

Role of Endoluminal Surgery in the Treatment of Rectal Tumors

REKTAL TÜMÖRLERİN TEDAVİSİNDE ENDOLUMİNAL CERRAHİNİN ROLÜ

Dr. F.STIPA, Dr.G.LUCANDRI, Dr.M.FERRI, Dr.A.CASATI, Dr.S.STIPA

Ist Department of Surgery, University "La Sapienza, Roma, ITALY

ÖZET

Amaç: Rektum sessis adenomalar (AD) ile bazı selektif adeno karsinomalar (ADC) in lokal eksizyon ile tedavisinin endikasyon ve sonuçlarının irdelenmesi.

Hasta ve Method: 199 hasta lokal eksizyonla tedavi edildi. Ancak 12 hasta bu çalışmaya dahil edilemedi. Araştırma grubundaki 107 hastanın 64'ü erkek (%58.9), 43'ü kadın (%40.2) olup ortalama yaş 65 ± 11 yıl idi (35-89). Patolojik inceleme sonucunda 42 hastada AD (%39.2), 65 hasta ADC (%60.8) bulundu. Bütün tümörler transrektal ultrasonografi (TRUS) ile evrelendirildi. ADC grubunda 25 hastaya preoperatif kemoradyasyon 12 hastaya postoperatif radyoterapi uygulandı. Lokal eksizyon transanal endoskopik mikrocerrahi (TEM) veya Parks tekniği ile yapıldı.

Çıkarımlar: AD alt grubunda operatif mortalite görülmedi. Hastane morbiditesi %11.9 idi. Ortalama 30.7 ± 14.2 ayda 3 rekürrens (%7.1) meydana geldi. Altı yıllık sağkalım %98 idi. ADC alt grubunda operatif mortalite görülmedi. 13 hastada postoperatif komplikasyon (%21) meydana geldi. Tamamlanan prosedürlerde (%74), nüks oranı Tis %10, pT1 %20, pT2 %11.7 ve pT3 %66.66 olup ortalama takip süresi 46.7 ± 16.1 ay idi. Toplam nüks oranı %20.8 (10/48) idi. T2 ADC'de preoperatif kemoradyasyon nüks oranını önemli derecede azalttığı görüldü (0/13-2/4 p<0.05)

Sonuçlar: Lokal eksizyon tüm adenomalar ve T1S ile T1 evresindeki rektal kanserler için güvenli bir yaklaşım metodudur. Kemoradyasyon T2 lezyonlardaki sonuçları iyileştirebilir, ancak uzun dönem sonuçlar mevcut değildir. T3 kanserlerinde lokal eksizyon sadece palyatif amaçlı olabilir.

Anahtar kelimeler: Rektal tümörler, endoluminal cerrahi

SUMMARY

Objective: To evaluate indications and results of local excision in the management of sessile adenomas (AD) and selected adenocarcinomas (ADC) of the rectum.

Patients and methods: 119 patients have been treated with local excision, but 12 of them were not eligible for this analysis; among the study group (107 patients), 64 were males (58.9%) and 43 females (40.2%), with a mean age of 65 ± 11 years (range 35-89); at pathological examination 42 patients were found to have an AD (39.2%) and 65 an ADC (60.8%). All tumours were staged by Transrectal Ultrasonography (TRUS). In the ADC group, 25 patients received preoperative chemoradiation and 12 patients postoperative radiotherapy. Local excision was carried out using Transanal Endoscopic Microsurgery (TEM) or the Park's technique.

Results: Among the AD subgroup we had no operative mortality and a 11.9% hospital morbidity. We observed 3 recurrences (7.1%) during a mean follow up of 30.7 months ± 14.2 . Six-year actuarial survival rate was 98%. In the ADC subgroup no operative mortality was observed, while 13 patients presented postoperative complications (21%). Among complete procedures (74%, recurrence rate were 10% (Tis), 20% (pT1), 11.7% (pT2) and 66.6% (pT3) during a mean follow up of 46.7 months ± 16.1 . Overall recurrence rate was 20.8% (10/48). In T2 ADC preoperative chemoradiation significantly

reduced the recurrence rate (0/13 vs 2/4 $p < 0.05$).

