

Endoscopic treatment of superficial colorectal neoplasms. Retrospective analysis of a single center technique and results

G. ACQUISTAPACE¹, F. MATERNINI¹, L. SNIDER², O. BELLINI², P. MOGLIA¹, P. CAPRETTI¹

SUMMARY: Endoscopic treatment of superficial colorectal neoplasms. Retrospective analysis of a single center technique and results.

G. ACQUISTAPACE, F. MATERNINI, L. SNIDER, O. BELLINI, P. MOGLIA, P. CAPRETTI

Endoscopic Submucosal Dissection (ESD) is a technique developed in Japan for “en bloc” resection of larger superficial neoplasms of the gastrointestinal tract as an alternative to the traditional Endoscopic Mucosal Resection (EMR), with removal of the lesion in multiple fragments (“piecemeal”). ESD offers a lower recurrence rate and allows a more accurate histopathological examination. This procedure is however considered technically difficult and therefore requires an adequate learning curve, it is time consuming with more discomfort for the patient, it has a higher complication rate, it is more expensive. To overcome these disadvantages, in the Western countries a hybrid technique called Circumferential Submucosal Incision - Endoscopic Mucosal Resection (CSI-EMR) has been developed and is especially employed for colonic lesions.

This article analyzes retrospectively the results obtained in a single centre by a single operator in the treatment of 23 patients (12 men and 11 women, average age 65,6 years), all suffering from superficial, larger than ≥ 20 mm colorectal neoplasms: 9 were treated with ESD for rectal lesions and 14 were treated with CSI-EMR for colonic lesions.

Findings show a technical success rate of 66,6% for ESD and 78,5% for CSI-EM, and a 0% recurrence rate during follow-up, 4,3% bleeding and 13% perforation complications. The histology of the removed lesions showed 13 (56,5%) low grade dysplasia adenomas, 8 (34,7%) high grade dysplasia adenomas, one grade 1 sigmoid colon adenocarcinoma infiltrating the submucosal layer without lymphovascular invasion, with free margins (R0), treated conservatively, and one grade 1 cecum adenocarcinoma, infiltrating the submucosal layer, with lymphovascular invasion and involved excision margin, treated surgically with no residual neoplastic disease in the surgical specimen.

These data are in line with the most significant ones in literature, except for the higher complication rate, which the authors ascribe to the “learning curve” and the smaller number of treated patients.

KEY WORDS: Superficial colorectal neoplasms - Endoscopic submucosal dissection (ESD) - Circumferential submucosal incision with endoscopic mucosal resection (CSI-EMR).

Introduction

Endoscopic removal is the treatment of choice for superficial colorectal neoplasms, the resection of which is essential for secondary prevention of colorectal cancer (1).

These superficial lesions may have a polypoid or non-polypoid morphology, and are nowadays defined according to the Paris-Kyoto classification (2, 3). How-

ever, recent data (4) show a significant incidence of cancer even in patients that have already been endoscopically treated for superficial neoplastic lesions. It is estimated that over one fourth of these neoplasms develops just because of inadequate resection techniques.

Endoscopic Mucosal Resection (EMR) is the technique of choice for the removal of mucosal and submucosal gastrointestinal neoplasms.

The majority of endoscopically diagnosed large bowel lesions are smaller than 20 mm and their complete one-piece (“en bloc”) resection with a diathermic snare, with or without base infiltration, is not too difficult.

Problems arise, however, for lesions larger than 20 mm when size and, at times, location do not allow “en bloc” resection with the usual diathermic snare. In these cases endoscopists make do with multiple fragment (“piecemeal”) resections. Unfortunately “piecemeal” resections, compared to “en bloc” resections, expose to

¹ General Surgery Department, Sant'Anna Hospital, Como, Italy
² Endoscopy Unit, Sant'Anna Hospital Como, Como, Italy

Corresponding author: Francesca Maternini,
e-mail: francesca.maternini@hsacom.org

© Copyright 2015, CIC Edizioni Internazionali, Roma

a higher risk of incomplete removal of the lesion with resulting higher recurrence rate. Moreover the polyp fragmentation of high grade dysplasia lesions does not allow the pathologist to assess the depth of submucosal invasion, which is decisive in differentiating superficial intramucosal neoplasms from superficial infiltrating ones. This often leads patients to surgery, which often proves to be an overtreatment.

This heartfelt need to radically remove (R0) superficial, larger than 20 mm neoplastic lesions in one piece gave rise to a new resection technique called Endoscopic Submucosal Dissection (ESD), evolution of EMR, which fully satisfies the typical surgical concept of sublesional tissue dissection. ESD was used for the first time in 1998 by Hosokawa at the National Cancer Center Hospital in Tokyo to treat an early gastric cancer (5) and later, thanks to the development of specific accessories, was applied to esophagus, rectum and, finally, large bowel. Unlike EMR, the endoscopist uses dedicated diathermic knives instead of a snare to make a mucosal perilesional incision and then progressively dissect the sublesional submucosa, after infiltrating the latter with various solutions to lift the neoplasm.

