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Transanal endoscopic microsurgery (TEM) vs radical surgery (RS) in the treatment of rectal cancer : Indications, limitations, prospectives. A review

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Abstract

Background and study aims : **Principal goal in the management of any patient with rectal cancer is to provide an optimal chance for cure while maintaining their quality of life. Transanal endoscopic microsurgery (TEM) is a minimal invasive procedure that allows full thickness local excision or rectal tumors. The role or TEM in the treatment of rectal cancer remains controversial. The aim of this study was to review the evidence related to the role of TEM compared to radical surgery in the treatment of rectal cancer.**

Patients and methods : **We reviewed 5 studies (two controlled randomized and three non-randomized) comparing outcome after TEM vs. radical surgery (RS), either open or laparoscopic, in patients with rectal cancer. We evaluated the results in terms of safety of the procedure as well as its efficacy.**

Results : **Hospital stay, complication rate and overall morbidity and mortality were lower in the TEM groups in all studies. With the exception of one study, recurrence was slightly (but non-significantly) increased in the TEM groups. No difference for T2 tumors with TEM vs. laparoscopic resection was seen though. Overall survival was not statistically different.**

Conclusions : **TEM is a safe, effective minimal invasive method for treatment of T1 rectal carcinomas and possibly T2 carcinomas in selected patients after neoadjuvant chemoradiation. Its role in advanced tumor stages should be further defined.** (Acta gastroenterol. belg., **2007**, 70, **374-380**).

Key words : transanal endoscopic microsurgery, TEM, radical surgery, rectal cancer.

Introduction

Colorectal cancer represents the second leading cause of cancer-related mortality in the western world (1). Cancer of the rectum is traditionally treated with anterior resection or abdominoperineal resection. These traditional curative resections have been considered "radical", but the advantages of radicality are countered by a high incidence of complications (2,3). Additionally many patients will have to carry a permanent colostomy, which inevitably limits their quality of life. On the other hand traditional local procedures such as the standard transanal resection have access to the lower rectum only. If the rumor is located in the middle or upper rectum it may be difficult to excise it completely. Anal retractors can be used, but visualization and access of the lesion are still problematic. At the same time standard local procedures are associated with an unacceptably high recurrence rate.

The technique of Transanal Endoscopic Microsurgery (TEM) was developed in 1984 by Buess in Germany as an alternative to major surgery, for local excision of both benign (adenomas) and malignant rectal lesions. Its results are promising, as far as morbidity, mortality and recurrence rate is concerned (4). TEM is a minimal invasive method that allows precise resection of tumors located 4-24 cm from the anal verge using an operative rectoscope. Although it is currently an established method for the treatment of rectal adenomas, its role in the treatment of rectal carcinoma is not completely clear.

The aim of this study is to evaluate the outcome of patients with rectal cancer treated with TEM compared to radical surgery. Evaluation was based on published studies comparing TEM with radical surgery.

The transanal endoscopic microsurgery (TEM) procedure

TEM is a minimally invasive surgical technique originally designed and introduced by Buess *et al.* in 1984 (4). Central component of the instrumentarium is a one-port system that consists of a rectoscope, handle and a four port-working insert. The rectoscope is introduced transanally and fixed onto the operating table with a Martin arm allowing positioning in every conceivable position. The position of the patient on the operating table depends on the tumor location, because the rectoscope must always face downward. The scope position is adjusted so that the lesion occupies the centre of the operative field. Depending upon these requirements a lithotomy, prone or lateral position of the patient can be chosen (5). An insufflator and a specially developed TEM pump are connected via a tube system and care for the establishment of the pneumorectum, pressure management, irrigation and suction. An electro-surgery unit or the harmonic scalpel is used for cutting and coagulation. The system is airtight, which is necessary for creating and maintaining the pneumorectum. Marking dots are placed at a 0.5 to 1 cm margin around the tumor followed by excision in the submucosal plane (mostly for adenomas) to full thickness excision (in the case of

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malignant tumors) (5). The different layers of the rectal wall and the perirectal fat can be clearly identified. After removal of the specimen, the defect is closed transversally with a running suture. Titanium clips are used as knots. The specimen is spread and pinned on a corkboard by means of fine needles in order to avoid anatomic distortion by the subsequent formalin fixation, and sent to the pathologist. The procedure is carried out under general (mostly) or spinal anaesthesia.

