Local Excision of Rectal Cancer with Transanal Endoscopic Microsurgery (TEM)

FRANCESCO STIPA1, GIORGIO LUCANDRI1, MARIO FERRI2, GIUSEPPE CASULA3 and VINCENZO ZIPARO2

1Third Department of Surgery, Hosp. S.Giovanny-Addolorata, Rome;
2First Department of Surgery, "Pietro Valdenti", University "La Sapienza", Rome;
3Department of Surgery, University of Cagliari, Italy

Abstract. Background: Local excision for T1 rectal cancers with Transanal Endoscopic Microsurgery (TEM) is an accepted standard of care. However for T2/T3 rectal cancers, the high local failure indicates that this is not a valid option. Materials and Methods: Between 1990 and 2000, 83 patients with rectal adenocarcinoma underwent complete full thickness local excision. The mean diameter of the tumor was 3.4±1.7 cm, 60% were located more than 5 cm from the anal verge; 43% of patients received radiation therapy (26 pre- and 10 postoperatively). Results: Postoperative complications occurred in 15 patients (18%); there were no postoperative deaths. Mean follow-up was 37 months (range 18-118). The pathological stage was: Tis 9, T1 39, T2 23, T3 12. The overall local recurrence rate was 0% for Tis, 13% for T1, 17% for T2 and 50% for T3. Recurrence was managed surgically in 65% and nonsurgically in 35% because of advanced disease or poor general condition. Overall 5-year survival rates were 100%, 92%, 75% and 69% for Tis, T1, T2 and T3, respectively. Conclusion: Local excision with TEM is effective for early (Tis,T1) rectal cancers. Patients with T2 tumors can be treated with preoperative chemoradiation and subsequently local resection. Patients with T3 should not be treated with local excision unless they are unable to tolerate more extensive surgery.

Local excision of locally advanced rectal tumors in association with chemoradiation has been reported with favorable results (1, 2). Preoperative radiation therapy may result in tumor downstaging which varies from partial to complete pathologic response with no evidence of residual tumor in the surgical specimen (3). Indeed the need for reduced surgery in a select group of patients with a complete response to neoadjuvant treatment is now questioned (4). Although endorectal ultrasound (ERUS) has proven to be helpful in the selection of patients, there is still a lack of any standard selection criteria and local excision for rectal cancer remains controversial. Few experiences have been reported and only one is prospective and randomized (5).

Traditionally these procedures have been performed using anal retractors. More recently the Transanal Endoscopic Microsurgery (TEM) device, which facilitates local excision of rectal lesions, has been adopted in some centers (1). In this study we present the results of our 10-year experience with local excision of malignant tumors of the rectum with the TEM instrument.

Materials and Methods

Between July 1990 and June 2000, at the First Department of Surgery-University of Rome "La Sapienza" and the Department of Surgery of University of Cagliari, Italy, 160 patients with a neoplastic lesion of the rectum underwent excision of their lesion with the TEM approach. Sixty-three patients (39%) had an adenoma and 97 patients (61%) a carcinoma. Of these, 83 patients (55.5%) who had a resection with curative intent formed the study group. There were 51 males (61.5%) and 32 females (38.5%), with a mean age of 66 years (range 35-89 years). Initial symptoms were rectal bleeding (N=55, 66.2%), with a mean age of 66 years (range 35-89 years). Initial symptoms were rectal bleeding (N=55, 66.2%) or change in bowel habits (N=23, 27.7%). In five patients (6%) the tumor was found during routine examination or endoscopy.

Preoperative assessment included digital rectal examination, total colonoscopy, proctoscopy with biopsy to evaluate the exact site and distance of the lesion from the anal verge (Table I). Patients were staged with ERUS, liver ultrasound or CT scan. Lesions included: uT1/T2 carcinoma less than 3 cm in size of the...
middle and low rectum, uT2 lesions following preoperative neoadjuvant treatment with partial or complete response, uT3 tumors and tumors greater than 3 cm in size who were medically unfit for major surgery or who refused permanent colostomy.