However, in spite of the undeniable advantages of “en bloc” removal of large superficial colorectal neoplasms, ESD has also some disadvantages compared to EMR such as: 1) it's a complex procedure, requiring an adequate learning curve at qualified centers, on animal models and with tutor supervision; 2) it's time consuming, taking up to 240 minutes for lesions larger than 50 mm, with notable discomfort for the patient, which often requires deep sedation or general anesthesia; 3) the complication rate, first of all perforation, is higher (6, 7); 4) it's more expensive.

For these reasons, a hybrid technique called Circumferential Submucosal Incision - Endoscopic Mucosal Resection (CSI-EMR) is gaining popularity, especially in Western countries. It consists of mucosal and submucosal perilesional incision with the knives used for classic ESD, thus creating a groove, which allows the diathermic snare to remove the lesion “en bloc”.

In a recent Australian study by Moss et al. carried out on animal models with sessile colonic lesions with an average size of 40 mm, CSI-EMR proved to be superior to EMR in terms of resection and complication rates (8). Another study by Sakamoto et al. carried out on 20-40 mm large lesions demonstrated that CSI-EMR has the same efficacy as ESD, but with lower procedure times and complication rates (9).

It can be therefore concluded that the advantages of circumferential incision are multiple: lower risk of incomplete resection and subsequent recurrence, simpler and time saving technique for an expert endoscopist, lower complication rate, adequate specimen for an optimal histopathological examination.

Patients and methods

Between October 2010 and March 2014 23 patients were treated at Sant'Anna Hospital in Como (Italy): 11 women and 12 men, average age of 65.6 yrs [51-89], with superficial neoplasms of average size of 25 mm [20-38]. Procedures were 9 rectal ESD and 14 colonic CSI-EMR (6 sigmoid colon, 1 ascending colon, 7 cecum).

Inclusion criteria were: lesions of size ≥ 20 mm, classified as 0-Is or 0-II according to the Paris-Kyoto classification, with pit pattern (evaluated with the use of high-magnification digitally enhanced endoscopes) included between type II and IV and removed “en bloc” with ESD or CSI-EMR.

Regarding the technique, rectal superficial lesions were excised with ESD, while colonic ones were removed with CSI-EMR. Since the beginning of 2013 Hook.Knife and IT.Knife (Olympus) have been used, the latter later substituted by SB Junior Knife (Sumitomo Bakelite). The diathermic snare used to complete the CSI-EMR was chosen according to the morphology of the lesion. Glycerol was used for submucosal infiltration until the end of 2012, later substituted by hydroxypropyl methylcellulose for longer lasting lifting effect. At the end of the excision, mucosal margins were treated with argon plasma coagulation. In the end specimens were mounted on styrofoam frames and sent to the anatomopathologists.

Results

The purpose of this retrospective analysis is to evaluate the effectiveness of ESD and CSI-EMR in the treatment of superficial colorectal lesions, that cannot be removed with traditional EMR because of their size. In this regard the following results have been evaluated:

1. histopathological diagnosis;
2. technical success rate (lateral and deep tumor free margins, R0);
3. clinical success rate (% of recurrence) evaluated through an endoscopic control after 30 days and scar biopsy in all cases;
4. complications;
5. follow-up.

• *Histopathological diagnosis:* 13 low grade dysplasia adenomas (56,5%); 8 high grade dysplasia adenomas (34,7%); one sigmoid colon grade 1 adenocarcinoma, infiltrating the submucosal layer, without lymphovascular invasion, with free margins (R0) in a 89 yrs old patient with whom an endoscopic surveillance at 3, 6 and 12 months together with a CT scan at 3 months were agreed upon; one cecum grade 1 adenocarcinoma, infiltrating

the submucosal layer, with lymphovascular invasion and involved excision margin. A right hemicolectomy was performed and no residual neoplastic tissue, nor lymph-nodal metastases were found in the surgical specimen.

- *Technical success rate:* ESD 66,6% (6/9), CSI-EMR 78,5% (11/14).

- *Clinical success rate:* absence of residual adenomatous tissue in 100% of cases.

- *Complications:* 1 delayed cecum bleeding case (4,3%), effectively treated endoscopically on the same evening, without need for blood transfusions; 3 perforations cases (13%), 2 of which were cecum perforations, immediately closed with clips, patients discharged after 5 days, asymptomatic; the third was a sigmoid perforation, immediately closed with clips, who, however, in the evening showed signs of peritonitis and required a laparoscopy, the positioning of more clips on the serosal side and a surgical drain, patient discharged after 7 days, asymptomatic.

- *Follow-up:* after the first negative endoscopic control after 30 days, our follow-up protocol plans a colonoscopy after 1 and after 3 years. This is the most common follow-up scheme reported in literature (10), even if an optimal surveillance timing after excision of large colorectal polyps has not yet been defined.

