Transanal endoscopic microsurgery combined with endoscopic posterior mesorectum resection in the treatment of patients with T1 rectal cancer – 3-year results

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Abstract

Introduction: *Rectum-sparing transanal endoscopic microsurgery (TEM) is a well-established treatment for T1 rectal cancer (RC). However, it is associated with an increased rate of local recurrence in comparison with extended resection. In most cases this failure is linked to inappropriate case selection and the presence of clinically non-detectable metastases in the regional lymph nodes. Endoscopic posterior mesorectal resection (EPMR) makes it possible to remove the relevant lymphatic drainage of the lower third of the rectum in a minimally invasive way, which in turn can help in adequate tumor staging.*

Aim: *To evaluate the long-term clinical results and influence of combined TEM and EPMR treatment on the anorectal functions.*

Material and methods: *Ten consecutive patients with T1 RC were operated on using TEM and EPMR as a two-stage procedure between 2007 and 2009.*

Results: *After a median follow-up of 42.6 (range: 36–80) months, none of our patients complained of symptoms of incontinence apart from one female patient with gas incontinence diagnosed preoperatively. There was no statistically significant difference in basal anal pressure, squeeze anal pressure, high pressure zone length or fecal continence assessed using the Fecal Incontinence Severity Index before and in follow-up months after the procedure. Postoperative morbidity consisted of one hematoma formation and one male patient complaining about sexual dysfunction until 6 months postoperatively. There was no evidence of locoregional recurrence.*

Conclusions: *Endoscopic posterior mesorectal resection in combination with TEM appears to be safe, feasible and with no impact on the basic anorectal functions in the 3-year follow-up.*

Key words: *transanal endoscopic microsurgery, rectal cancer, endoscopic posterior mesorectal resection.*

Introduction

Rectum-sparing transanal endoscopic microsurgery (TEM) is a well-established treatment for T1 cancer of the rectum. A low complication rate, a short hospital stay, and the preservation of anal sphincter function make TEM an attractive option for these patients as well [1–5]. However, it is associated with an increased rate of local recurrence in comparison with extended resection [6, 7]. That is why Zerz *et al.* introduced the endoscopic posterior mesorectal resection (EPMR) procedure, which allows resection of the lymphatic field in this region without sacrificing the rectum. According to the results published in the literature, this technique seems to be safe and feasible. It removes a relevant lymphatic field of the lower rectum, which in turn allows for a complete

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staging of the tumor and radical treatment in case of positive lymph nodes (LN) [8, 9].

The TEM procedure alone is connected with transanal introduction of a 4-cm diameter operational rectoscope, which can influence anorectal functioning [10–13]. Although there are no data on fecal incontinence after EPMR in the scarce published literature, resection of this part of the mesorectum, including dissection of small nerves reaching the rectum, may potentially influence the continence.

Aim

That is why we conducted this prospective study with the aim of assessing safety and efficacy and determining the influence of TEM combined with EPMR on the long-term anorectal functional outcome.

Material and methods

Patients with T1 cancer of the lower third of the rectum were examined in the prospective study between 2007 and 2009. All the patients were treated with TEM in combination with EPMR in a two-stage procedure.

Preoperative staging

The location, staging and grading of the tumor were assessed during sigmoidoscopy with a biopsy and pathological examination, endorectal ultrasonography (ERUS) and in some cases 3D ultrasound imaging. In addition, we performed colonoscopy (to exclude synchronous lesions) and standard preadmission laboratory diagnostics. All the patients had a chest X-ray, and a computed tomography (CT) of the abdomen and pelvis. In addition, their preoperative carcinoembryonic antigen (CEA) serum level was measured. However, the inclusion criterion for the study was the confirmation of T1 stage by the final pathological examination.

Functional evaluation

To obtain the functional results a full anorectal manometry was performed using a six-channel catheter (Medtronic) on the day of admission to the hospital for TEM and for EPMR. We evaluated the following parameters: basal anal pressure (BAP), squeeze anal pressure (SAP), length of the zone of maximum pressure (high pressure zone length – HPZL), presence of recto-anal reflex when coughing (reflex sphincter contraction – RSC) and rectoanal inhibitory reflex (RAIR). The Fecal Incontinence Severity Index (FISI) was used to provide a subjective assessment of the ability to control defecation.