Patients/materials and methods

We included in our study only comparative studies (randomised or non randomised) for the main analysis in order to evaluate several aspects of TEM procedure for the treatment of rectal malignant tumors in comparison to radical surgery (RS). In these settings studies referring to TEM and adenomas were not included. Factors and aspects evaluated included peri- and postoperative mortality ; peri- and postoperative morbidity or complications, operating time, length of hospital stay, survival and recurrence rate, and finally costs.

Searches were conducted on published English-and German-spoken literature for the period between 1984 and November 2006. Searches were based on Medline (last search time : November 2006). Articles retrieved were carefully evaluated to confirm they met the selection criteria.

Under these settings we located five comparative studies : Two controlled randomised trials (CRT) by Winde *et al.* (6,7) and Lezoche *et al.* (8) comparing TEM with open and laparoscopic RS respectively and three non-randomised comparative studies (Heinzt F *et al.*, Langer C *et al.*, Lee *et al.*) (9,10,11), comparing TEM with open RS.

Study presentation

In their controlled prospective randomised trial Winde *et al.* (6,7) stratified the patients in four groups according to preoperative histological and endosonographical diagnosis. Among patients with uT1 rectal carcinoma, 25 were submitted to TEM and 28 to anterior resection (AR). For adenoma patients, 98 underwent TEM and 90 perianal submucosal excision (PSE). Patients after TEM operation were followed up for a median period of 40.9 months (min : 13.3-max : 110.6 months) and 45.8 months (min : 7.1-max : 107.2 months) after AR.

In their prospective randomised study Lezoche *et al.* (2005) (8) compared the results and the oncologic outcomes of TEM (n = 20) with laparoscopic resection (LR) (n = 20) in 40 patients with T2N0 rectal cancer after their being submitted to neoadjuvant radiochemotherapy. Actually this is the only published study comparing TEM with minimal invasive (laparoscopic) radical surgery. Inclusion criteria specified low rectal cancer staged as T2-N0-G1-2, tumor diameter up to 3 cm and tumor location within 6 cm from the anal verge. Patients in both groups received a standardised neoadjuvant radiochemotherapy. TEM procedure included full-thickness excision of the tumor with negative margins, including the adjacent perirectal fat. Laparoscopic procedures included either low anterior resection or abdominoperineal resection (Miles procedure). Primary end point of the study was the probability of survival after 3 and 5 years of follow-up evaluation. Secondary end points included morbidity and 30-day mortality, operative time, blood loss, analgesic use and hospital stay. Median follow-up period was 56 months (range 44-67 months) for both groups.

In their retrospective study (1985-96) Heintz *et al.* (9) compared the results obtained in 103 patients with T1 rectal carcinomas undergoing TEM or radical surgical therapy. All patients underwent rectoscopy to determine the location and size of tumor and were biopsied. Consistent with the criteria proposed by Hermanek *et al.*, tumors were differentiated as low risk (well or moderately differentiated adenocarcinoma without lymphatic invasion) or high-risk carcinoma (poor differentiated or undifferentiated adenocarcinoma with lymphatic invasion) (12). Until 1988 radical surgery was routinely performed when preoperative histology revealed a carcinoma. After 1988 patients were submitted to primary local excision (LE) when preoperative staging revealed Low risk T1 carcinoma. Meanwhile a radical surgery was performed when postoperative histology showed high-risk T1 carcinoma. In the low risk group (n = 80) 44 patients were treated with TEM (2 with LE according to Parks) and 34 with radical surgery. In the high risk group (n = 23) 11 patients were treated with TEM (and 1 with LE) and 11 patients radical surgery.

