Endoscopic mucosal resection of large colorectal polyps : prospective evaluation of recurrence and complications

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Abstract

Background : Endoscopic mucosal resection (EMR) is a major therapeutic advance in the treatment of sessile and flat colorectal polyps. The aim of the study was to prospectively evaluate the success, complications and recurrence with EMR in colon.

Methods : From Jun/2008 to Jan/2012, patients referred for EMR of polyps ≥ 20 mm were included. Inject and cut EMR technique was used. Rates of complications and recurrence were assessed at 3, 12 and 36 months.

Results : From 78 referred polyps, 73 EMR were performed in 71 patients (54% men, 65.8 ± 10.6 years). Median polyp size was 30 (20 ; 35) mm, 64.4% sessile and 37% in rectum. Piecemeal removal performed in 86.3%. Median follow-up time was 12 (7 ; 15) months. Histological analysis revealed low-grade dysplasia in 51%, high-grade dysplasia in 37%, intramucosal carcinoma in 11% and invasive carcinoma in 1%. The case of invasive carcinoma was referred for surgery. There were 6 complications (8.2%) resolved without surgery : 5.5% of delayed bleeding, 1.4% of post-polypectomy syndrome and 1.4% of perforation. Recurrence was observed in 22.2% at 3 months, 11.1% at 12 months and 0% at 36 months. By logistic regression, a location near the pectinate line (OR 26.13) and a previous history of polypectomy (OR 7.70) became independent factors related to recurrence.

Conclusions : In our experience, EMR was a relatively safe procedure with all complications managed conservatively. We had an acceptable percentage of local recurrence and all cases of recurrence were treated endoscopically. (Acta gastroenterol. belg., **2013**, 76, **225-230**).

Key words : Colonoscopy, endoscopic mucosal resection, large colorectal polyps, recurrence, complications.

Introduction

In the era of colorectal cancer screening, the detection of large and sessile colon polyps has increased, making endoscopic mucosal resection (EMR) the treatment of choice of these lesions (1).

The most common EMR technique used is the "inject and cut" technique (2). This involves the injection of a solution into the submucosal layer, in order to lift the lesion and expand the submucosal away from the *muscularis propria*, reducing the risk of perforation and bleeding and facilitating "en bloc" and complete resection.

The lesions can be removed "en bloc" or in pieces (piecemeal). "En bloc" is recommended because it provides more accurate histological assessment and reduces the risk of recurrence. However, in the majority of polyps bigger than 20 mm, that is not possible and piecemeal resection is performed. In this case, careful should be taken in getting as bigger and fewer pieces as possible, and to retrieve all pieces to histological analysis (3).

EMR is a technique with a small learning curve and good results at long *follow-up*. The most common complications, hemorrhage (0.4-16%) and perforation (0-5%) can be controlled with endoscopic methods in the majority if situations, rarely requiring surgery (1,4-8).

The major concern is the recurrence rate that can vary from 3-39% (8-16), but usually is managed endoscopically. For this reason, guidelines recommend that after piecemeal resection in sessile adenomas, follow-up evaluation should be performed at short intervals (2-6 months) to verify complete removal, and once this has been achieved, subsequent evaluation should be individualized (17).

The aim of the study was to prospectively evaluate the efficacy, rate of recurrence and complications, in a series of consecutive patients submitted to EMR of colonic polyps, with size higher than 20 mm. The study was performed in a single tertiary Centre, by five gastroenterologists with very different expertise and skills, being the closest as possible to every daily clinical scenario.

Material and methods

Study population

Between June 2008 and January 2012, all patients referred to endoscopic resection of sessile or flat colorectal polyps ≥ 20 mm, were submitted to EMR, and prospectively included in the study if a minimum of 3-month *follow-up* was performed.

Exclusion criteria was the presence of non-lifting sign during EMR, lesions that could not be removed by EMR due to location conditioning difficult endoscopic access (more than two consecutive folds, more than 50% of the bowel wall circumference beyond the rectum and involving the appendix or diverticula orifices) and cases where patient preferred surgery.

Written informed consent was obtained from all patients before the procedure, but no ethics committee

consent was demanded as this study reports on conventional clinical practice.

Patient's data such as previous history of neoplasia, abdominal surgery, colonic polyps, prior polypectomy attempt and concomitant medications were recorded.