Operative technique

Full thickness local excision using TEM was performed in the first stage. All patients received bowel preparation, subcutaneous thrombosis prophylaxis and a single intravenous infusion of antibiotic prophylaxis (ceftriaxone sodium 2.0 g + metronidazole 1.0 g *i.v.*). All the procedures were performed by a single surgeon and under general anesthesia. Before the introduction of the proctoscope, a nitroglycerin ointment was used routinely to achieve relaxation of the anal sphincter. The surgical procedure was performed using an operative rectoscope (Storz, Germany) 4 cm in diameter and 20 cm long. The patient was positioned so that the tumor was localized downwards in the operating field according to preoperative sigmoidoscopy. The operating technique was performed as described by Buess. To obtain radical margins, the planned resection line was marked with diathermy spots at least 10 mm from the tumor. All the defects were closed by running 4-0 monofilament sutures secured with titanium clips. Macroscopic control of the margins and the diameter measurement were made after the excised specimen had been pinned out on a cork board.

As in the second stage, EPMR was performed four to 6 weeks after the former operation. The procedure was performed as described by Zerz *et al.* and in our previous paper [8, 14].

Follow-up

All the patients had proctologic follow-up including ERUS and an anorectal manometry. A consecutive oncologic examination, based on an accepted follow-up program (history, physical examination, rectoscopy) was performed every 3 months for a period of 2 years and every 6 months for a further 3 years. Colonoscopy and computed tomography of the thorax, abdomen and pelvis were performed every 12 months.

The local institutional ethics committee approved the study.

Statistical analysis

Data on all patients were entered into a prospective database. The data are presented as mean val-

Table I. Patient characteristics

Parameter	Results
Gender:	
Female	5
Male	5
ASA score:	
1	3
2	3
3	4
Tumor size* [mm]	30.9 (range: 22–43)
Location:	
Anterior wall	2
Posterior wall	8
Follow-up [Mo]	42.6 (range: 36–58)

**Tumor size – maximum length of the tumor measured after fixation of the specimen on a cork board*

Table II. Histological findings

Parameter	Results
Grading:	
1	2
2	7
3	1
Submucosal invasion:	
Sm1	2
Sm2	6
Sm3	2
Cancer cells in lymphatic or blood vessels	No
Status and number of harvested LN	6.9 (range: 4–11)

ues. The statistical analysis was based on the ANOVA test with repeated measures (Statistica 10.0 for Windows). A *p*-value of less than 0.05 was deemed to indicate statistical significance.

Results

Ten patients (5 female and 5 male; ranging in age from 69 to 78 with a mean of 73.5 years) took part in the prospective study during a period from 2007 to 2009. The patients' characteristics are summarized in Table I.

The primary tumor could always be radically excised using TEM with a radial margin of at least 10 mm (full thickness excision). In all cases during the EPMR procedure it was possible to create a sufficient presacral operating space and resect the mesorectum up to the promontory. The mean EPMR operating time was 89 (range: 65–145) min. There were no intraoperative complications apart from one small rectum perforation during EPMR, which did not require conversion and was treated endoscopically with two additional sutures. Postoperative morbidity consisted of one hematoma formation, which resolved itself without any additional treatment, and 1 male patient complaining about sexual dysfunction until 6 months postoperatively. However, the symptoms resolved later without any additional treatment. There was no mortality. The median length of stay was 4.5 days (range: 4–8 days).

Histological findings and follow-up

After a median follow-up of 42.6 (range: 36–80) months, there was no evidence of locoregional recurrence. The histological findings are summarized in Table II.