Langer *et al.* (10) performed a retrospective comparative study with 182 operations on 162 patients with early rectal carcinoma (pT1, G1/2) or adenoma to compare the outcome following four different kinds of surgical resection : Radical resection (RS) (anterior or abdominoperineal resection ; n = 27), conventional transanal resection using Park's retractor (TP ; n = 76), TEM with electrosurgery (TEM-ES ; n = 45), and TEM with UlrtaCision (TEM-UC ; n = 34), thus a total of 79 patients for the TEM group. The adequacy of resection was reported as 'complete' (R0), incomplete (R1) or doubtfully complete (RX). Median follow up was 33.7 months (range 1-138) in the RS group, 33.4 (range 1-130) in the TR group and 21.6 (range 1.75) in the TEM groups. These differences between TP and TEM were statistically significant (p = 0.0253), but not that between RS and TEM (p = 0.0979).

Lee *et al.* (11) retrospectively compared the feasibility and results of TEM as a treatment of rectal cancer with those of radical surgery in patients with T1 and T2 cancers. 74 patients with rectal cancer were included in the TEM group : 52 patients with T1 cancer (70.3%) and 22 patients with T2 cancer (29.7%). Radical surgery group included 114 patients with T1N0M0 and

T2N0M0 rectal tumors : 42 of them underwent abdominoperineal resection and 72 low anterior resection. 14 patients were excluded and finally 100 patients with rectal cancer were included in the radical surgery group : 17 patients with T1 cancer (17%) and 83 patients with T2 cancer (82%). The study was not randomised. It is important to mention that for T1 lesions TEM was preferred and for T2 lesions radical surgery was the treatment of choice and TEM was performed when patients were not suitable for radical procedures. Mean postoperative follow-up was 31 months for the TEM group and 34.6 months for the radical surgery group.

Results

In the RCT by Winde *et al.* (6,7) reported perioperative mortality was zero. For the above-mentioned follow- up period one death in each group were reported (1/28 in the anterior resection-AR- group and 1/25 in the TEM group). The death case in the AR group was attributed to distal metastasis and it was not clear whether the death in the TEM group was related to cancer. There was no significant difference in the early complication rate between TEM (20%, 5/25) and AR group (35.7%, 10/28). No differences were reported concerning individual complications except blood loss. Five complications were reported in the TEM patients : one case of rectal bleeding, one perforation, one ischemic compartment syndrome and two cases of micturition disturbance. Ten complications were observed in the AR group, namely, one case of rectal bleeding, one leakage or suture dehiscence, four wound healing impairments, one stricture, one small bowel obstruction and two cases of micturition. Operating time was significantly less for TEM patients (mean, 103 (SD < 46) minutes) than for AR group (mean, 149 (SD, 54) minutes). Hospital stay was also significantly shorter for TEM patients (mean 5,7 (SD 4) days) than for AR patients (mean 15,4 (SD2) days) ($p < 0{,}001$). A 4% local recurrence rate and 96% 5-year survival rate after TEM for T1 cancers was reported.

Quite interesting were the results of the second prospective randomised trial by Lezoche *et al.* (8) comparing TEM with laparoscopic radical surgery. The authors reported significantly lower operative time for TEM (median values 95 min for TEM and 170 min for LR, $P < 0.001$). Blood loss, analgesic use and hospital stay was also significantly lower in TEM group compared to LR group ($P < 0.001$ for all these parameters). Perioperative mortality was zero in both groups. Minor postoperative complications were observed in 2 cases in TEM group (2/20, 10%), namely partial suture leakage which was conservatively treated, and in 2 cases (2/10, 10%) in LR group (anastomotic leakage, conservative treatment). 1 major complication was observed in each group (1/20, 5%) namely a perianal phlegmon in a TEM patients which was treated with laparoscopic ileostomy, and a pelvic peritonitis in a RL patient which was treated surgically with laparoscopic ileostomy and peritoneal washing. In a median follow up of 56 months one local recurrence was observed in TEM group, (1/20, 5%). The patient was treated with laparoscopic abdominoperineal resection. One case of local recurrence was also observed in the LR group and the patient died 3 months later. The authors report a probability of survival at the end of the follow-up evaluation 95% for TEM group and 83% for LR group ($P = 0.358$).