Conclusion: Local excision represents a safe and appropriate approach for all adenomas and rectal cancers staged as Tis and T1; chemoradiation may improve results in T2 lesions, but long-term results are not available. In T3 cancer local excision has only a palliative purpose.

Keywords: Rectal tumors, endoluminal surgery

The choice of the most appropriate procedure for treating distal rectal tumors is influenced by many features, such as size, location, macroscopic aspect, histopathologic parameters and extent of the tumor growth (local spread, lymphnode involvement); patient's age and compliance also play an important role.

Local methods are being widely applied in the treatment of rectal sessile adenomas (AD): They include transcoccygeal, transphinteric or transanal approach; this last technique should be preferred: The recurrence rate is comparable (2-20%), but the morbidity is lower (0-11% vs 10-22%) (1,2). Transanal excision can be performed by using Parks or Pratt retractor or Transanal Endoscopic Microsurgery (TEM). This operation allows a precise dissection and complete removal of the AD, even if it requires optimum surgical skills.

As regard rectal adenocarcinomas (ADC), the diffusion of accurate diagnostic devices (spiral CT scan, NMR, TRUS), the development of magnified endoscopic microsurgical technique (TEM) and the combination of local excision with adjuvant therapies (preoperative or postoperative chemoradiation) improved the results of local treatment and led many authors to compare this approach with more demolitive surgery.

Patients with T1 distal rectal carcinoma with favorable clinical and histopathologic characteristics treated with local excision alone have a local control rate of greater than 90% (3). A recent randomized trial comparing TEM and anterior resection in T1 rectal cancer demonstrated that lower morbidity, similar rate of local recurrence and survival favored the first approach (4). Chemoradiation improves local control for T1 tumors with unfavorable features (5).

As regard cancer limited to the muscularis propria without transmural penetration (T2), controversies still exist: A critical limitation of local excision is the inability to widely resect perirec-

tal and mesenteric lymphatics; in fact the rate of lymphnode metastasis (LNM) rises progressively with tumor's penetration into the rectal wall, ranging from 17.9% to 22% in large series (6,7). However predictors of LNM, such as tumor's size, macroscopic aspect, grading, lymphovascular involvement and colloid histologic characteristics, have been identified (8); a proper analysis of these features could select T2 tumors with favourable histology and ideal cases, suitable for local approach. Moreover the combination with chemoradiation may be of benefit in reducing local recurrence, even if no randomized controlled trials have been published since today. Both preoperative (preRT) and postoperative radiotherapy (postRT) have been used, with better results for preRT. Unsatisfying results of postRT can be explained by a less effective tumoral cells damage in perirectal tissue, made scarred and more hypoxic by previous surgery. A recent multicentric Swedish trial has demonstrated that preRT reduces overall recurrence rate (11% vs 27%, $p < 0.001$) and improves long term survival (58% vs 48%, $p = 0.004$) in patients treated with transabdominal resection of rectal ADC (5); it has been used a short term schedule (25 Gy given in 5 daily fractions), which can be compared, by using the theoretical model of Cumulative Radiation Effect, to the conventional 5 weeks treatment. Tumor can also completely disappear, as a consequence of preRT and only scarring tissue may be found in the resected specimen: This result has been described to occur in different rates (8-32%) by some authors (9,10,11). Recent reports demonstrated that chemotherapy with 5-FU enhanced the effect of radiation, particularly if given as a continuous infusion (12,13); the short half-life of 5-FU, the reduced toxicity for normal tissues, the rate of tumoral cells submitted to radiosensitization support this route of administration. At present preRT with continuous 5-FU infusion represents the best approach for patients carrying rectal ADC.

TABLE 1: RECURRENCE RATE. COLLECTIVE DATA

	T1	T2	T3
Local Excision	22/235 (9.3%)	34/158 (21.5%)	12/32 (37.5%)
Local Excision + RT +/-CT	7/124 (5.6%)	22/230 (9.5%)*	21/63 (33.3%)
Local Excision + RT + CT	-	2/39 (5.1%)**	-

Stearns 1984, Grigg 1984, Killingback 1985, Cuthbertson 1986, Balslev 1986, Willett 1989, Horn 1989, Gerard 1989, Otmezguine 1989, Despretz 1990, Gall 1992, Summers 1992, Shafik 1992, Ota 1992, Said 1993, Takahashi 1994, Minsky 1994, Bannon 1995, Coco 1995, Fortunato 1995, Winde 1996, Bleday 1997, Pers. Exp. 1998 (*p=0.03, **p=0.001).

