Transanal endoscopic microsurgery after endoscopic resection of malignant rectal polyps: a useful technique for indication to radical treatment

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Abstract
Background
Management of malignant rectal polyps (MRPs) after endoscopic polypectomy (EP) is still debated. It is sometimes difficult to decide whether to simply follow-up (FU) or to treat such a removed lesion. Transanal endoscopic microsurgery (TEM) could have a role both in T staging and in treating MRPs after EP.
Methods
Patients who underwent a full-thickness TEM within 3 months after an EP between January 2008 and October 2012 were retrospectively analyzed. If post-TEM histology showed locally advanced rectal cancer, patients underwent a total mesorectal excision (TME) within 4–6 weeks. Patients without malignant disease or pT1sm1 cancers at post-TEM histology were followed up every 3 months for 2 years with clinical examination, flexible rectal endoscopy, and neoplastic markers monitoring.
Results
A total of 39 patients were included. Post-EP histology was adenocarcinoma in 27/39 cases (69.2 %) and adenoma in 12/39. Mean operative time was 64.2 min; no 30-day mortality occurred; 30-day morbidity was 2.7 % (rectal bleeding in 1/39 cases). Post-TEM histology showed a T2 cancer in 5/39 patients, four with and one without a previous cancer diagnosis, who were further treated by TME (four RARs and one APR) and are disease free with a mean FU of 24.2 months. Post-TEM histology showed adenoma in 10/39 cases and fibrosis in 24/39. These patients are disease free with a mean FU of 13 months.
Conclusions
A full-thickness TEM after EP of MRPs can establish the presence of residual malignant disease and its depth of invasion, precisely defining the indication to TME. In event of benign post-EP histology, TEM must be performed in presence of macroscopic residual disease, in order to obtain an RO resection and finally exclude cancer, while, in absence of macroscopic residual disease, only close FU is required.
Keywords
Rectal polyps Endoscopic mucosal resection Transanal endoscopic microsurgery Total mesorectal excision

Colorectal cancer (CRC) represents the most frequently diagnosed neoplasm in Europe (436,000 new cases/year, i.e. 13.6 % of diagnosed tumors) [*1*] and accounts for 8 % of deaths for neoplasm in the world and 12.2 % in Europe [*2*]. With the introduction of a screening program, the incidence of early CRC increased. Early CRC is defined as a tumor extended to the mucosal or submucosal layer (pT1 according to the TNM classification). The Paris classification [*3*] further sub-stages this kind of tumor, as originally suggested by Haggitt et al. [*4*] and Kikuchi et al. [*5*], to define more accurately the risk of recurrence and lymphatic dissemination in peduncolated and sessile lesions, respectively [*6*]. For pedunculated carcinomas, the classification includes four levels of invasion; level 4 lesions (which extend beyond the polyp stalk but do not invade the muscularis propria) are predictive of negative patient outcome [*4*]. For sessile lesions, Kikuchi et al. defined three levels of

submucosal invasion, split into superficial (sm1), middle (sm2), and deep (sm3) thirds of the submucosa. The frequency of lymph node metastases is proportional to the degree of depth being 2, 8, and 23 %, respectively [*6*]. The Paris classification [*3*], revised in Kyoto in 2008 [*7*], defines every lesion extended no more than 1 mm in the submucosal layer as 'sm1'. Forty percent of CRCs are located in the rectum. Rectal polyps can be removed either by endoscopic resection, with endoscopic mucosal resection (EMR) [*8*] or endoscopic submucosal dissection (ESD) [*9*], or by transanal endoscopic microsurgery (TEM) [*10*]. Pathological examination of the specimen should identify the presence of cancer cells and assess if local excision has been curative or requires surgical radicalization by total mesorectal excision (TME) [*11*]. This is not so easy, especially after endoscopic resection, because it is sometimes impossible to define the level of submucosal invasion, lymphatic and vascular invasion, budding, and other risk factors for local recurrence [*5*, *12–14*].