In their retrospective comparative study Heintz *et al.* (9) reported perioperatively 2 deaths out of 34 low risk carcinoma patients undergoing radical resection (6%). Complication rate was significantly lower in the TEM group (2.1%, 1/46) with a case of rectoviginal fistula, than in the radical surgery group (15%, 5/34) ($p = 0.04$). Mean follow-up period for low-risk patients was 52 months (+-22.7) and 42.8 months for high-risk patients. No difference in the actuarial five-year survival for TEM/LE patients (62%) compared to radical resection (67%) was observed ($p = 0.47$). In the follow up period 6 of 58 cases (10.3%) of local recurrence were observed in the TEM/LE patients. Two of these were in the low-risk carcinoma category (with one death) and four were high risk (three deaths). In the radical resection patients 3 of 45 (6.7%) local recurrences were observed (one in low risk and two high risk who had undergone previous local excision, no deaths).

In the comparative study of Langer *et al.* (10), one patient in the RS group died of sepsis due to anastomotic leakage after a low anterior resection (1/27,3.7%). Mortality in TP and TEM groups was zero. 15 cases with complications were observed in RS group (15/27, 55.5%). Among them an anastomotic leakage, a case of wound abscess, an appendicitis, a transient urine retention, 1 ileus, 4 cases of wound infection, 4 cases of increased stool frequency and 2 cases of circulatory collapse. In the TEM_ES group complications observed (3/45) were leakage, a rectovaginal fistula and a case of bleeding. A case of bleeding, a leakage and a transient neurasthenia (nerve femoralis lat) as observed in the TEM – UC group (3/34). The comparison of complications for TEM vs. RS group showed a significantly lower rate for TEM (Wilcoxon test, $P = 0.0001$).

RS group showed the best results in terms of completeness of excision, with no R1 or RX status of resection. On the contrary a significantly higher incidence of R1 (37%) and RX- resections (16%) was observed in the TP group than in the TEM group (R1 : 19% and RX : 5%). ($P = 0.001$). The lowest recurrence rate was found in RS with 3.7%. In the TP and TEM group the overall recurrence rate was 26.3% and 8.9% respectively [TP group : 31.5% for adenomas and 15% for carcinomas, TEM group : 8.8% (5/57) for adenomas and 10%(2/20) for carcinomas)] and this difference was statistically significant ($p = 0.0055$). Interestingly use of TEM-UC was connected with lower recurrence rate (2.9%) than TEM-ES (13.3%). The procedure 2-year survival rate was 96.3% for the RS group and 100% in the TP and TEM

group. Risk factors for the development of recurrent tumor found to be statistically significant were tumor size (p = 0.0236) and recurrent tumor at the time of operation (p = 0.0231).