Thirty-six patients (43.3%) received radiation therapy either preoperatively or postoperatively. Neoadjuvant treatment with chemoradiation was administered to 26 patients (4 uT1, 14 uT2, 8 uT3). Preoperative radiation was delivered with 15 Mv linear accelerator, 45 Grays (Gy) to whole pelvis in 5 weeks (5 days a week, 1.8 Gy per fraction), excluding the anal canal. Concurrent chemotherapy was administered by 5-FU (500 mg/m²/day) continuous infusion during the first and last week of radiation therapy. Patients were operated within 4 weeks of completing treatment. Postoperative treatment with either chemoradiation or radiation alone was administered postoperatively to 10 patients (3 uT1, 4 uT2, 3 uT3).

All patients received perioperative antibiotic drugs (cefotetan 2 g, metronidazole 1.5 g) and preoperative bowel preparation (polyethylene glycol 230 g in 4 litres of water). Local excision was performed using the Transanal Endoscopic Microsurgery (TEM) instrument (Wolf, Klittingen, Germany) according to the original technique described by Buess and coworkers (1). Tumors were resected with a margin of at least 1 cm. Full thickness excision of the rectal wall, including the perirectal tract, was always achieved. The defect of the rectal wall was closed with running absorbable suture. The mean duration of the surgical procedure was 178±98 min.

Follow-up evaluation included physical examination, CEA and CA 19.9, chest X-ray, EUS, liver ultrasonography and proctosigmoidoscopy at 3 months and then every 6 months. Colonoscopy and abdominal CT scan were performed every 12 months. Median follow-up was 37 months (range 18-118). Seventy-one patients (85.5%) had minimum follow-up of 24 months. In patients with T2 tumors who underwent preoperative chemoradiation the minimum follow-up was 25 months in 88% of patients.

The Chi-square test was used to assess difference between proportions. Survival was estimated by Kaplan-Meier analysis. A log-rank test was used to compare outcomes.

Results

Postoperative complications occurred in 15 patients (18%) (Table II). Two patients with rectal perforation had the defect repaired transanally, one patient required laparotomy and closure and two patients required anterior resection. One patient with bleeding and one patient with rectovaginal fistula required reoperation. All other patients were managed conservatively. There were no differences in complications between patients receiving neoadjuvant treatment or those that had not. Six patients (7.2%) required blood transfusions (1 unit each). The length of hospital stay was 1-7 days in 68 patients (82%), 8-10 days in 10 patients (12%) and >10 days in 5 patients (6%), who had complications. For T1 lesions the sensitivity for ERUS was 88% and specificity 100%. It was not possible to determine sensitivity and specificity for T2/T3 lesions as many had undergone neoadjuvant therapy with subsequent partial or complete response.

Among 26 patients receiving preoperative chemoradiation, 7 (27%) had a complete response (2 uT1 and 5 uT2) according to ERUS; 17 patients had a partial response but only in ten cases was a downstaging observed (6 uT2 → uT1 and 4 uT3 → uT2); in the remaining 2 patients there was no change in stage. We observed perineal erythema in one patient and temporary moderate proctitis in six patients.

The pathological T-stage is shown in Table III. Four patients had one or more lymph nodes in the resected specimen; all nodes were tumor-free.
The overall local recurrence rate was 18% (15/83). This rate decreased with time. In 1990-1994 it was 33% and between 1995-2000 it was 17% (*p* = 0.7). In four patients the local recurrence was associated with systemic disease. Median time to recurrence was 9.3 months (range 2-25).

Table IV. Rectal carcinomas: recurrence according to pathological T-stage.

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Total recurrence rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis</td>
<td>0/9 0%</td>
</tr>
<tr>
<td>T1</td>
<td>5/39 13%</td>
</tr>
<tr>
<td>T2</td>
<td>4/23 17%</td>
</tr>
<tr>
<td>T3</td>
<td>6/12 50%</td>
</tr>
<tr>
<td>Total</td>
<td>15/83 18%</td>
</tr>
</tbody>
</table>

Local control rates were affected by the choice and the type of adjuvant treatment (Table V). Among patients with T1 tumor, none who received adjuvant treatment had local recurrence. Among patients with T2 tumor, those who received preoperative neoadjuvant treatment had no recurrence. In this subgroup, 88% of patients had been followed-up for a minimum of 25 months. In patients with T3 tumor, the adjuvant treatment did not influence the outcome.