Management of malignant rectal polyps (MRPs) after endoscopic resection is still debated. The key point is to obtain an accurate pathological definition of T stage and risk factors. Full-thickness TEM provides the pathologist with an adequate specimen to define T stage and submucosal extension. Therefore, TEM could have a role, both curative and diagnostic, in treating MRPs after endoscopic resection. The aim of this study was to assess the results of TEM after incomplete endoscopic polypectomy in terms of residual disease, recurrence, and need of further surgery.

Methods

A prospectively maintained rectal database was searched for all patients who underwent TEM between January 2008 and October 2012. The present study included all patients undergoing TEM within 3 months after rectal endoscopic polypectomy either after partial polypectomy (macroscopic residual disease confirmed by rigid rectal endoscopy and multiple biopsies) or complete endoscopic resection. Every lesion was removed by EMR, piece meal in the majority of the cases. In presence of macroscopic residual disease, both benign and malignant lesions underwent TEM, while after a complete endoscopic excision only MRPs or high-grade dysplasia (HGD) adenomas were further treated by TEM. Preoperative assessment included rectal digital examination, complete colonoscopy, rigid rectal endoscopy and endorectal ultrasonography (EUS). Under general anesthesia, a full thickness TEM was performed and the rectal wall defect always repaired with an absorbable monofilament running suture secured with silver clips [*15*].

On the basis of post-TEM histology, patients fit for surgery with locally advanced rectal cancer underwent radical abdominal surgery by TME, either rectal anterior resection (RAR) or abdominoperineal resection (APR). When TEM excision was considered radical (no residual malignant disease or pT1sm1 cancers), patients were followed-up every 3 months for 2 years, with clinical examination, flexible rectal endoscopy, and monitoring of neoplastic markers.

Statistical analysis included analysis of patients' characteristics and assessment of rate of recurrence after treatment. Analysis was conducted according to the intention-to-treat principle, in order to assess the efficacy of TEM after polypectomy.

Results

Between January 2008 and October 2012, a total of 238 TEM were performed at the Department of Surgical Sciences, University of Turin, Turin, Italy. Of 238 patients, 39 underwent TEM to further treat a rectal neoplasm after an endoscopic polypectomy performed within the previous 3 months (median 2.8; range 0.8–3). Patients' characteristics are summarized in Table 1. Mean age was 67.7 ± 10 years (range 41–84); mean distance of the inferior margin of the lesion or scar from the anal verge was 7.41 ± 2.58 cm (range 2–15). After endoscopic polypectomy, 27/39 cases (69.2 %)

had a diagnosis of adenocarcinoma, 21 of which (53.8 %) with residual macroscopic disease; 12/39 (30.8 %) had a diagnosis of HGD or low-grade dysplasia (LGD) adenoma, nine of which (23.1 %) with residual macroscopic disease. Patients with an MRP underwent TEM because (i) it was not possible to define staging in ten cases, due to a piece-meal excision; (ii) it was not possible to define the deep margin in 11 cases; and (iii) there was gross residual disease in six cases. Patients with a diagnosis of adenoma underwent TEM because of a previous piece-meal removal in three cases and because there was gross residual disease in nine cases. A total of 22 patients (56.4 %) underwent a pre-operative EUS. In the remaining patients, EUS was not performed because in 12 cases residual disease was macroscopically clear and because in five cases inflammation induced by the recent endoscopic procedure would have made the exam unreliable. Correspondence rate between ultrasonographic (uT) and pathological (pT) stage was 54.5 % with an understaging rate of 13.6 % (Table 2). Mean operative time was 64.2 ± 31.2 min (range 25–150). Peritoneal opening occurred in one case, but was immediately sutured without complications; neither conversion to abdominal surgery nor diverting stoma was necessary. No meaningful bleeding occurred, no intra- or postoperative blood transfusions were necessary. No 30-day mortality occurred, while 30-day morbidity was 2.7 %; 1/39 cases developed a grade IIIa complication according to Dindo–Clavien's classification [*16*] consisting of rectal bleeding 10 days after surgery, successfully treated by endoscopic clip positioning. Mean postoperative stay was 4.1 ± 1.2 days (range 2–7).