In their retrospective study Lee W *et al.* (11), mean tumor size in the TEM and radical surgery group was 23.5 +-9.5 mm and 37.8 ± 15.3 mm respectively and the difference was significant (p = 000.9). Complications after TEM were considerably rare compared to radical surgery : only three cases of complications were observed all in the early postoperative period (bleeding, urinary difficulty, fecal incontinence) making a complication rate of 4.1%. Early complications in the radical surgery group included urinary difficulty (n = 17), anastomotic leak (n = 2), postoperative bleeding (n = 1) and a rectovaginal fistula (n = 1), all except the first were surgically managed. Late complications included faecal soiling (n = 8), sexual problems (n = 8), anastomotic site stenosis (n = 4), intestinal obstruction (n = 3) and stoma problems (n = 7). Overall complication rate after radical surgery 48%. Six cases of recurrence were observed in the TEM group (3 with local recurrence and 3 with distal metastasis) compared to 11 cases in the radical surgical group (five patients local recurrence, five with metastatic disease an 1 patient with both). The overall 5 year local recurrence rate was for the T1 stage 4.1% in the TEM group and 0% in the RS group. For T2 tumors recurrence rate was 19.5% and 9.4% respectively. Though the difference was non significant for T1 stage (p = 0.94), a statistical significance was observed in the T2 group (p = 0.035). 5- year disease-free survival rate was 95.9% in the TEM group and 94.1% in the RS group for T1 stage (p = 0.35). For T2 tumors 5- year disease-free survival rate was 80.5% and 83.3% respectively (p = 0.12). The overall %-year survival rate was 100% in TEM and 92.9% in RS group for T1 tumors (p = 0.07). For T2 tumors rate was 94.7% and 96.1% respectively (p = 0.48). No statistical significance was observed.

Discussion

Carcinoma of the rectum is conventionally treated by radical surgery (RS) such as abdominoperineal resection or low anterior resection (13). The evolution in the treatment of rectal cancer has led to a drastic fall in the local recurrence rate, from 15-40% to 7-10%, which can be attributed mainly to the total mesorectal excision (TME). However the benefits of the these gold standard procedures, which show excellent results in terms of local recurrence and survival rate, are paid for by a high rate of complications and a strong limitation of the quality of life as a result of frequent anorectal, sexual and urinary dysfunction (10,11).

A great variety of techniques have been developed for the local excision of rectal neoplasms including the standard transanal excision, the transphicteric approach (York-Mason) and the transcoccygeal approach (Kraske) and of course the transanal endoscopic microsurgery (TEM). The transanal approach has benefits such as low morbidity and early recovery, but for technical reasons by the help of this method the surgeon can only reach low- and mid-rectal lesions. Apart from that it has a high local recurrence rate. The transphicteric approach can reach higher lesions, but the subsequent complication rate is also high (6,11,14).

Transanal endoscopic microsurgery (TEM) was first introduced by Buess in Tuebingen –Germany in 1984. This method combines the advantages of radical and conservative procedures for rectal lesions and is currently an accepted method for the surgical treatment of benign rectal neoplasms (adenomas) (6,15,16). Its role in the treatment of rectal cancer is still under investigation.

In the current study we attempted to elucidate the role of TEM in the treatment of rectal cancer. When TEM is compared with radical surgery, the method is associated with shorter operative, hospitalization and ventilation times, lower loss of blood, less peri- and postoperative complications and almost zero mortality. In addition most of these parameters are also statistically significantly lower in most of the studies presented. The evaluation of economical aspects of the procedure produces a total cost corresponding to two thirds of the costs for the usual radical procedures for both rectal adenoma and cancer (17).

The reason why TEM is superior to traditional methods is that it has special advantages such as better exposure of the lesion, superior 3-D optics of operative field and pneumorectum. These allow a full-thickness transanal excision, and access to lesions located not only in the lower but also in the middle and upper part of the rectum. It is now possible to carry out formal transanal resection by means of a rectoscope, which provides excellent access and vision of the entire rectum.

The complication rate after TEM is reported between 5 and 15% (18). Among the complications are postoperative bleeding, rectovaginal fistula, leakage, transient urine retention or incontinence, and rarely cardiorespiratory complications (19). In all the presented comparative studies complication rate is lower in the TEM group than in the RS group, with statistical significance (9,10) or not (7,8).

