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Research Article

Endoscopic Surveillance at 3 Months Post EMR for Early Detection of RRA

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Abstract

Background: Endoscopic mucosal resection (EMR) is an increasingly used technique for large sessile and flat-laterally-spreading (LST) colorectal lesions. As residual or recurrent adenoma (RRA) may occur in 10-40% of non-pedunculated lesions, surveillance colonoscopies are encouraged but optimal time intervals are unclear.

Purpose: To analyze characteristics of resected lesions and to assess frequency of RRA and provide follow-up suggestions.

Setting: All consecutive (May 2016 - 2017) EMR for flat or sessile adenomas ≥ 15 mm with high-grade dysplasia, Ca *in situ*, or pT1 were included.

Methods: we performed all procedures after evaluation of Paris, NICE, Kudo classification and lifting sign. Colonoscopies were repeated at 3, 6 and 12 months. Endoscopic and histological findings were collected, and their correlation analyzed for all primary lesions and RRA.

Results: 70 patients were included. Mean size of lesions was 25 mm (range 15 - 90 mm), 60% of lesions were removed en-bloc, 40% piecemeal. 40% polyps were sessile, 35% LST granular, 25% LST non-granular. NICE patterns were II (28; 40%), II/III (32; 45.7%) and III (10; 14.3%). Pit pattern according to Kudo was IIIs (28; 40%), III L/IV (32; 45.7%), IV/V (8; 11.4%) and V (2; 2,9%). End clips were used as bleeding prophylaxis in 38%, for intraprocedural bleeding in one patient. No post-procedural bleeding or perforation occurred. 11 lesions were pT1 (15.7%), 15 had at least some foci of Ca *in situ* (21.4%), 35 showed high grade dysplasia (HGD) (50%), 9 low grade dysplasia (LGD) (12.8%). Only 3 cases were surgically treated after polypectomy due to histological findings. At 3 months control, RRA was found only in 5 cases (7%). At 6-month controls, RRA was again detected in 2 of these patients. New cases of RRA were not found at 6 months, while at 12 months we had 2 primary RRA and 1 tertiary RRA.

Conclusions: EMR is a technique safe and effective particularly for lesions removable en-bloc. The RRA-risk after EMR was in line with the literature. Moreover, RRA seems to be ever early suggesting a close follow-up in the first period after EMR. NICE and Kudo classifications help better circumscribe the lesion to perform a complete resection with unscathed margins to avoid piecemeal resection. The analysis of a larger number of patients would be useful to combine endoscopic and histological parameters and produce a predictive model to better plan treatment and surveillance.

Keywords: *Endoscopic Surveillance; EMR; RRA*

Introduction

EMR is increasingly used to remove colonic polyps. This technique is specifically chosen for resection for sessile polyps and laterally spreading lesions according to guidelines [1,2]. Previous studies have demonstrated good feasibility and efficacy of this procedure, even if with recurrence rates depending on specific risk factors, such as the size of the lesion, intraprocedural bleeding, argon plasma uses to refine mucosectomy [3]. Indeed, in clinical practice, interval time for first surveillance colonoscopy can depend on decision making of each endoscopy unit, according to current guidelines always within six-twelve months from the EMR [1].

Aim of the Study

The aim of the study was to assess recurrence rates after mucosectomy at first and subsequent control colonoscopies, to establish the most appropriate interval time for surveillance.

Patients and Methods

We included all consecutive patients between May 2016 - 2017 that underwent colonoscopy and EMR for sessile polyps or LST of diameter > 1.5 cm histologically diagnostic for high grade dysplasia adenoma, Ca *in situ* or pT1 at Gastrointestinal Endoscopy Unit, Regina Elena National Cancer Institute of Rome. The EMR was performed with the inject and resect technique only if the lesion showed complete lifting after submucosal injection with sodium chloride solution, adrenaline 1:10000 and methylene blue. All procedures as well as surveillance colonoscopies were realized by two expert endoscopists with Olympus colonoscopies 190 series. The interval time chosen to run out the first surveillance colonoscopy was 3 months. Second and third colonoscopies were assessed at 6 and 12 months after EMR. All endoscopies were performed in white light, zoom magnification and NBI vision to correctly assess NICE, Paris and Kudo classifications [2,4,5]. Polyps' histological diagnosis was defined according to guidelines by an expert pathologist [6].