Table 1

Patient characteristics in relation to histological examination

Patients	**Total (N = 39)**	**Post-EMR histology**	
		Malignant disease (N = 27)	**Benign disease (N = 12)**
Sex			
Male	22 (56.4)	17 (63)	5 (41.6)
Female	17 (43.6)	10 (37)	7 (58.4)
Age (years)	67.7 ± 10	68.1 ± 9.3	66.8 ± 11.8
Polyp distance from the anal verge (cm)	7.41 ± 2.58	7.76 ± 2.27	6.63 ± 3.12
Macroscopic residual disease			
Yes	30 (76.9)	21 (77.7)	9 (75)
No	9 (23.1)	6 (22.3)	3 (25)
Post-TEM histology			
Adenoma	10 (25.6)	4 (14.8)	6 (50)
HGD	8 (20.5)	4 (14.8)	4 (33.3)
LGD	2 (5.1)	0	2 (16.7)
Carcinoma	5 (12.9)	4 (14.8)	1 (8.4)
T1	0	0	0
T2	5 (12.9)	4 (14.8)	1 (8.4)
Fibrosis	24 (61.5)	19 (70.4)	5 (41.6)

Data are presented as n (%) or mean ± SD

EMR endoscopic mucosal resection, HGD high-grade dysplasia, LGD low-grade dysplasia, TEM transanal endoscopic microsurgery, SD standard deviation

Table 2
Correspondence between ultrasonographic stage (uT) and pathological stage (pT) in patients who underwent endoscopic polypectomy

	Pathological stage								
	Fibrosis	**pT0**	**pT1**	**pT2**	**pT3**	**Tot**	**CR (%)**	**Overstaging (%)**	**Understaging (%)**
Ultrasonographic stage									
Fibrosis	8	2	0	0	0	10	80	0	20
uT0	1	3	0	0	1	5	60	20	20
uT1	3	0	0	0	0	3	0	100	0
uT2	0	1	0	1	0	2	50	50	0
uT3	0	2	0	0	0	2	0	100	0
Total	12	8	0	1	1	22	54.5	31.9	13.6

CR correspondence rate

Post-TEM histology revealed in 100 % of cases a lateral margin >3 mm and full-thickness excision in every specimen. Among the 27 patients with previous cancer diagnosis, four (14.9 %) had a pT2 cancer at post-TEM histology; two patients had residual and two did not have residual macroscopic disease after polypectomy. These four patients underwent salvage surgery by TME (three RAR and one APR). Post-TEM histology showed HGD adenoma in 4/27 (14.9 %) cases (one with and three without residual macroscopic disease after polypectomy) and fibrotic tissue in 19 cases (70.2 %), three with and 16 without residual macroscopic disease after polypectomy. Among the 12 patients with previous adenoma diagnosis, the three without residual macroscopic disease after polypectomy (25 %) had fibrotic tissue at post-TEM histology, while the nine with residual macroscopic disease (75 %) had fibrotic tissue in two cases (16.7 %), LGD adenoma in two cases (16.7 %), HGD adenoma in four cases (33.3 %), and pT2 cancer in one case (8.3 %), further treated by TME (RAR) (Table 3). Mean follow-up (FU) was 14.3 ± 13.4 months (range 6–49). In the five cases who underwent radical abdominal surgery, mean time between TEM and TME was 30 days. All patients are disease free at 8, 22, 29, 30, and 32 months, respectively, from the abdominal operation. Pathological examination of the five specimens showed neither residual disease nor lymph node metastasis. All patients with a previous diagnosis of cancer but a post-TEM histology negative for malignant residual disease (23/39) are disease free, with a mean FU of 12.9 ± 12.3 months (range 6–43). All patients (10/39) with a post-TEM histology of adenoma, four of whom had a previous cancer diagnosis, are disease free, with a mean FU of 13.2 ± 13.0 months (range 6–41).

