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Local Excision of Early Rectal Cancer by Transanal Endoscopic Microsurgery (TEM): The 23-Year Experience of a Single Centre

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Abstract

Aim: Transanal endoscopic microsurgery (TEM) is an effective, minimally invasive alternative approach to traditional surgery. This study reviews the characteristics of a series of patients affected by early rectal cancer and discusses the results of this treatment. Methods: From 1992 to 2014, 187 patients with rectal cancer staged as pT1 by preoperative endorectal ultrasound, computerized tomography and/or magnetic resonance imaging were treated by TEM at our institution. We analysed age, gender, size of lesion, distance from the anal verge, histological grading and stage. Furthermore we considered operative time, intra and post-operative complications and hospital stay. Patients were also enrolled in a tight follow-up for recurrence and survival. Results: There were no intraoperative complications or conversions to other procedures. There were minor complications (partial suture dehiscence, stool incontinence, rectal haemorrhage) in 24 patients (12.8%) and a major complication (perianal phlegmon) in one (1.5%). Two (5%) of the 40 patients with pT3 disease before neoadjuvant therapy experienced a local recurrence and one (2.5%) died for metastasis. Conclusion: TEM is a safe technique characterized by low morbidity and mortality and excellent oncological outcomes. These advantages, coupled with its ability to be applied to a strikingly high proportion of rectal tumours, suggest that it should be considered as the gold standard approach to early rectal cancer in accurately selected patients.

Keywords

Transanal Endoscopic Microsurgery, Rectal Cancer

1. Introduction

Over the past few years, rectal cancer surgery has progressed at a fast pace, culminating in the development of

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minimally invasive local excision techniques. The evolution has benefited from concurrent advances in diagnostic imaging like transanal endoscopic ultrasound (EUS), computed tomography (CT) and magnetic resonance imaging (MRI)—which have been providing increasingly accurate preoperative staging—as well as in non-surgical approaches, chiefly radiotherapy (RT) and chemotherapy. However, despite the effectiveness of the latter approaches, surgery remains the gold standard treatment for rectal cancer, and minimally invasive techniques have become its mainstay.

Transanal endoscopic microsurgery (TEM) was developed by Gerhard Buess in 1983 [1]; 30 years on it is still considered as an innovative technique that affords radical yet minimally invasive tumour excision in selected patients.

The current point of view is to consider local excision curative in T1 N0 rectal cancer without high risk features [2] and TEM, as we stated in our previous works, can be considered the best choice in these tumors [3]-[5].

Aim of this study was to validate this assumption, showing our results in a large series of selected patients with early rectal cancer treated by TEM at a single centre and demonstrate the feasibility and safeness of this surgery and its oncological outcomes.

2. Patients and Methods

From February 1992 to September 2014, 187 patients affected by rectal adenocarcinoma underwent TEM at our institution.

The selection criteria of the patients were adenocarcinoma staged preoperatively as T1 N0 M0 with absence of high risk features and lymphovascular invasion [6].

The data collected included age, gender, size of lesion, distance from the anal verge, histological grading, lymphovascular and depth of invasion.

Tumour grade was evaluated according to Broders' classification [7] and the depth of submucosal invasion to the Kikuchi system (Sm1, 2, 3) [8].

Enrolment was based on an accurate preoperative workup that included clinical examination (digital rectal exploration), laboratory testing including tumoral markers (CEA and CA 19.9) and colonoscopy with macrobiopsies to determine tumour grading.

Patients underwent accurate preoperative staging by transanal EUS and thoracic, abdominal and pelvic CT and/or MRI to evaluate tumour risk based on depth of invasion, lymphovascular invasion and differentiation [6] and to exclude those with high-risk tumours.

Rigid rectoscopy provided information on tumour distance from the anal verge, longitudinal extension, and circumferential location. The latter information enables planning the patient's decubitus position, because the TEM equipment is designed to operate from the top down [3]-[5]; accordingly, prone decubitus is required for anterior lesions, the lithotomy position for posterior lesions, and left and right lateral decubitus for right and left lesions, respectively.

Patients with T1-N0 lesions underwent TEM immediately, those with T2 or T3 N0 M0 tumours received first neoadjuvant RT in a 10 - 15 MV linear accelerator according to a standard protocol (daily dose, 180 cGy; total dose, 5040 cGy; 28 fractions over 5 weeks). Since January 1997, patients aged less than 75 years with a good performance status received preoperative chemotherapy with continuous infusion of 5-fluorouracil (200 mg/m^2/d), used as a radiosensitizer; from 2003 they received capecitabine (1650 mg/m^2/d) during RT. Restaging was performed by digital rectal exploration, rectoscopy, transanal EUS, and MRI or CT 30 days after RT. Patients who had achieved downstaging (T1-N0-M0) and had mobile lesions < 3 cm diameter underwent TEM 40 - 50 days after neoadjuvant treatment.