Results of preoperative chemoradiation and conventional surgery (low anterior or abdominoperineal resection) should be extended and compared with local approach, but few experiences have been reported since today and none is prospective and randomized. On Table 1 we attempted a comparison, by collecting recent series of local approach to rectal ADC, in which patients are stratified according to the different treatment protocols and depth of invasion. Our experience is included. In T2 tumors we observe the best results for preoperative chemoradiation even if the number of patients is small, the rate of recurrence seems to be comparable to that of Heald's procedure (5%, 14). Results of local treatment in T2 rectal tumors needs to be confirmed, careful selection of patients eligible is expected and patient must be compliant and

reliable because a close follow up is extremely important, especially if a salvage procedure is expected to be successful.

For T3 tumors the rate of recurrence is unacceptable (30-40%, Table 1) despite adjuvant therapies and local procedure may be considered only for palliative purpose or when patient clearly refuses demolitive surgery and permanent colostomy (15).

We began our experience with local treatment of rectal tumors in November 1991 and now we report the consecutive series of patients operated upon.

MATERIALS AND METHODS

We treated 119 patients; 12 of them (10%) are excluded from this analysis because of intra-

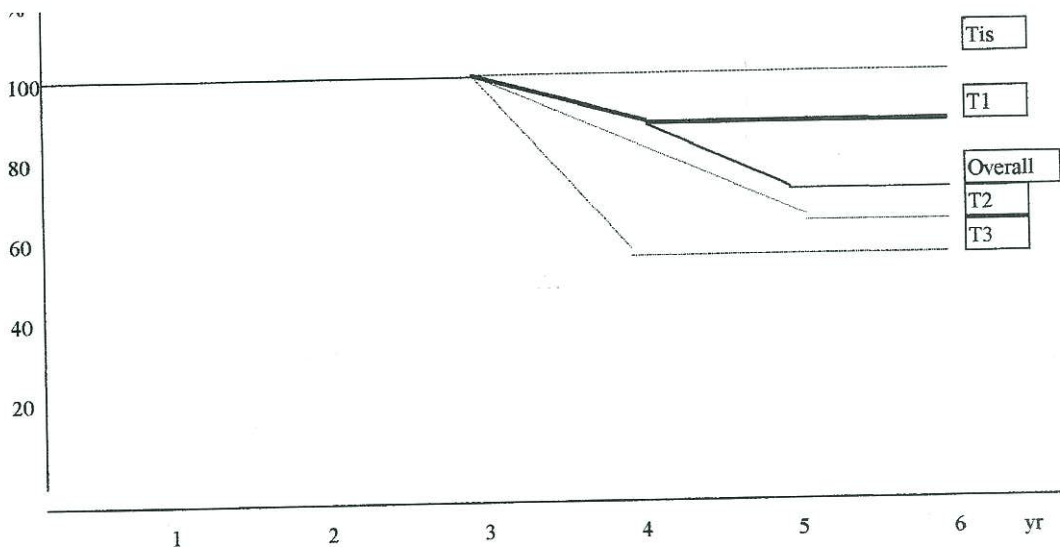


Figure 1: Complete Procedures: Overall and stage-related survival

TABLE 2: ADJUVANT TREATMENT ACCORDING TO T-STAGE

	Tis	T1	T2	T3	Overall
PreRT	0	1	16	8	25(38%)
PostRT	0	3	5	4	12(18.4%)
Overall	0/10	4/16	21/25	12/14	37/65 (56.4%)

operative conversion to open colectomy (2), rectal mucosectomy in colonic polyposis (1), lesions other than epithelial tumors (4 inflammatory pseudopolyps, 1 solitary ulcer, 1 anal condiloma, 1 squamous carcinoma, 1 leiomyoma and 1 carcinoid).