With respect to statistical analysis: Student t or Mann-Whitney tests were used to compare the distribution of continuous variables by outcome. Pearson's χ^2 or Fisher's exact tests were used to test for association between categorical variables and outcome.

Results

The present study included 70 patients with mean age 64 ± 9 years, 59% females. Table 1 enlists the characteristics of the lesions treated by EMR. Mean size of lesions was 25 mm, median size 20 mm (dimensional range 15 - 90 mm). According to Paris classification, lesions were classified as sessile (28; 40%), granular LST (24; 35%) and non-granular LST (18; 25%). The lesions showed NICE patterns II (28; 40%), II/III (32; 45.7%) and III (10; 14.3%). Pit pattern according to Kudo was IIIs (28; 40%), III L/IV (32; 45.7%), IV/V (8; 11.4%) and V (2; 2,9%). Most frequent sites of EMR were sigmoid colon (31.4%), rectum (21.4%) and descending colon (18.6%). Forty-two lesions (60%) were removed en-bloc, 28 (40%) in piecemeal. Endoclips were used for bleeding prophylaxis in 38%, for intraprocedural bleeding only in one patient. No post-procedural bleeding or perforation occurred. As to histological findings after EMR: 11 lesions were pT1 (15.7%), 15 had at least some foci of Ca *in situ* (21.4%), 35 showed high grade dysplasia (HGD) (50%), 9 low grade dysplasia (LGD) (12.8%). Three pT1 were surgically treated after EMR due to histological findings (> sm^2 sec. Kikuchi). An endoscopic suspicion of RRA at 3 months endoscopy was observed in 8 patients and therefore the suspect RRA was removed by biopsy/cold snare polypectomy/EMR, accordingly to its dimension and aspect. Histological confirmation of RRA was observed only in 5 (RRA 7%): two cases between the lesions removed en bloc and three cases between those resected in piecemeal. RRA showed LGD (2/5), HGD (2/5) and foci of Ca *in situ* (1/5). All RRA occurred within primary lesion ≥ 2 cm (5/5) and with morphology 0-Is (4/5) or LST non-granular (1/5) according to Paris classification. At 6-months colonoscopies, we only observed 2 secondary RRA (one LGD and one HGD). Finally, at 12-months endoscopic controls, we found 2 primary RRA (both LGD) and 1 tertiary RRA (HGD). None of the analyzed factors showed a statistically significant prognostic correlation with RRA.

Lesions	(N)	(%)
Size		
< 2 cm	18	25.7%
≥ 2 cm	52	74.3%
Paris Classification		
Sessile	28	40%
0-Is	21	
0-Isp	7	
Granular LST	24	35%
Non-granular LST	18	25%
NICE Pattern		
II	28	40%
II-III	32	45.7%
III	10	14.3%
Kudo Classification		
IIIs	28	40%
III L/IV	32	45.7%
IV/V	8	11.4%
V	2	2.9%
Location		
Caecum	6	8.6%
Ascending colon	9	12.8%
Transverse colon	5	7.1%
Descending colon	13	18.6%
Sigmoid colon	22	31.4%
Rectum	15	21.4%
Resection		
En bloc	42	60%
Piecemeal	28	40%
Histology		
LGD	9	12.9%
HGD	35	50%
Ca in situ	15	21.4%
pT1	11	15.7%