Whenever possible, patients on antiplatelet medications were instructed in the way of discontinuation. Patients on anticoagulation drugs were switched to low molecular weight heparin until the day before the procedure. After the EMR, patients on antiplatelet agents were instructed to reassume the drug after 7 days, while patients on anticoagulant agents were maintained on low molecular heparin and warfarin until accomplish the desired prothrombin time.

Polyps were classified using the Paris classification (18) and colorectal adenomas according to the Vienna classification (19).

Resection technique

The procedure was performed with a standard Olympus Exera II 160 series colonoscope using the "inject and cut" technique.

The first step of the procedure was the submucosal injection with a disposable injection needle (Olympus EndoTherapy NM-200U-0425, Japan) of 25G and 4 mm long, to create a submucosal cushion for safety and better resection. The injection solution contained saline solution with adrenaline 1:100,000 and methylene blue 1:200,000. The volume varied with the size of the lesion.

Marking of the edges with argon plasma coagulation (APC) before the submucosal injection was only done in cases of a type IIb lesions, at a 20W power with effect 2 settings (Olympus PSD-60 electrosurgical station with endoplasma unit).

After the submucosal injection, a disposable electrosurgical snare (Olympus EndoTherapy SD-230U-20) of 20 mm diameter was placed around a portion of the polyp and gently pressed against the mucosa, while closing until resistance was felt. Then, the portion of the polyp was moved away from the bowel wall and a small opening of the snare was done to allow the muscular layer eventually trapped to release from the snare. The snare was closed again until resistance. The polyp was then cut using the electrosurgical unit selecting the endo-cut forced mode at a 20W power with effect 2 settings.

When en bloc resection was technically impossible, piecemeal removal was performed and the procedure was repeated until complete removal of the lesion with visualization of the *muscularis propria*.

APC was then used at a 20W power, effect 2 settings, to ablate any residual polyp that could not be removed with a snare, and, in most cases, at the edge or margins of the mucosectomy ulcer, according to the endoscopist's judgment.

All resected specimens were retrieved for histopathological analysis, using a polyp retrieval net (Roth Net, US Endoscopy, Ohio, USA) of 25 × 30 mm diameter, placed after stretching in a cork plate.

Follow-up

Surveillance colonoscopy was scheduled by protocol to be performed at 3, 12 and 36 months.

Rates of complications (bleeding, perforation or post-polypectomy syndrome) were evaluated at the procedure, and one month after by an appointment with the patient.

Bleeding was defined as intraprocedural (during EMR), early (within the first 24 hours after EMR) or delayed (more than 24 hours after the procedure). Post-polypectomy syndrome was defined as the presence of abdominal pain with localized peritoneal signs, associated with fever and leucocytosis. Perforation was confirmed in one patient during the exam when the peritoneum was seen through the polypectomy scar.

Per-protocol, malignant polyps with unfavorable histology such as deep submucosal invasion (≥ 1000 μm), angiolymphatic invasion or poor differentiation was referred for surgical treatment.

Resection was considered complete if no residual adenomatous tissue was noted following completion of the EMR. Recurrence was defined as reappearance of adenomatous tissue in an apparently previous complete resection scar, while persistence or residual polyp was defined as the persistence of adenomatous tissue on follow-up, when the previous resection hadn't been complete. Both were demonstrated by pathology.

In case of recurrence or persistence of adenomatous tissue, removal was done with a snare or destroyed using the APC at the same settings. In this case, surveillance of the scar was tightened and scheduled within 3 months interval, to allow for healing and correct assessment of the scar for further recurrence.

Statistical analysis

Continuous data are described with mean and standard deviation if the distribution was normal, or with median and interquartile range if the distribution was skewed.

To compare continuous variables we used *t*-student or Mann-Whitney, according to the distribution. For categorical variables χ^2 or Fisher's exact test were used. *P* values < 0.05 were considered statistical significant.

For logistic regression we used the Wald test, assuming a Model coefficients < 0.05 and a Hosmer and Lemeshow Test > 0.05. Univariate analysis was performed previous to multivariate, including in the last one only the clinical variables with statistical significance. Results are presented as Odds Ratio (OR) with 95% interval confidence. Success is presented in an intention-to-treat analysis.