Among the study group (107 patients), 64 were males (58.9%) and 43 females (40.2%), with a mean age of 65 ± 11 years (range 35-89); at pathological examination 42 patients were found to have a rectal AD (39.2%) and 65 an ADC (60.8%).

Transrectal Ultrasonography (TRUS) has been performed by the same operators, using a real time rotating transrectal ultrasound with a 7.5 MHz probe; comparing its data with postoperative pathological examination, it showed a 77.5% sensibility and a 100% specificity for uTis and uT1 lesions, with an accuracy rate of 88%. Results for uT2 and uT3 cancer cannot be discussed in this series because most of them were submitted to preRT. In 4 patients perirectal lymphnodes have been detected by TRUS (3 uT2 and 1 uT3 lesions): After preRT and full-thickness excision, no nodes have been found on 2 specimens, only reactive nodes in the remaining 2.

Thirty-seven patients received adjuvant treatment (Table 2). Preoperative chemoradiation was performed in T2 and T3 lesions, whenever possible according to technical feasibility, patient's compliance and physical conditions. Recently, preoperative chemoradiation has been performed also for T1 lesions. Few patients have been submitted to postoperative radiotherapy in the early phase of our experience. No sandwich treatment has been performed. Chemoradiation was performed in the same department, using the same device (6 mV linear accelerator with 3-field or 4 field technique and the same schedule (external beam pre or postRT, 5 times per week, with a daily fraction of 180 cGy and total pelvic

dose of 45 to 50 Gy). All patients had bladder distension or an external bladder compression device, in order to exclude small bowel from the fields and received continuous 5-FU infusion (500 mg/m²/day) during RT. Control TRUS has always been performed 3 weeks after the end of chemoradiation. Patients were considered as complete responders whenever a complete disappearance of the tumoral bulk could be demonstrated, partial responders in case of significative reduction of the lesion (50-75%, non responders in the absence of any reduction. No significative systemic and/or local side effects have been observed.

Patients were considered eligible for local approach when rectal neoplasms was less than 3 cm. in diameter, confined to the rectal wall, involving less than 50% of the rectal circumference and whose upper margin was located within 15cm. (posterior-sided lesions) or 12 cm. (anterolateral sides lesions) from the anal verge. As far as ADC is concerning, all lesions confined to rectal wall satisfying the above-mentioned criteria were candidate to local excision. T3 tumors were included when a significant downstaging could be demonstrated after preRT or in case of palliative surgery.

Local excision, by using standard or microsurgical techniques, has always been performed 1 month later. In 94% of patients the operation was performed under general anesthesia. According to the preoperative staging, we performed rectal mucosectomy (AD, Tis) and partial wall excision (T1) or full-thickness technique (T2, T3) with or without dissection of the perirectal fat. In the latter group the rectal defect has been closed transversely, by using a 4/0 PDS continuous running suture. All specimens had intraoperative pathological examination. Electrocoagulation (ECG) has been delivered using a bipolar probe. Operations have been considered as complete whenever free pathological

TABLE 3: RECURRENCE RATE ACCORDING TO T-STAGE. COMPLETE PROCEDURES

Tumors recurrence(%)	
Tis	1/10(10)
T1	3/15(20%)
T2	2/17(11.7%)
T3	4/6(66.6%)

margins could be obtained.

Patients have been followed with endoscopic, ultrasonographic and biochemical controls at 1 and 3 months since the operation, there after every 6 months.

RESULTS AND CONCLUSIONS

We performed TEM procedure on 100 patients (93.4%), Parks operations in 5 cases (4.6% and electrocoagulation (ECG) in 2 (1.8%).

Among the AD subgroup, mean operation time was 173 min \pm 169; we had no operative mortality and a 11.9% hospital morbidity. 3 intraoperative perforations, treated with transanal suture; 1 bleeding treated with medical therapy; 1 large recto-vaginal fistula, operated with success. Only 1 patient required blood transfusions (2.3%); mean hospital stay was 5 days \pm 2.2. We observed 3 recurrences (7.1%) during a mean follow up of 30.7 months \pm 14.2; 1 patient has been treated with low anterior resection, 1 had repeated ECG and 1 a new TEM procedure. Six-year actuarial survival rate is 98%.