Patients were informed of the oncological risks associated with local excision, *i.e.* of the possibility of local recurrence and distant metastasis, and of the main potential complications of the procedure, *i.e.* bleeding, suture dehiscence, temporary gas or stool incontinence, and possibility of conversion to laparotomy with colon resection and colostomy, and provided their consent.

Preoperative washout of the colon was performed the day before the operation with 4 l of an osmotic laxative. All patients were given short-term antibiotic prophylaxis and were operated on under general anaesthesia.

The patient was placed on the table; than the 12 or 20 cm modified rectoscope with 3D vision and 3 operative channels was inserted, the lesion was located, and the rectoscope was fixed in position with a Martin arm (Wolf, Tuttlingen, Germany), a three-elbowed device attached to the operating table.

The rectum was inflated with CO^2 to achieve dilatation and to determine the most appropriate plane of excision for dissection. Endoluminal pressure was kept around 12 - 15 mmHg and continuously monitored by the endosurgical unit. Full-thickness excision was performed with a margin of at least 1 cm of normal mucosa. The largest possible amount of local perirectal fat was removed. In posterior and lateral lesions the dissection was carried out at the level of the avascular plane of mesorectal fascia, and for posterior lesions at the level of the prostate capsula or of the vaginal septum. The incision was made in such a way as to remove a pyramid-shaped tissue block, with the tip on the side of the lumen, that included perirectal fat and tumour. The rectal defect was closed with an endoluminal running suture [3]-[5]. The surgical specimen was then stretched out and its margins were pinned on cardboard to facilitate microscopic evaluation (**Figure 1**).

The following variables were measured: operative time, intraoperative complications, postoperative complications, the incidence and severity of post-operative pain, hospital stay and recurrence rate.

Follow-up was at 6-month intervals until 24 months, and yearly thereafter.

The data regarding continuous variables are presented as median with the 25th to the 75th percentile in parentheses. The cumulative probability of failure (local recurrence or distant metastasis) and the probability of disease-free survival (DFS) were estimated using the Kaplan-Meier method. A level of 5% was used for statistical significance.

3. Results

Data analysis showed that patients with a preoperative diagnosis of T1 adenocarcinoma (n = 122) were more frequently male (66.4%) and had a median age of 68.3 years (25th - 75th percentile: 60 - 74). Final pathology confirmed a pT1 carcinoma in all 122 patients. Patients with preoperative T2-T3 adenocarcinoma (n = 40) staged as yT1 after neoadjuvant treatment were also more frequently male (57.5%) and had a median age of 69.7 years (25th - 75th percentile: 68 - 73). Final histology disclosed pT1 lesions in 25 more patients (13.6%) who had a preoperative diagnosis of adenoma; these, too, were more frequently male (76%), and had a median age of 67.4 years (25th - 75th percentile: 61.5 - 73.5) (**Table 1**).

The median distance of the tumour from the anal verge was 7.9 cm (25th - 75th percentile: 5 - 10). Median tumour diameter was 5 cm (25th - 75th percentile: 2 - 7) (**Table 2**).

Median operative time was 85 min (25th - 75th percentile: 60 - 120), but in the procedures carried out over the last 4 years it fell to 43 min.

There were neither intraoperative complications nor conversions to other surgical procedures.

Patients were allowed liquids on the first postoperative day and solid food the following day. All were able to walk freely within 12 h of the procedure.

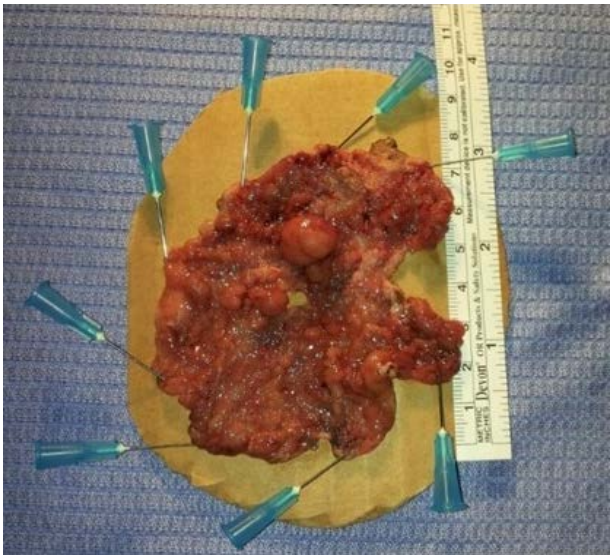

Figure 1. Surgical specimen pinned to cardboard after excision (diameter, 8 cm).