Table 3
Accordance between post-endoscopic mucosal resection (EMR) histology and post-transanal endoscopic microsurgery (TEM) histology, considering the presence or not of macroscopic residual disease (MRD)

	Post-TEM histology				
Post-EMR histology	**Cancer**	**Adenoma**	**Fibrosis**	**Total**	**Accordance rate (%)**
No MRD cancer	2	3	16	21	9.5
MRD cancer	2	1	3	6	33.3
No MRD adenoma	0	0	3	3	0
MRD adenoma	1	6	2	9	66.6
Total	5	10	24	39	15.4

Discussion

Management of malignant colorectal polyps (MCPs) after endoscopic polypectomy is still largely debated. It is sometimes difficult to decide whether to simply FU or to treat an endoscopically removed lesion. For rectal polyps, representing about 35 % of MCPs, there is a high risk of morbidity if abdominal surgery is chosen, with about 8 % of anastomotic leakage in RAR [*17*]. Accurate staging and assessment of risk factor for local recurrence and lymph node metastasis should be obtained on every specimen. Gill et al. [*18*] in a large retrospective analysis of MCPs in the UK, showed that a clear resection margin from 0.1 mm appears sufficient to avoid surgery, but locally advanced T1 lesions [*3*], [*4*]) have a greater risk of residual cancer and lymph node metastases found at surgery [*18*]. In this series, 76.7 % of patients having surgery had no residual tumor in the specimen after an initial local excision. Butte et al. [*19*] retrospectively analyzed 143 colectomies performed after polypectomy for MCPs, finding residual invasive disease in the colon wall and lymph node in 11 and 7 %, respectively, of patients following gross complete polypectomy. Positive (<1 mm) or unknown polypectomy margins were associated with residual disease in the colonic wall, and lymphovascular invasion was associated with lymph node metastases. Kim et al. [*20*] published a series of 85 radicalized polypectomy (23.5 % for rectal polyps), showing that positive vertical margin (>pT1sm1) and inadequate lifting sign could be predictors of the presence of residual tumor or lymph node metastases in surgical specimens after non-curative endoscopic resection for early CRC.

This study analyzes the role of TEM in the management of MRPs. In our series, TEM allowed an accurate staging in 100 % of lesions after EMR with no 30-day mortality and a very low morbidity rate. Correct staging provides the certainty of having or not having radically treated every polyp, reserving radical surgery for only high-risk neoplasms. TEM does not jeopardize the oncological quality of a delayed TME if performed within 4–6 weeks [*21*]. In our series, only 4/27 patients with a previous cancer diagnosis (14.9 %) needed a TME for a T2 cancer, in line with the literature. It is very interesting that 1/9 patients with a previous adenoma diagnosis and macroscopic residual disease (11.1 %) had a locally advanced rectal cancer: 85 % of patients avoided unnecessary major abdominal surgery, that was mandatory in the unexpected case. On the other hand, benign rectal lesions completely removed by EMR (3/12) did not have residual disease on post-TEM histology, showing that, in the absence of macroscopic residual disease, neither HGD nor LGD rectal adenomas need further treatment, but only close FU.

No risk factors for locally advanced rectal cancer reached statistical significance in our series, probably due to the small number of cases. In particular, macroscopic residual disease in the presence of cancer cells does not affect tumor depth of invasion.

The correct way to assess the indication for radical surgery is to verify the grade of involvement of the submucosal layer. Unfortunately, this is not possible when, as in our series, specimens are removed by piecemeal EMR, because this is technically difficult and rarely assessed by routine pathology examination. We would have liked to review these data, but the majority of polypectomies were performed at centers other than ours. It must be said that ESD might overcome this limitation, defining submucosal involvement more precisely. Nevertheless, ESD is rarely performed in Europe as it is considered technically challenging, while it is affected by a consistent rate of complications (29.2 %) and allows a rate of R0 resections of no more than 72.9 % of cases [*22*]. Considering our data, it would be advisable to resect rectal polyps >2 cm directly by TEM, in order to obtain a correct T stage and possibly a radical minimally invasive treatment. Nevertheless, even after EMR, TEM represents a useful procedure either in staging or in treating MRPs.

Conclusions

Decision making regarding MRPs after endoscopic resection is challenging. TME is a major surgical procedure, with high morbidity rates, that could be avoided in 85 % of patients with MRPs. A full-thickness rectal wall excision by TEM following polypectomy allows the definition of the presence of residual disease and the depth of invasion, thus establishing a correct indication for further TME. Conversely, only strict FU is recommended for endoscopically removed benign lesions in the absence of macroscopic residual disease.

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