Table 1: *Characteristics of lesions removed by EMR.*

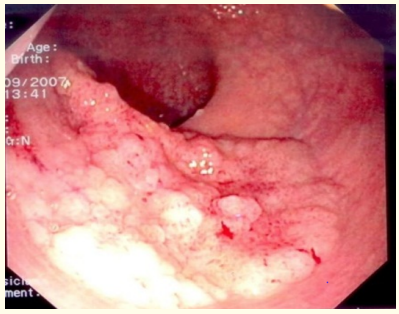

Figure 1: *LST granular.*

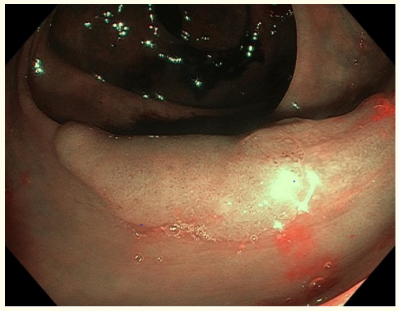

Figure 2: *Flat adenoma in NBI.*

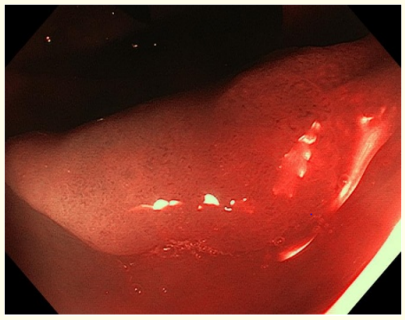

Figure 3: *Flat adenoma in NBI.*

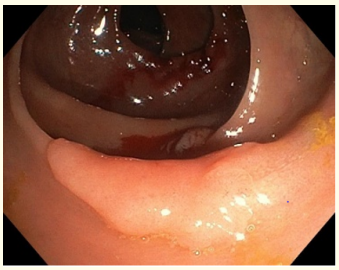

Figure 4: *Flat adenoma in White Light.*

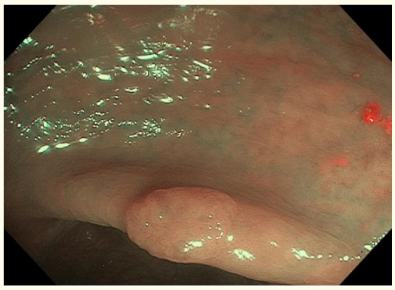

Figure 5: *RRA at 3 months colonoscopy NBI vision.*

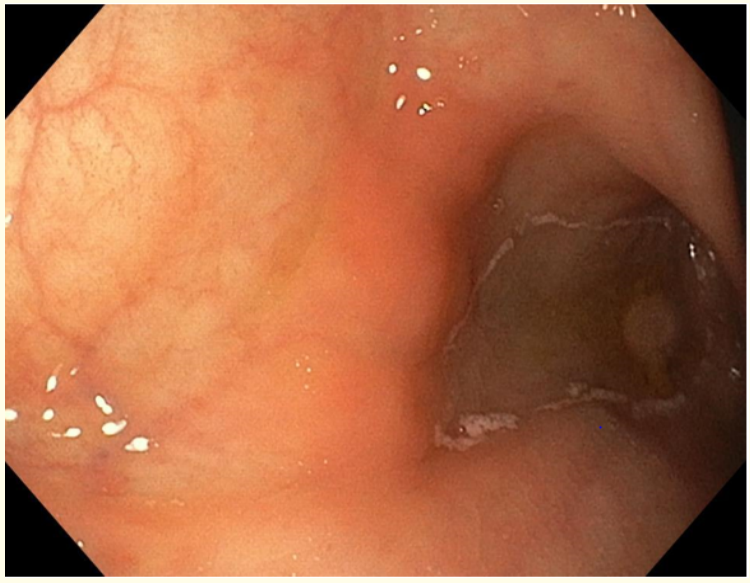

Figure 6: *Other scar at 3 months colonoscopy with sign of endoclips.*

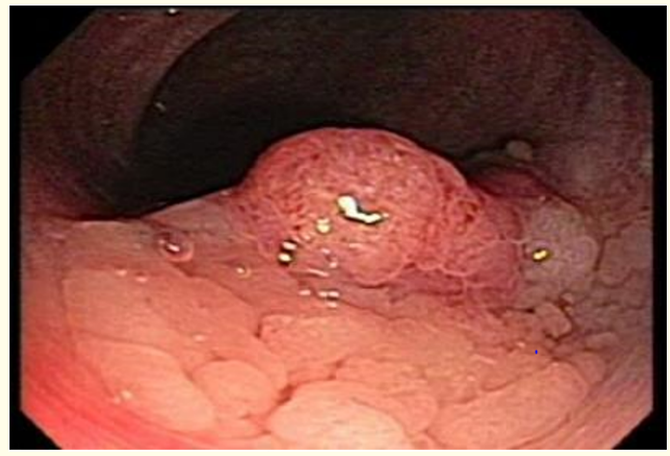

Figure 7: *Sessile polyp.*

Figure 8: *Flat adenoma.*

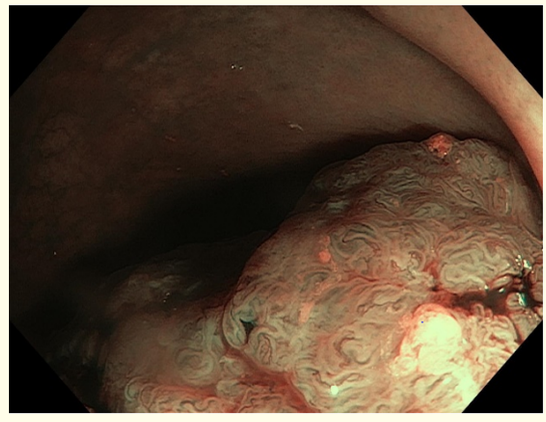

Figure 9: *Large sessile polyp in NBI vision.*

Figure 10: *Large sessile polyp in White Light vision.*

Figure 11: *Scar at 3 Months Colonoscopy.*

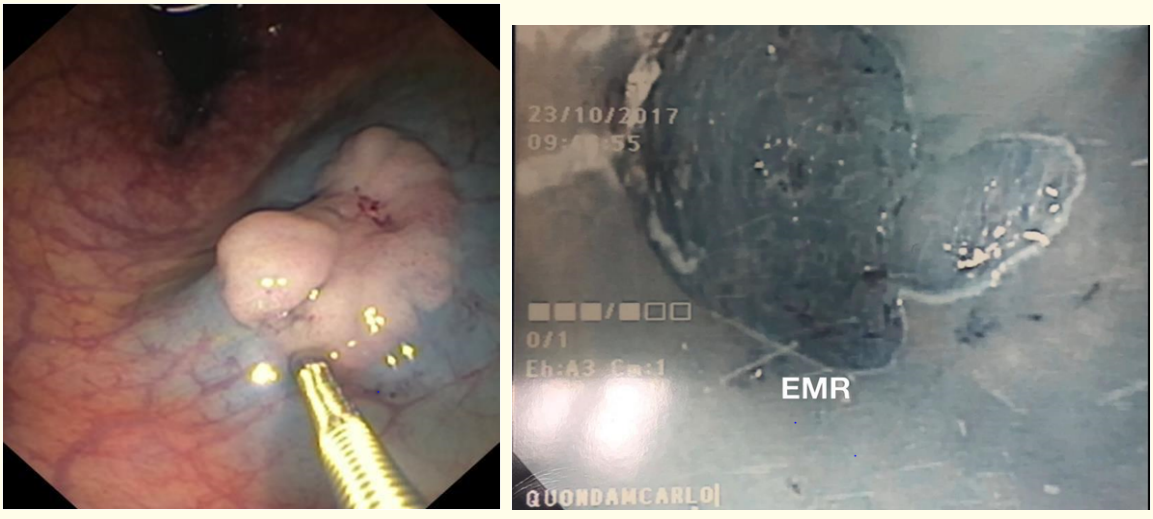

Figure 12: *EMR sessile polyp.*

Figure 13: *Metallic endoclicps use.*

Discussion

In the population on study we had good percentages of en bloc EMR and low rates of RRA at control colonoscopies performed at 3, 6 and 12 months after endoscopic resection. In the literature, some risk factors for RRA have been reported, like size of the lesion > 20 mm, piecemeal resection, intraprocedural bleeding and others. Zhan T., *et al.* in a study conducted on 129 patients submitted to EMR for large flat colo-rectal lesions, found polyp size and piecemeal resection as main risk factors for local recurrence [7]. Our data are aligned with the literature, showing even lower rates of primary RRA than those generally reported, probably as a result of the combination between a relatively small number of polyps on study and a particularly short interval between EMR and first endoscopic control. A 3 months interval is not frequently reported in the literature, however in our experience it has proved to be ideal to re-treat precociously the RRA, not being too early to intercept the RRA, because we did not find any primary RRA at 6 months, but only re-recurrences (secondary RRA). The small sample size on study, hindered the research of a statistical correlation with any of the characteristics analyzed, however all RRA occurred in lesions > 20 mm, in line with other studies. Moss., *et al*. found a 14% of primary RRA at 4 months control colonoscopies and a 4% primary RRA at 16 months control in a population of 128 patients submitted to EMR. Between those treated at 4 months control for a primary RRA, 20% showed a secondary RRA at 16 months control. Risk factors for recurrence were a polyp size > 20 mm, an intraprocedural bleeding and the use of argon plasma coagulator to refine the mucosectomy [3]. A study conducted by Bahin., *et al.