In the ADC subgroup, chemoradiation led to a significant downstaging of cancer, with pathological complete response rate of 30% in uT2 complete procedures (4/13). Absence in reduction of tumoral bulk has been observed only in 2 uT3 patients.

Mean operation time was 197 min. \pm 109; according to the depth of surgical excision, we performed 8 mucosectomy (12.3%), 11 partial wall excision (17%), 46 full-thickness operations (70.7%), including perirectal fat in 28 cases. Mean resected surface (cm²) was 19.23 \pm 14.35, with neoplastic and disease-free values of respectively 9.12 \pm 10.6 and 10.21 \pm 8.5.

No operative mortality was observed; 13 patients presented postoperative complications

(21%). Five perforations (7.7%), treated with transanal (2) or transabdominal suture (3 cases); in 4 patients tumor arised from the anterior aspect of the rectal wall, while in the remaining it was left-sided. Four bleedings (6.1%), treated with medical therapy (3 cases) and Hartmann emergency procedure (1). One small recto-vaginal fistula (1.5%), which did not require surgical correction; one transient stenosis (1.5%), treated with pneumatic proctoscopic dilatation; one moderate incontinence (1.5%) and one cystitis (1.5%), both treated with medical therapy.

Five patients required blood transfusions (7.7%): 3 patients had pT2 tumors, 2 pT3 lesions; only 1 patient required more than 1 unit. Mean hospital stay was 5 days \pm 1.5.

We considered 48/65 operations as complete (74%): 10/10 were staged as Tis (100%); 15/16 as T1 (94%); 17/25 as T2 (68%) and 6/14 as T3 (43%). Overall recurrence rate was 20.8% (10/48) during a mean follow up of 46.7 \pm 16.1 months. The recurrence rate according to T stage is reported on Table 3. In T2 tumors preoperative chemoradiation significantly reduced the recurrence rate (Table 4). Lower recurrence rate was also observed in patients whose tumor did not exhibit ulcerative configuration (11% sv 26%, $p < 0.01$) and when resected neoplastic surface was less than 10 cm² (2.7% vs 75%, $p < 0.0001$). Salvage procedures were performed in 9 patients (6 Miles operations, 1 anterior resection, 1 Parks procedure and 1 ECG), with success in 8 cases (88.8%). Only 1 patient refused any treatment.

At the follow up, we have 45 patients alive disease-free (93.75%), while report 2 cancer-related deaths at 22 and 25 months since the date of local treatment (15.3%) and 1 cancer-unrelated death (liver cirrhosis). The 6 year actuarial survival rate is 100%, 88%, 66% and 66% respectively for pTis, pT1, pT2 and pT3 patients; overall actuarial survival rate is 72% (Figure 1).

TABLE 4: RECURRENCE RATE ACCORDING TO T-STAGE. COMPLETE PROCEDURES

	RT+	RT-
pT2*	0/13	2/4(50%)
pT3	3/3(100%)	2/3(66%)

*p < 0.05 (Fisher's exact test)

TABLE 5: RESULTS OF LOCAL EXCISION IN RECTAL NEOPLASMS

	Adenomas	Carcinomas
Mean operation time (min)	173±169	197±109
Blood transfusion	1 pt (2.3%)	5 pts (7.7%)
Operative mortality	-	-
Hospital morbidity	11.9%	21%
Recurrence	3 pts (7.1%)	10 pts (20.8%)

*Complete procedures

As regard the comparison with conventional treatment of rectal ADC, we report similar recurrence rates both for T1 and T2 patients submitted to local treatment or not (respectively 20% vs 18.3% and 11.7% vs 12.3%, $p = n.s.$); however the different rates of patients submitted to RT in the subgroups (81% and 19%) don't allow us to state definitive conclusions.

Among incomplete procedures (17 patients, 26%), 8 patients (47%) had been submitted to preRT, while 6 patients underwent post-RT after evidence of residual in the specimen (35%).