Colonoscopy after 1 year on 15 patients is negative for recurrence. Colonoscopy after 3 years on 4 patients is still negative for recurrence, with the finding of 2 tubular adenomas, smaller than 10 mm, in two patients.

Discussion

The majority of published articles regards retrospective studies, carried out in a single center, by a single operator, without any rigorous “intention to treat” method and often without adequate follow-up data; our study is no exception.

Thus the choice of studies to refer to was carried out on the base of the Authors’ experience, not coincidentally mostly Japanese (11).

Summary Table 1 of the main studies on colorectal ESD

The higher complication rate reported by our study, compared to literature, is the price ascribed to the “learning curve”. As a matter of fact all of them occurred in the first two years, and ultimately only one perforation case needed surgery, which was minimally invasive.

In the light of our experience, we believe that the hydroxypropyl methylcellulose longer lasting lifting effect, the use of SB Junior Knife for sublesional dissection and, of course, the endoscopist’s longer standing experience are key factors in the prevention of complications.

The other sobering fact was our recurrence rate, substantially in line with literature, despite the lower radical (R0) resection rate. We believe that this is due to: 1) argon plasma treatment of the mucosal resection margins; 2) erosion of the mucosal perilesional margins secondary to the coming and going of electrified instruments during the sublesional dissection.

In closing, our follow-up was too short and the number of patients too small to allow us definitive conclusions. However we’d like to point out that after both ESD for rectal lesions and CSI-EMR for colonic lesions there was no recurrence in long term controls, reflecting the equal effectiveness of the two methods in the hands of a single endoscopist.

Conclusion

Endoscopic submucosal resection is a complex, risky, operator-dependent, expensive procedure and we are still far from being able to standardize it as a large scale, reproducible treatment for all large superficial colorectal lesions. Despite these limitations, ESD and its variation CSI-EMR are gaining increasing popularity even in Western countries as promising alternatives to traditional surgery for the treatment of large flat colorectal neoplasms. Even in our series, the 8 patients with high grade dysplasia adenomas (34,7%) would have very likely be subjected to a surgical overtreatment, if they had undergone a traditional endoscopic “piecemeal” mucosectomy.

TABLE 1 - SUMMARY OF THE MAIN STUDIES ON COLORECTAL ESD.

Authors	Number of lesions	% R0 resections	% recurrence	% bleeding	% perforations
Tanaka et al.	70	-	-	1,4%(1)	10% (10)
Saito et al.	200	83%	0%	0,5% (1)	5% (10)
Repici et al.	20	90%	-	0%	10% (2)
Kabayashi et al.	28	93%	0%	-	-
Hayashi et al.	267	95,9%	2,25%	0%	5,6%
Acquistapace et al.	23	66,6% rectum 78,5% colon	0%	4,3% (1)	13% (3)

References

1. Winaver SJ, Zauber AG, Ho MN, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup. *N. Engl J Med.* 1993;329:1977-81.
2. The Paris endoscopic classification of superficial neoplastic lesions: esophagus, stomach and colon. The Paris Workshop. *Gastrointest Endosc.* 2003;58(Supp 6):S3-S27.
3. Kudo S, Lambert R, Allen J, et al. Nonpolypoid neoplastic lesions of the colorectal mucosa. *Gastrointest Endosc.* 2008;68(4):S3-S47.
4. Luigiano C, Consolo P, Scaffidi MC, et al. Endoscopic mucosal resection of large and giant sessile and flat colorectal polyps: a single-center experience with long-term follow-up. *Endoscopy.* 2009;41:829-835.
5. Hosokawa K, Yoshida S. Recent advances in endoscopic mucosal resection for early gastric cancer. *JPN J Cancer Chemoter.* 1998;25:483.
6. Saito Y, Fukuzawa M, Matsuda T, et al. Clinical outcome of endoscopic mucosal resection of large colorectal tumors as determined by curative resection. *Surg Endosc.* 2010 Feb;24(2):343-352.
7. Kabayashi N, Yoshitake N, Hirahara Y, et al. A matched case-control study comparing Endoscopic Submucosal Dissection and Endoscopic Mucosal Resection for colorectal tumors. *J Gastroenterol Hepatol.* 2011 Oct;17.
8. Moss A, Bourke MJ, Tran K, et al. Lesion isolation by circumferential submucosal incision prior to endoscopic mucosal resection (CSI-EMR) substantially improves en-bloc resection rates for 40mm colonic lesions. *Endoscopy.* May 2010;42(5):400-404.
9. Sakamoto T, Matsuda T, Nakajima T, Saito Y. Efficacy of endoscopic mucosal resection with circumferential incision for patients with large colorectal tumors. *Clin Gastroenterol Hepatol.* 2012;10(1):22-26.
10. Kaltenbach T, Soetikno R. Endoscopic resection of large colon polyps. *Gastrointest Endoscopy Clin N Am.* 2013;23:137-152.
11. Angeletti S, D'Ambra G, Cipolletta F. Risultati a lungo termine della EMR e ESD nel tratto digestivo inferiore. *Gior Ital End Dig.* 2010;33:29-33.