In the previous years, lesions above the peritoneal reflection were considered to be a contraindication for TEM and the intraoperative full thickness excision was contraindicated or was an indication for laparotomy. Today it is accepted that all malignant masses mandate full thickness excision. Proximal, anterior, or lateral tumors are most likely to be within the peritoneal cavity and full-thickness excision will result in intraperitoneal penetration. This is not a contraindication to TEM, but it does make the procedure technically more challenging. The defect can be safely repaired endoscopically if the surgeon has adequate endoscopic suturing skills without conversion to a laparotomy (20,21). The consequences of the intraperitoneal suture line disruption will be more

severe. Therefore, in cases the integrity of the rectal wall is still in doubt, we suggest a diagnostical laparoscopy should be performed with eventual additional intraperitoneal suturing of the rectal wall, as we practice in our Department. The theoretical disadvantages of intraperitoneal tumor cell dissemination may be potentially worrisome (21). Iadvertent perforation of the bowel or tumor is a relatively common complication during resection of rectal cancer. In a prospective national cohort study of 2873 patients undergoing major open resection for rectal carcinoma Eriksen *et al.* reported an overal perforation rate of 8.1% (234 of 2873 patients). The 5-year local recurrence rate was 28.8% following perforation, compared with 9.9% in patients with no perforation ($p < 0.001$). Subsequent survival rates were 41.5 and 67.1% respectively ($p < 0.001$). The authors concluded that the intraoperative perforation has an independent negative effect on the local recurrence and survival rates of patients undergoing resection of rectal cancer and it should be therefore avoided (22).

Insertion of the 40 mm rectoscope into the rectum and the subsequent mechanical trauma are responsible for the functional changes in the sphincter mechanism. It seems that operative time longer than two hours are more often related to these disorders, which are mostly subclinical or are manifested with fecal incontinence improving in time (23). Cataldo *et al.* evaluated prospectively the functional results of TEM and observed no differences in the number of bowel movement per 24 hours, fecal incontinence severity Index scores and quality of life in patients submitted to TEM (24).

The role of TEM for the treatment of rectal cancer is still controversial. What has strongly been criticized with TEM is the ability to achieve an oncological accepted excision in cases of malignant tumors. Radical surgeries for rectal cancer such as low anterior resection and abdominoperineal resection have led to good results in terms of local and 5-year survival rates. A major disadvantage of local therapy (TEM included) is the inability to deal with lymph node metastasis. Several studies have reported low lymph nodes metastasis rate of 0% to 12% for T1 cancer, although for T2 tumors the rate amounts 12.5 to 28% (11). After transanal resection local resection for T1 tumors the rate ranges from 0 to 27%. Infiltrated lymph nodes left behind after surgery are considered to be a major cause or local recurrence (10). Many authors have advocated histopathological criteria to predict nodal involvement (10,11,12).

Small size of the tumor, good or moderate differentiation, no venous or lymphatic involvement, and minimum invasion of the rectal wall (tumor confined to the mucosa or submucosa) are associated with low incidence of lymph node metastasis (10,11,12). In potentially curable patients transanal ultrasound or MRI should be performed to identify depth of invasion and lymph node status (T and N stage respectively). Endorectal sonography has a reported accuracy of up to 93% and 81% in showing the depth of invasion and lymph node involvement respectively (1). Patients with perirectal lymphadenopathy (Stage III) should undergo a radical resection as TEM can not evaluate or treat regional lymph nodes (21).

The resection margin of the local specimen is considered by some authors of critical importance in relation to the development of recurrence. Heinzt *et al.* reported tumor free resection margins of the surgical specimens in 78%(35/45) in cases of low risk T1 carcinoma and only in 58% (7/12) for high-risk carcinoma. To achieve local radical excision and to avoid uncertain margins in the final histology the margin of clearance should be 5 mm in cases of adenomas and 10 mm in carcinomas (25). Other authors emphasize on the role of lymph node involvement only, meaning that positive excisional margins should not be considered a risk factor, rather it should be viewed as an insufficient therapy, which requires further treatment (1).