Table 1. Patient characteristics.

Variables	
pT1 (187 patients)	
Preoperative diagnosis of adenoma (n = 25)	
Sex	
Male	19 (76%)
Female	6 (24%)
Age	
Median (25^{th} - 75^{th} percentile)	67.4 (61.5 - 73.5)
Preoperative T1 (n = 122)	
Sex	
Male	81 (66.4%)
Female	41 (33.6%)
Age	
Median (25^{th} - 75^{th} percentile)	68.3 (60 - 74)
Preoperative T2-T3 (n = 40)	
Male	27 (67.5%)
Female	13 (32.5%)
Age	
Median (25^{th} - 75^{th} percentile)	69.7 (68 - 73)

Table 2. Lesions characteristics.

Variables	
Distance from anal verge (cm)	
Median (25^{th} - 75^{th} percentile)	7.9 (5 - 10)
Diameter (cm)	
Median (25^{th} - 75^{th} percentile)	5 (2 - 7)

Median hospital stay was 3 days (25^{th} - 75^{th} percentile: 3 - 4).

Minor complications arose in 24 patients (12.8%) and included partial suture dehiscence in 14 (7.4%), stool incontinence in 3 (1.6%), and rectal haemorrhage in 7 patients (3.7%). Postoperative pain, evaluated according to Numeric Rating Scale (NRS) [9], was minimal and only 12 patients (9%) required analgesics over the first 48 h. Partial suture dehiscence was managed with antibiotics; stool incontinence with physiotherapy and anal sphincter biofeedback, resolving within two months of the operation; and haemorrhage with blood transfusion.

One patient (1.5%) experienced a major complication, a perianal phlegmon, which required a drain and a temporary laparoscopic ileostomy (**Table 3**).

Two patients (5%) with disease stage pT3 before neoadjuvant therapy experienced a local recurrence at 12 and 18 months respectively. They were treated by laparoscopic anterior rectal resection and are tumour-free at 2 and 3 years, respectively.

Twenty-two patients with T1 stage before the operation died from other causes, with a probability of death at the end of follow-up (median 82 month, 25^{th} - 75^{th} percentile: 48 - 144) equal to 47% (95%CI: 21% - 64%) (**Figure 2**).

One patient (2.5%) with tumour stage T2 before RT developed distant metastasis. He underwent adjuvant chemotherapy and died at 2 years from the operation (**Figure 3**).

Table 3. Operative data.

Variables	
Operative time (min)	
Median (25th - 75th percentile)	85 (60 - 120)
R0 resection [no. (%)]	185 (98.9%)
Intraoperative complications	0%
Hospital stay (days)	
Median (25th - 75th percentile)	3 (3 - 4)
Postoperative complications [no (%)]	
Pain	12 (9%)
Partial suture dehiscence	14 (7.4%)
Stool incontinence	3 (1.6%)
Rectal haemorrhage	7 (3.7%)
Perianal phlegmon	1 (0.5%)

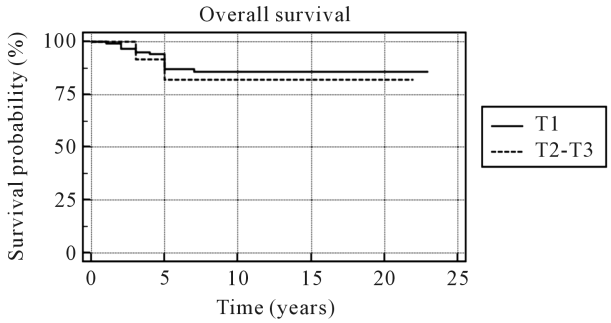

Figure 2. Overall survival.

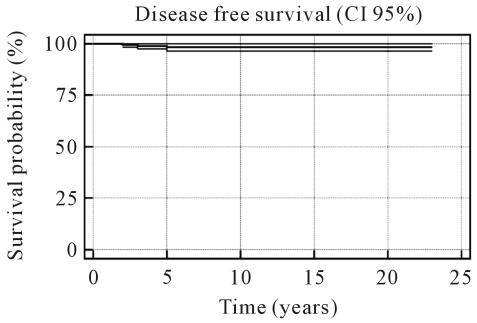

Figure 3. Disease free survival.