The software applied was SPSS for Windows version 16.0 (IBM Corporation, USA).

Results

From June 2008 - January 2012, 78 potentially removable polyps were identified. 5 polyps were excluded for the following reasons : 1 with non lifting sign during the
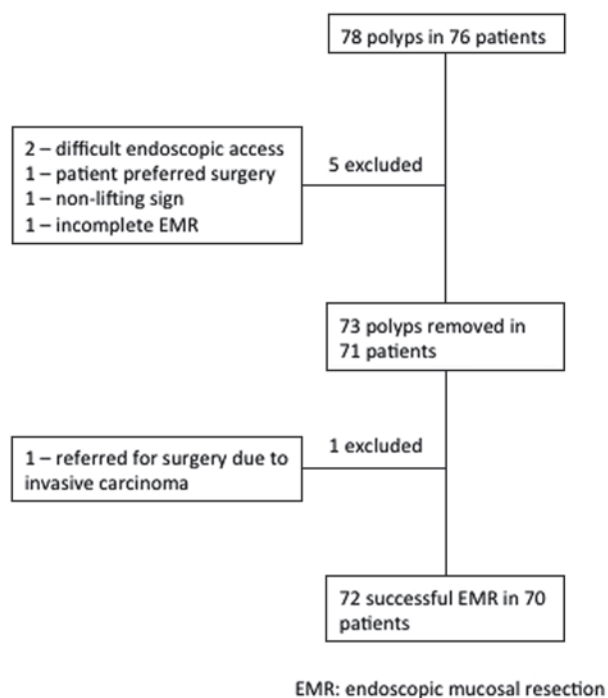
Fig. 1. — Flowchart of patients

Table 1. — **Demographic and clinical data of the patients (n = 71)**

Age (years)[1]	65.8 ± 10.6
Sex[2]	
Male	38 (53.5%)
Female	33 (46.5%)
Medical records[2]	
Concomitant colon cancer	12 (16.9%)
Previous abdominal surgery	30 (42.3%)
Other polyps	47 (66.2%)
Medication with antiplatelet or anticoagulant[2]	26 (36.7%)

[1]Mean ± SD ; [2]Number of patients (percentages).

Table 2. — **Characteristics of polyps (n = 73)**

Size (mm) †	30 (20; 35)
Type ‡	
Sessile	47 (64.4%)
Non-polypoid	26 (35.6%)
Previous polypectomy in the same place ‡	7 (9.9%)
Location ‡	
Left colon	38 (52.1%)
Right colon	35 (47.9%)
Technique of removal ‡	
Piecemeal	63 (86.3%)
"En bloc"	10 (13.7%)
Application of Argon Plasma Coagulation ‡	55 (75.3%)

† Median (interquartile range); ‡ Number of polyps (percentages).

exam, 1 case where patient preferred surgery, 1 that was unable to be totally removed, and two with difficult endoscopic access. In the final, 73 EMR of polyps ≥ 20 mm were performed in 71 patients (Fig. 1).

The demographic and clinical data of the patients are presented in Table 1. Mean age was 65.8 ± 10.6 years, and 53.5% were male. Characteristics of the polyps removed and technique of removal are shown in Table 2.

According to Paris Classification, 47 (64.4%) were polypoid (0 – Is) and 26 (35.6%) non-polypoid (11% 0 – IIa, 1.4% 0 – IIb and 23.3% 0 – IIa+IIb). Median polyp size was 30 (20 ; 35) mm, with 16 (21.9%) larger than 40 mm.

Regarding lesion site, 27 (37%) were located in the rectum and, of these, 8 (29.6%) reaching the pectinate line. Among the others, 6 (8.2%) were located in the sigmoid colon, 6 (8.2%) in the descending colon, 14 (19.2%) in the transverse colon, 15 (20.5%) in the ascending colon and 5 (6.8%) in the cecum.

Piecemeal resection was performed in 63 (86.3%) polyps and "en bloc" in 10 (13.7%). Argon plasma was applied in 55 (75.3%) cases. 67 polyps (91.8%) were removed in one single session. The remaining needed more procedures because EMR was considered incomplete in the first session. Characteristics of polyps according to type of resection are shown in Table 3.