One pT1 patients had his residual treated by a new TEM procedure at 2 months. Four out of 8 pT2 patients had clinical evidence of residual disease (50%): 1 patient was submitted to a Miles procedure at 8 months, 1 patient refused any further treatment, while the remaining 2 patient were judged not suitable for other treatment because of poor conditions; 4 patients with microscopic residual disease entered a close follow up program without clinical evidence of disease at 11, 29, 29 and 39 months. Eight pT3 patients developed clinical evidence of residual disease, but only 4 had some kind of treatment; a new TEM procedure (1 case), a colo-anal anastomosis (1 case) and chemotherapy (2 cases). After a mean follow up of 28.75 ± 19.3 months, 5 patients are alive without clinical evidence of residual disease (29.4%), 3 patients are alive with disease (17.6%), while we account 9 cancer-related deaths (53%). We report a 13% 6-year overall actuarial survival rate. Cumulative data concerning both AD and ADC are summarized on Table 5.

Our experience indicates that local treatment with preoperative chemoradiation seems to provide an alternative to conventional surgery in properly selected patients with rectal ADC; this regimen is a safe treatment option, with acceptable local control rates and survival. TEM

procedure in particular is related with less morbidity, blood loss and hospital stay. Intraoperative pathological examination is always required, in order to obtain a radical surgical procedure. Close follow up is mandatory to early detect local recurrence and submit patients to salvage procedure with success. Definitive conclusions on T2 tumors will be state only with randomized studies. We wish them and hope the collaboration of other Departments.

KAYNAKLAR

1. Parks AG, Stuart AE: The management of villous tumors of the large bowel. *Br J Surg* 1973;60:688-695.
2. Said S, Stippel D: Transanal Endoscopic Microsurgery in large, sessile adenomas of the rectum. A ten-year experience. *Surg Endosc* 1995;9:1106-1112.
3. Ng AK, Recht A, Busse PM: Sphincter preservation therapy for distal rectal carcinoma. A review *Cancer* 1997;79(4):671-683.
4. Winde G, Nottberg H, Keller R, Schmid KW, Bunde H. Surgical cure for early carcinomas (T1). *Transanal Endoscopic Microsurgery vs Anterior Resection. Dis Colon Rektum* 1996;39:969-976.
5. Swedish Rectal Cancer Trial: Improved survival with preoperative radiotherapy in resectable rectal cancer. *New Engl J Med* 1997;336(14):980-987.
6. Brodsky JT, Richard GK, Cohen AM, Minsky BD: Variables correlated with the risk of lymphnode metastasis in early rectal cancer. *Cancer* 1992;69:322-326.
7. Hermanek P, Marzoli GP: *Local therapie der Rektumkarzinomas. Berlin, Springer Ed, 1994.*
8. Takahashi T, Nivatvongs S, Batts KP: Local excision for carcinoma of the rectum. *Dis Colon Rektum* 1994;34:28.
9. Marks JH, Marks GJ, Brady L: Full-thickness local excision for selected distal rectal cancer. *Pers*

- Com.
10. Gerard JP: *The use of radiotherapy for patients with low rectal cancer: An overview on the Lyon experience.* NZJ Surg 64:457-463.
 11. Horn A, Halvorsen JF, Dahl O: *Preoperative radiotherapy in operable rectal cancer.* Dis Colon Rectum 1990;33:823-828.
 12. O'Connel MJ, Martenson JA, Weiend HS: *Improving adjuvant therapy for rectal cancer by combining protracted infusion fluorouracil with radiation therapy after curative surgery.* N Engl J Med 1994;331:502-507.
 13. Palmhan L, Glimelius B: *The value of adjuvant radio(chemo)therapy for rectal cancer.* Eur J Cancer 1995;31:1347-1350.
 14. Heald RJ, Ryall RD: *Recurrence and survival after total mesorectal excision for rectal cancer.* Lancet 1986;1:1479-1482.
 15. Minsky BD: *Results of local excision followed by postoperative radiation therapy for rectal cancer.* Radiat Oncol Investig 1997;5(5):246-251.
-

YAZIřMA ADRESİ:

Dr.Sergio Stipa
Istituto di Clinica Chirurgica,
Policlinico Umberto I
00161 Roma, ITALY