4. Discussion

No-surgical operative techniques for early rectal cancer therapy have been introduced over the past few years. They include endoscopic mucosal resection (EMR), piecemeal EMR, and, more recently, endoscopic submucosal dissection (ESD) [10] [11]. They are minimally invasive procedures that can be executed without general anaesthesia. However, they still entail considerable drawbacks and a higher risk of complications [11], chiefly incomplete resection, which involves a high recurrence rate and may negatively affect pathological evaluation of invasion depth, state of resection margins, and vessel invasion; this is especially true of piecemeal EMR [11].

Spreading non-granular tumours (LST-NG) ≥ 20 mm and laterally spreading granular lesions (LST-G) ≥ 20 mm are currently considered as indications for *en bloc* resection of early rectal cancer [11] [12]. According to the literature, *en bloc* resection with EMR can be performed in 66.5% - 80% of tumours, but it is not recommended for lesions > 20 mm. *En bloc* resection with ESD can be performed in 80% - 94.5% of tumours, regardless of lesion size and site, but it is heavily operator-dependent and is greatly affected by patient condition and lesion status. Moreover, even with ESD incomplete vertical resection of a T1 rectal carcinoma makes it difficult for the pathologist to evaluate the tissue specimen [11].

Recurrence rates for *en bloc* resection of malignant lesions vary greatly according to different reports (0% - 14%); however, such estimates do not include the recurrence of adenomatous lesions at the site of endoscopic resection. Incomplete resection with positive lateral or deep tumour margins involves even higher rates (18.4%, 23.1%, and 30.7% at 5, 12, and 24 months, respectively).

Analysis of the latest and largest studies of endoscopic resection discloses that EMR and ESD have in fact been applied to treat a fairly small proportion of rectal cancers [13]-[19]. It is therefore difficult to assess their value in treating rectal malignancies. Moreover endoscopic resection, especially ESD, carries a high risk of perforation (1.4% - 10.4%), both immediate and up to 14 h after the procedure (delayed perforation) and bleeding (5%) [11] [12] [20] [21].

TEM is a safer technique that allows performing complete tumour resection in 98.9% of cases in this study.

TEM affords a magnified 3D binocular vision, which provides a clear view, maximizing the scope for obtaining free margins. Lately high-magnification chromoscopic colonoscopy has become available, but this technique provides 2D vision, and sometimes doesn't allow a direct view of the lesion.

In early rectal cancer patients, TEM provides results that are comparable to open surgery [22], as we stated in previous studies.

Our results show that TEM can reach tumours located in the upper rectum as far as 20 cm from the anal verge, and to excise lesions 2 - 3 cm from the anal ring, where complete endoscopic resection would be difficult to perform. In our series there were only two cases (1.06%) of positive resection margins on pathological examination.

Lesion diameter is not a limitation for TEM, as demonstrated by the successful excision of extensive circumferential lesions in some of our patients. TEM also allows full-thickness excision, *i.e.* removal not limited to mucosal and submucosal layers but extending into perirectal fat, even in cases of very low lesions [3].

Another factor contributing to patient outcome is that surgical specimens removed by TEM afford optimum pathology material, thus providing reliable submucosal invasion information (Sm1, Sm2 and Sm3) to guide in decision-making for further surgical treatment.

No intraoperative complications arose in the present series of 187 patients. However, our experience indicates that even in case of rectal perforation TEM allows to suture the tear without need for emergency surgery.

TEM technique involves fewer postoperative complications, most of which can be managed conservatively (transfusion for bleeding and antibiotic therapy in case of suture dehiscence and fever).

The features discussed above allow achieving excellent oncological outcomes with very low recurrence rates and high disease free survival rates. There were only two local recurrences in our series and one cancer related death.

Several studies have documented a correlation between pathological T-stage and lymphnode involvment. It has been demonstrated that low-risk T1 rectal cancer have a very low rate of lymphnode metastasis which allow to consider TEM a safe procedure [19] [23]-[26]. The indications for TEM have considerably expanded since its introduction, in parallel with technical advances and surgeon experience, but patient accurate preoperative selection is the key element to the successful performance of TEM.

The limitations of TEM include a long surgeon learning curve (over than 50 operations) and the steep cost of the equipment.

Moreover one of the limits of our study is that we presented on a retrospective series and non randomized. Other studies will be necessary to confirm our observations.

TEM has been enabling surgeon to achieve all key treatment goals: complete tumour resection with negative margins, preservation of normal anatomy, minimization of morbidity and mortality, and preservation of sphincter function.

These considerations indicate that TEM could now be considered as the gold standard approach to early rectal cancer in selected patient.

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