Histological analysis revealed low-grade dysplasia in 37 (50.7%), high-grade dysplasia in 27 (37%), intramucosal carcinoma in 8 (11.0%) and invasive carcinoma in 1 (1.4%). The only case of invasive carcinoma was referred for surgery, but no carcinoma cells were observed in the histopathological specimen.

Malignancy was statistically significant related to polyp size (35 mm vs. 30 mm, $P = 0.03$). There was no relation between malignancy and age or type and location of lesions.

Complications occurred in 6 procedures (8.2%) and included 4 (5.5%) cases of delayed bleeding, one (1.4%) case of post-polypectomy syndrome and one (1.4%) case of immediate rectal perforation. There were no cases of immediate or early bleeding.

The cases of delayed bleeding occurred 1, 3, 4 and 6 days after the procedure. The bleeding was controlled in all, three with endoscopic hemostasis (*clips* in two and APC in another), and the other one spontaneously.

Two patients with delayed bleeding submitted to hemostasis with *clips* needed hospital stay (duration of 2 and 5 days), and one needed blood transfusion with 2 units of red blood cells.

The patient with the rectal perforation had a conservative treatment with immediate endoscopic closure using *clips*, followed by antibiotic and 48 hours fasting. The case of post-polypectomy syndrome also had conservative treatment with favorable result.

Bleeding was not significant related to polyp's size, location, technique of removal, use of APC, malignancy and medication with antiplatelet or anticoagulant agents.

Table 3. — **Characteristics of polyps according to type of resection (n = 73)**

	Piecemeal resection N = 63	"En bloc" resection N = 10
Size (mm) †	33.5 ± 13.5	23 ± 4.8
Type ‡	Sessile – 39 (61,9%) Flat – 24 (38,1%)	Sessile – 8 (80%) Flat – 2 (20%)
Location ‡	Left colon – 34 (54%) Right colon – 29 (46%)	Left colon – 4 (40%) Right colon – 6 (60%)
Total (%)	63 (86.3%)	10 (13.7%)

† Mean ± SD ; ‡ Number of polyps (percentages within type of resection).

Follow-up colonoscopy was performed in 70 patients (98.6%). As referred earlier, one patient was sent for surgery after the EMR because histology revealed an invasive adenocarcinoma.

The median follow-up time was 12 (7 ; 15) months. Colonoscopy at 3 months was performed in 72 (98.6%) polyps, at 12 months in 54 (74%) and at 36 months in 8 (11%).

Persistence or recurrence was observed in 16 polyps (22.2%) at 3 months, in 6 polyps (11.1%) at 12 months and in none at 36 months. From the 6 cases of one-year recurrence, 4 (7.4%) had no visible lesion in the colonoscopy performed earlier at 3 months.

All the cases of persistence or recurrence were submitted to additional polypectomy or multiple biopsies followed by APC, and the follow-up was tightened until full disappearance of adenomatous tissue. All cases are cured without the need of surgery.

Recurrence was higher in the presence of previous attempts of polypectomy at the same place (71.4% vs. 23.1%, $P = 0.02$) and in polyps near the pectinate line (87.5% vs. 20.3%, $P < 0.001$). Persistence or recurrence of lesion was higher if APC was applied (33.3% vs. 11.1%, $P = 0.06$), and this was particularly seen at 3 months, and in bigger polyps (38.3 ± 4.1 vs. 29.7 ± 1.4, $P = 0.06$). By regression, location near the anus, OR 26.1 (95%CI : 2.82-242.01, $P = 0.004$) and previous attempt of polypectomy at the same place, OR 7.70 (95%CI : 1.17-50.5, $P = 0.03$) were the only independent factors interfering with recurrence, among seven clinical variables that were related to recurrence in previous works (size and type of polyp, malignancy, resection technique, previous polypectomy at the same place and location near the pectinate line). These results are shown in Table 4.

In our series, EMR had a success rate of 92.3% (72/78), with six cases being excluded or referred for surgery.

Discussion

This study aimed to demonstrate the efficacy and safety of EMR in the management of large colorectal polyps. In our experience, EMR had a success rate of 92.3%.

We found a complication rate similar to that described in other works. Bleeding is the most common complication described with EMR, with rates that can vary from 0.4%-16% ; perforation is another possible complication, less frequent, that has been reported for 0%-5% (1,4-8). In our series we had 5.5% of delayed bleeding and 1.4% of rectal perforation and post-polypectomy syndrome.