Ten patients out of 15 who recurred had salvage operations. Treatment and follow-up of these patients are shown in Table VI. The other 5 patients received nonsurgical treatment, due to disseminated disease or poor general condition. The T stage-specific disease-free 5-year survival rates were 100%, 92%, 75% and 69% for Tis, T1, T2 and T3 tumors, respectively (Figure 1).

**Table VI. Salvage operations in 10 patients with recurrent disease.**

<table>
<thead>
<tr>
<th>T-stage</th>
<th>Time to recurrence (months)</th>
<th>Operation</th>
<th>Follow-up (months)</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>5</td>
<td>LE</td>
<td>48</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T1</td>
<td>2</td>
<td>APR + ADJ</td>
<td>8</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T1</td>
<td>10</td>
<td>APR</td>
<td>25</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T1</td>
<td>2</td>
<td>LE</td>
<td>51</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T1</td>
<td>12</td>
<td>LAR</td>
<td>60</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T2</td>
<td>7</td>
<td>APR</td>
<td>3</td>
<td>Died, disease</td>
</tr>
<tr>
<td>T2</td>
<td>24</td>
<td>APR + ADJ</td>
<td>26</td>
<td>Alive, disease</td>
</tr>
<tr>
<td>T3</td>
<td>14</td>
<td>APR</td>
<td>44</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T3</td>
<td>12</td>
<td>APR + ADJ</td>
<td>47</td>
<td>Alive, DF</td>
</tr>
<tr>
<td>T3</td>
<td>4</td>
<td>APR</td>
<td>13</td>
<td>Alive, disease</td>
</tr>
</tbody>
</table>

*Follow-up after salvage operation
LE = local excision; APR = abdominoperineal resection; LAR = low anterior resection; ADJ = adjuvant treatment; DF = disease-free.

**Discussion**

Local excision has gained wide acceptance over past decades as a treatment modality for rectal adenomas. The are several advantages of this approach; less morbidity and mortality, shorter hospital stay, avoidance of a colostomy and overall better quality of life have been reported (5-9).

The overall local recurrence rate was 18% (15/83). This rate decreased with time. In 1990-1994 it was 33% and between 1995-2000 it was 17% (*p* = 0.7). In four patients the local recurrence was associated with systemic disease. Median time to recurrence was 9.3 months (range 2-25).

Recurrence rate according to T-stage is outlined in Table IV. In 71 patients with minimum follow-up of 24 months the recurrence rate was 14% (10/71): 0/8 Tis, 5.8% T1 (2/34), 13% T2 (3/23), 41.6% T3 (5/12).

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**Table VII. Local recurrence after local excision (Literature cumulative data)**

1. Ref. 1, 5, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 28 pers. exp.; range F.U. 4 - 108 months.
2. Ref. 6, 10, 11, 16, 17, 18, 20, 21, 22, 29, pers.exp.; range F.U. 4 - 112 months.
3. Ref. 7, 12, 17, 19, 23, 24, 25, 26, 27, 30 pers.exp.; range F.U. 4 - 112 months.

**Table VII. Local recurrence after local excision (Literature cumulative data)**

<table>
<thead>
<tr>
<th>T-stage</th>
<th>L.E. (1)</th>
<th>L.E. + RT (2)</th>
<th>L.E. + RT + CT (3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
<td>60/519 (11.5%)</td>
<td>106/291 (36.1%)</td>
<td>13/36 (36.1%)</td>
</tr>
<tr>
<td>T2</td>
<td>27/310 (8.7%)</td>
<td>30/147 (20.4%)</td>
<td>9/36 (25%)</td>
</tr>
<tr>
<td>T3</td>
<td>0/20 (0%)</td>
<td>15/128 (11.7%)</td>
<td>5/38 (13.1%)</td>
</tr>
</tbody>
</table>

*p* = 0.001 (L.E. vs L.E. + RT + CT)

"p" = 0.06 (L.E. vs L.E. + R.T.)