When the above criteria are met, results of TEM are comparable with these of radical surgery. Actually in the presented randomized and non-randomized comparative studies no statistically significant differences were observed between the TEM and radical surgery (RS) groups, as far as local recurrence and survival for each follow- up period is concerned (Table 1), with the exception of T2 tumors in the study of Lee *et al.* (11). Lee *et al.* found a 5-year local recurrence rate of 4.1% and 5-year survival of 100% after TEM for T1 tumors. For T2 tumors the 5-year local recurrence rate was statistically higher after TEM than after RS ($p = 0.04$), though no difference was observed as far as survival was concerned. On the contrary Lezoche *et al.* in their PRT found no differences in local recurrence between TEM and laparoscopic resection for T2 tumors. The authors concluded that a wide local excision (TEM) or T2 rectal cancers with preoperative high dose radiotherapy and chemotherapy can achieve probabilities of local failure and survival that are comparable with those of laparoscopic resection (8).

Other non-comparative series studies favor TEM for treatment of T1 rectal tumors. For T2 cancer, with its relatively high lymph node metastasis rate, there are few reports of the therapeutic effect of TEM. Again Lezoche *et al.* in a previous non-randomized study in 2002 evaluated the outcome of 35 patients with pT2 rectal tumors treated with preoperative high dose radiotherapy followed by TEM. The authors report once case of local recurrence (2.85 5) and probability of surviving 96 months after completion of treatment 83% (18). The authors concluded TEM of pT2 rectal tumor combined with preoperative high doses of chemotherapy could achieve similar survival to the one observed after open or laparoscopic surgery. This study has the methodological problem that it is not randomized. Additionally only patients with well- or moderately differentiated tumors not exceeding 4 cm in diameter, and without evidence of vessel or lymphatic tumor cell invasion. Thus tumors with histopathological features that involve in a lower

Table 1. — **Studies compairing TEM and radical surgery (RS) for the treatment of rectal cancer : Patients, follow-up, recurrence- and survival rate**

		Patients		Follow up*		Local Recurrence		Survival	
		TEM	RS	TEM	RS	TEM	RS	TEM	RS
Winde *et al.* (6,7)		25	28	40.9	45.8	1/25(4%)0	96%	96%[a]	
Lezoche *et al.* (8)		20	20	56	56	1/20	1/20	95%	83%[b]
Heintz *et al.* (9)	LR	44	34	52		2/46	1/34	79%	81%[a]
	HR	11	11	42.8		4/12	2/11	62%	69%
Langer *et al.* (10)		79	27	21.6	33.7	10%	3.7%	100%	96.3%[c]
Lee *et al.* (11)	T1	52	17	31.0[+]	34.6[+]	4.1%	0%	100%	92.9%[a]
	T2	22	83	31.0[+]	34.6[+]	19.5	9.4**	94.7%	96.1%

LR : Low-risk T1 rectum Ca
HR : High-risk T1 rectum Ca
*Follow-up in months (median value except [+] : mean value)
**Statistical significant difference
[a] Five-year survival
[b] Survival at the end of the follow up
[c] Two year survival.

rate of nodal metastasis. Guerrieri *et al.* reported disease survival rate in T2 and T3 patients 81% and 59% respectively at a mean follow up time 46 months (26).

Stipa *et al.* examined the outcome of patients with Tis, T1, T2, and T3 tumors treated with TEM receiving pre- or postoperative radiotherapy (27). With a recurrence rate of 0%, 13%. 17% and 50% for each stage Tis to T3 and 5 year survival rates of 100%, 92%, 75% and 69% respectively the authors concluded that TEM is effective for early (Tis, T1) rectal cancers. Selected Patients with T2 tumors can be treated with preoperative chemoradiation and subsequently local resection (TEM). Patients with T3 tumors should not be treated with local excision, unless they are unable to sustain more extensive surgery. In a recent study Lezoche *et al.* report at a median follow-up of 55 (range 7-120) months a local failure rate was 5 per cent for patients with T2-T3 rectum neoplasms treated with TEM following a neoadjuvant radiotherapy (28).