* on 884 LST treated with EMR, found the same risk factors for RRA and showed a 10.1 - 11.7% of primary RRA at 4 months endoscopic controls. A second control was run out at 12 months, but the authors did not mention the RRA at this time [8]. These data confirm that primary RRA are inclining to arise rapidly and, interestingly, when it happens, there is a considerable higher risk of re-recurrence, as also reported in our experience. Here we confirm that EMR can be broadly considered an effective treatment of endoscopic adenomas but, if it fails to be radical at first intention, there is a considerable risk of repetitive failures, as also shown by Kim HG., *et al*, that analyzed 64 consecutive patients with recurrent lesions after initial piecemeal EMR of nonpedunculated adenomas > 2 cm, finding a 34% of second recurrences and, after a second treatment by EMR, a 20% of third recurrences [9]. At the end of our study, three patients underwent curative surgery, whereas the others obtained eradication by endoscopy but at the cost of seriated EMR. A systematic review and large metanalysis by Belderbos TD., *et al.* found piecemeal resection (versus en bloc) as the only independent risk factor for recurrence (3% versus 20%) [10]. In light of all these results, in case of lesions with *a priori* high risk of RRA, endoscopic submucosal dissection (ESD) should be considered an alternative treatment to EMR, because it enables the removal "en bloc" of large flat lesions, thus reducing RRA and also efficaciously preventing the submucosal invasion. ESD is also undoubtedly preferable to EMR when, after injection, there is no positive lifting sign [1,11]. Moreover, Saito Y., *et al.* obtained better outcomes with ESD versus EMR in case of LST-G exceeding 30 mm and LST-NG exceeding 20 mm [12], even if in our experience EMR proved to be safe and effective in these cases too. ESD is widely used in Eastern countries, but the procedure usually takes sensibly longer times than EMR and can be burdened with major complications like perforation and bleeding in percentages that