Local treatment of rectal cancer is less accepted. The only published prospective randomized trial comparing local excision with TEM and anterior resection in the treatment of T1 rectal adenocarcinomas demonstrated that operating time, operative blood loss, length of hospitalization and postoperative analgesic demand were in favor of the local approach. In addition mortality, morbidity, overall and disease-free long-term survival did not differ significantly (5).

We have reviewed experiences in the literature for local excision, classifying patients according to stage and type of treatment (Table VII): there is evidence that the association of chemoradiation with local excision provides satisfying results.
for T2 tumors: the recurrence rate is the same as radical surgery with the current technique. Concerning survival rates, our results are comparable to Enker’s (31) and Heald’s (32) who reported 5-year survival rates of respectively 86% and 83% for Dukes stage B and 66% and 67% for Dukes stage C (Figure 1). We would like to emphasize that none of the 14 T2 patients who received neoadjuvant treatment have had local recurrence to date and none died during follow-up. Although we recognize that follow-up is short at this time, 88% of them have had a minimum follow-up of 25 months.

It is established that preoperative RT provides better results than postoperative RT (33) and continuous infusion of 5FU should be preferred to bolus administration (34, 35). We therefore used this protocol and found that significant downstaging can be obtained by preoperative chemoradiation. In the recent report by Janjan et al. a complete response was observed in 27% of patients, with downstaging in 45% of patients (3). However the results of chemoradiation should be taken with caution: in the report of Dahlberg et al. (36) significant side-effects (partial incontinence, toilet dependence, difficulty in rectal emptying) were observed in 30-50% of treated patients. We did not experience such a rate of side-effects.

A limitation of local treatment is the inability to remove nodes. Lymph node metastases can be found in 20% of T2 tumors and 70% of T3 tumors (37). This makes adjuvant treatment mandatory. Furthermore, histological examination of the primary tumor needs to be accurate. As a routine, patients should be assessed for the presence of other prognostic factors, in order to select “low risk” rectal carcinomas for this procedure. These include, extramural venous invasion, perineural invasion, nodular-shaped lymphatic reaction, vascular invasion and tumor vascularity determined as an increase in vessel count (38-40).

We have found ERUS the most useful modality for determining rectal wall involvement: its accuracy for staging of tumor penetration ranges from 64% to 94%, with an average of 84% (41, 42). The most common error is overstaging of T2 lesions, due to peritumoral inflammation.
Among the currently available local excision modalities TEM has the advantage of allowing optimal exposure by distending the rectal wall and magnifying the surgical field. It allows resection of high lesions which are not suitable for excision with the use of anal retractors. Mid and low rectal lesions are also resectable with full-thickness excision with better clearance of lateral and deep margins. It is also a safe technique. No cause-related mortality was observed in our experience and the morbidity rate was low. The disadvantages are the high cost and the learning curve necessary to master the technique.

Another controversial matter concerns the indications and results of salvage operations in patients who exhibit local recurrence: in our experience, out of 10 patients surgically treated for local recurrence, 9 are still alive with a mean follow-up of 36.3 months. The other 5 patients died of systemic disease. A close follow-up is mandatory to detect local recurrence in order to allow salvage operation.

We believe that patients with rectal cancer should be carefully selected using ERUS and primary pathology findings. Patients with T3 tumors have an unacceptable rate of local recurrence, unrelated to adjuvant treatment if treated with local excision; we suggest that they should be treated with TEM for palliative purposes. Only selected patients with T2 tumors may be eligible for TEM after preoperative combined treatment as part of a prospective study; operation margins should be carefully checked for adequate tumor clearance. Patients with T1 rectal cancer with good pathologic features can be treated safely with local excision alone.

References


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