This conclusion seems to precisely depict the actual role of TEM in the surgical treatment of rectal Ca. T1 lesions (confined to the mucosa and submucosa) are ideal candidates. Further randomized control trials especially for advanced tumor stages (T2, T3) are necessary in order to establish the role of TEM in the treatment of these tumor stages (6-11,18,27,28,29). The impact of radiotherapy and chemotherapy on surgical treatment must also be taken into account as these therapies are currently and integral part of the multidisciplinary approach to rectal cancer treatment and can lead to tumor down staging and lymph node sterilization improving resectability (8).

It is obvious that careful patient selection is crucial to TEM outcome. Preoperative staging must be precise and should be done by the surgeon himself. In any case, TEM is a technically challenging procedure that requires significant experience before dexterity is achieved.

What will the future of TEM in the treatment of rectal cancer ? Undoubtedly TEM is a safe and effective procedure even in rectal cancer when appropriate selection criteria for the patients are applied. Though it is not possible to rule out a higher local recurrence rate for TEM than radical resection for tumor stages T2 or more (17), multidisciplinary approach with new aggressive radio-chemotherapeutic protocols is quite promising. Anyway TEM will be applicable and effective in many patients with rectal Ca, and those with a local recurrence have always the option of a subsequent radical resection or salvage operation (2,8). We have to point out that authors, who found higher recurrence rates after TEM for rectal cancer, emphasize on the role of radical surgery in cases of advanced stages. Floyd *et al.* identified 2 recurrences in 75 patients undergoing TEM for T1 cancer, both of which were salvaged with radical resections, for a 0% cancer specific mortality (30). Maslekar *et al.* reported local recurrence rates after TEM4.5% (range 0-14) for benign rectal lesions, 6% (0-13) for T(1) cancers, 14% (range 0-50) for T(2) cancers and 20% (range 14-67%) for T(3) cancers. Local recurrences after TEM could be surgically salvaged with good disease free survival rates. In the same series three patients with a recurrence after a TEM for T2 rectal cancer were submitted to salvage resection and were free of recurrence until at least two years after surgery (31).

In their TEM series Bretagnol F treated 52 patients with rectal cancet with TEM. Histopathological stage (pT) was stage 1 in 31 patients, pT2 in 17 and pT3 in four. Immediate salvage surgery was performed in seven patients (13 per cent). At a median follow-up of 34 (range 1-102) months, eight patients (15 per cent) with carcinomas had developed local recurrence. The overall and disease-free 5-year survival rates for patients with carcinomas were 76 and 65 per cent respectively (32) The authors conclude that TEM might be

oncologically safe for carcinomas, provided that resection margins are clear,but strict patient selection is required.

Borschitz T *et al.* treated 44 patients with pT2 rectal cancer with TEM. All of them were recommended a radical operation. Local recurrence rates after local R0 resection alone of low-risk T2 carcinomas were 29 percent, whereas patients with unfavourable criteria developed recurrences in 50 percent. After immediate reoperation, the local recurrence risk in patients without lymph node filiae was significantly reduced to 7 percent. The authors concluded that local R0 resection of low-risk pT2 carcinomas represents an inadequate therapy. In pT2N0M0 rectal carcinomas, the recurrence rate can be reduced through immediate reoperation to a level similar to primary radical surgery (33). These studies might cause scepticism about the role of TEM in rectal cancer treatment.

Conclusion

Most of the published studies lead to the conclusion that TEMs offers oncologic outcomes similar to those of radical resection for T1 tumors. In order to define the exact role of this procedure in the rectal cancer therapy, further controlled randomized trials with increased number of patients examining the efficacy of TEM in advanced tumor stages (> T2) in conjunction with other neoadjuvant or adjuvant therapeutical modalities (radio-, chemotherapy) in an adequate follow-up period are necessary. Until then radical surgery remains an established treatment modality for these advanced cancer stages.

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