once complete removal has been established. In our study, surveillance colonoscopy was performed at various intervals, at the discretion of the clinician in charge

of the individual patient's care. Local recurrence occurred in 17 cases, 12 within the first twelve months after EMR (mean 6.2 ± 0.8 months) and the remaining 5 during the second year of follow-up (mean 18.6 ± 1.9 months). Notwithstanding, the majority of recurrences published in the literature were detected at the first surveillance colonoscopy at 3–6 months,<sup>13,16</sup> supporting the generalized adoption of this schedule for an appropriate evaluation. Nevertheless Walsh, et al.<sup>32</sup> reported that half of recurrences after piecemeal EMR occurred after a negative first follow up examination. In order to address late recurrence Khashab, et al.<sup>44</sup> conducted a follow-up study of large adenomas submitted to EMR. A normal macroscopic appearance of the resection site and a negative scar biopsy specimen at the first follow-up predicted long term eradication, thus selecting the patients who would benefit from more than one surveillance colonoscopy.

Published studies report a surgical referral rate of lesions submitted to the different EMR modalities ranging from 0–54%.<sup>33</sup> In our series the referral rate was 14.3% (excluding the referral due to perforation). The 2 major indications for colectomy were incomplete resection of the index lesion and invasive CRC, thus emphasizing the need for an appropriate patient selection prior to EMR.

As stated, resection of lesions > 20mm in diameter is usually accomplished with a piecemeal technique, leading to a difficult assessment of pathological completeness of removal and to a higher recurrence rate. To avoid this problem, Japanese endoscopists have developed and proposed endoscopic submucosal dissection (ESD) as a superior resection technique. ESD allows a higher *en bloc* excision rate of large colorectal neoplasms (87 – 98.6%), thus providing a more accurate histological evaluation (R0 resection in 71 to 95.6% of the cases) and an extremely lower recurrence rate (0 – 2.8%).<sup>45-47</sup> However ESD is associated with a higher perforation rate (1.4–10%),<sup>45-47</sup> is far more technically demanding than EMR, requires the use of specialized accessories and has a high learning curve and prolonged resection times.

Available data points in favour of the complementarity of these techniques. The use of ESD in very large lesions or in recurrences not manageable with EMR will possibly further reduce the need for surgery in these patients.

## CONCLUSIONS

This study represents the largest reported series of colonic EMR in Portugal, confirming that it is an effective and safe minimally invasive procedure. EPMR was the method of choice for lesions larger than 20mm that was not associated to a higher recurrence rate opposing some literature reports. A very low major complication rate of just 1.4% was registered, which confirms the safety of this technique. Surveillance colonoscopy plays an essential role following EMR, as local recurrence is not infrequent and is amenable to endoscopic management in the majority of cases.

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## CONFLICT OF INTERESTS

None stated.

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