Although we haven't found any association between the presence of complications and clinical variables, it has been described in other studies in relation with malignancy (3), piecemeal removal and size (4,6).

All cases were managed conservatively, with endoscopic hemostasis efficient in three and without need of surgery. As described in literature the use of *clips* is the preferable mode of endoscopic hemostasis (20) in cases of hemorrhage, because it has lower perforation rates.

Previous studies have reported recurrence rates ranging from 3% to 39% (8-16).

We had a recurrence rate of 22.2% at 3 months and 11.1% at one year. Although the majority of the studies describe that most recurrences appear within the first 6 months, in our series we had four cases with no recurrence at 3 months but with lesion at 1 year.

This phenomenon had already been described (21), and proves the importance of a continuous surveillance, especially in the long-term as 1 or 3 years. Also, it is very important to look careful at the circumferences of the edge and base of the ulcer after the procedure to avoid persistence of adenomatous tissue.

Recurrence is often related with the resection technique, presence of malignancy, polyp type and size (4,14, 22,23), location near the pectinate line (24) and previous attempt at removal the polyp (16).

In multiple logistic regression analysis we concluded that the independent predictive factors of recurrence were the location near the anus (OR 26.1) and previous polypectomy at the same place (OR 7.70). This highlights the importance of the first procedure in order to be successful and can identify the patients with a higher probability of recurrence that should be submitted to an even more careful surveillance, possibly with biopsies of the area in every endoscopic revision.

The relation between recurrence and previous polypectomy at the same site can be explained by the presence of fibrosis that makes complete removal of adenomatous tissue more difficult.

Treatment with APC to reduce recurrence is controversial ; in some studies, APC has proven to reduce the recurrence rate after piecemeal resection (8,25) ; in others, it was found to be a risk factor (16). In our study, recurrence was higher in cases when APC was applied, particularly at 3 months, but these were also the cases with larger polyps. APC was used in our series to eliminate any residual polyp unable to be removed with a snare, or in the edge of the scare at the end of the procedure. The higher rate of recurrence can be related to those cases with residual tissue ablated with APC. We cannot take conclusions about the prophylactic application at the

Table 4. – **Odds Ratio of recurrence associated with clinical variables (n = 73)**

	Odds ratio	95% CI	*P*
Univariate analysis			
Polyp size	1.048	1.007-1.09	0.02
Type of polyp	0.59	0.21-1.7	0.33
Location near the anus (n = 8)	27.43	3.1-243. 4	0.003
Technique of removal	3.98	0.47-33.6	0.21
Application of APC (n = 55)	0.25	0.05-1.21	0.09
Malignancy at histology (n = 9)	1.67	0.36-7.7	0.52
Previous polypectomy (n = 7)	8.33	1.47-47.4	0.017
Multivariate analysis			
Location near the anus	26.13	2.82-242.01	0.004
Previous polypectomy	7.70	1.17-50.5	0.034

CI : confidence interval ; APC : Argon plasma coagulation.

margins of the mucosectomy in preventing recurrence because it was not systematically used.

The development of new techniques of endoscopic submucosal dissection (ESD) has lower rates of recurrence (26-30) because it raises the "en bloc" and the R0 resection rates. Nonetheless it has a higher rate of complications, specially perforation and hemorrhage, implies a higher procedure length, and technically is more demanding than EMR, with longer learning curves, making it difficult to become routinely performed (31,32).

Our study has limitations that should be named, as the relatively low sample size.

The fact that five different endoscopists performed the procedures can be seen as a disadvantage because there are different technical skills levels, which can influence recurrence and complication rates. Nonetheless, in our opinion, has the advantage of traducing a real study with conditions similar to the majority of endoscopic Units in daily practice.

In conclusion, EMR was a safe procedure in our series, with a complication rate within the values described in other works and it was effective, with a manageable rate of recurrence and all (except one with invasive carcinoma) patients cured without the need of surgery.

From our results we think that EMR can be routinely used in all Endoscopic Units in the treatment of large colorectal polyps, without the need for advanced training, but extreme care should be taken with surveillance and recurrence, especially in cases of previous polypectomy or polyps involving the pectinate line.

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