reach respectively 14% and 2.2% versus only 0.8% and 1.7% observed in EMR [13,14]. All considered, an evaluation of cost-effectiveness must be done case by case and, for sure, ESD should be restricted to highly experienced Centres, for those cases not treatable with EMR or at high risk of RRA or when a deep submucosal invasion is highly suspected. With respect to this last point, surgery remains the natural competitor of ESD and comparative studies shows similar results as to disease control rates, with generally less serious morbidity with the endoscopic treatment. For this reason, in the absence of clear endoscopic signs of deep neoplastic invasion, surgery is usually chosen as rescue therapy after EMR/ESD if histological examination shows negative prognostic signs, like submucosal invasion ≥ 1000 μm, positive lymph vascular invasion, positive vertical/horizontal margins of the resected lesion [15]. In our study, we have decided to perform or not EMR based on the evaluation of the macroscopic aspect of the lesions, applying NICE and Kudo classifications. It has been demonstrated that in white light vision, neoplastic lesions (adenoma and adenocarcinoma) and hyperplastic polyps can be distinguished with a sensitivity, specificity and diagnostic accuracy around 80-82%, while NBI system and chromoendoscopy for pit pattern definition reach higher and similar sensitivity, specificity and accuracy, respectively of 95.7%, 87.5%, 92.7% [16,17]. In this study we confirm that capillary network analysis and pit pattern evaluation are easily applicable by expert endoscopists, highly reproducible and trustworthy for decision making because we had low rates of "rescue surgery", all occurring in Kudo classes IIIL/IV and V, that are known to be diagnostic of high dysplasia and early cancer lesions [5].

Conclusions

EMR is a safe and effective technique, particularly for lesions removable "en-bloc". The RRA-risk post- "piecemeal" EMR was the same of literature. Moreover, RRA seems to be ever early, suggesting a close follow-up only in the first period. The analysis of a larger number of patients and larger size of polyps would be useful to combine different endoscopic and histological parameters to produce a predictive model to better plan treatment and surveillance.

Conflict of Interest

The authors declare no conflict of interest.

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