Functional results

None of our patients complained of any symptoms of incontinence in the postoperative period apart from one female patient with fecal incontinence diagnosed preoperatively (gas incontinence). We observed a deterioration of subjective symptoms 1 month after EPMR. However, 3 months after the procedure the intensity of the symptoms was already comparable with that assessed preoperatively. There were no statistically significant differences in BAP, SAP, HPZL and in fecal continence control assessed using the Fecal Incontinence Severity Index before, after TEM alone and 1, 3, 6, 12 and 36 months after the EPMR procedure (Tables III and IV).

Discussion

This is also the first study assessing the long-term influence of combined TEM and EPMR treatment on the anorectal functions of patients with T1 rectal cancer. Only a few studies have dealt with the postoperative functional results, but only after TEM

Table III. Manometry results before and after the procedure

Parameter	Before TEM	Before EPMR	1 Month postop.	3 Months	6 Months	12 Months	36 Months	Value of *p*
BAP [mm Hg]	58.3	49.8	54.2	56.7	57.5	58	58	NS
SAP [mm Hg]	141.7	142.2	140.8	140.8	142.5	142.4	144	NS
HPZL [cm]	2.6	2.5	2.5	2.6	2.6	2.6	2.6	NS
RAIR [+/n]	6/6	6/6	6/6	6/6	6/6	6/6	6/6	NS
RSC [+/n]	6/6	6/6	6/6	6/6	6/6	6/6	6/6	NS

BAP – basal anal pressure, SAP – squeeze anal pressure, HPZL – high pressure zone length, RSC – reflex sphincter contraction, RAIR – rectoanal inhibitory reflex

Table IV. Mean FISI scores before and after the procedure

	Before TEM	Before EPMR	1 Month postop.	3 Months postop.	6 Months postop.	12 Months postop.	36 Months postop.	Value of *p*
Overall	2.7	2.8	2.8	2.7	2.6	2.7	2.7	NS

alone. Most of them have shown that even though manometric alterations can be observed in the early postoperative follow-up, manometric values return to normal with time, and no detrimental effects on fecal continence can be seen. We discussed the studies in detail in our preliminary study assessing functional results after 12 months [14]. Since that time we have not found in the literature any other studies dealing with this problem.

In our study we did not observe any statistically significant differences in BAP, SAP, HPZL, RSC and RAIR before, after TEM alone and after the combined TEM + EPMR procedure. Moreover, we also did not observe statistically significant differences in FISI score providing a subjective assessment of the ability to control defecation. One female patient with fecal incontinence diagnosed preoperatively (gas incontinence) complained of a slight deterioration in her symptoms one month after the EPMR procedure. At the 3-month follow-up the intensity of the symptoms were already comparable with those reported preoperatively. However, none of the above studies used nitroglycerin ointment (as a donor of NO) before the introduction of the operational proctoscope. In our department this type of ointment is applied in the anal canal as a standard procedure, just before the TEM rectoscope is introduced. It causes rapid sphincter relaxation, and decreases BAP pressure by approximately 30 mm Hg without any major effect on blood pressure. Furthermore, none of the published studies assessed the functional outcome after combined TEM and EPMR treatment, which is why comparison with this published paper is not possible. In the study of Zerz *et al.*, 1 female patient reported transient defecation problems in the sense of inertia recti for 6 weeks [8]. We can only hypothesize that it may be due to dissection of small nerves reaching the rectum. In our study group we did not observe such a complication. Koeninger *et al.* also did not report any postoperative complications, in the sense of deterioration of continence control [15]. Of course we are aware of a limitation of this study. A potential difference in anorectal functions compared to the preoperative results may remain statistically undetected due to the small sample size.

This technique is safe and effective. In a study of 18 patients carried out in Sankt Gallen the mortality rate was zero and the morbidity rate was low. Tarantino *et al.* observed 3 cases of intraoperative perforation, treated endoscopically with additional sutures, with no clinical consequences in the postoperative period. In the postoperative period they also reported 1 case of transient rectal inertia, paresthesia in the posterior femoral region and wound dehiscence. There were also two major complications after EPMR, 1 case of pulmonary embolism and 1 case of postoperative bleeding that required endoscopic evacuation [9]. Koeninger *et al.* also observed no intra- or postoperative complications in a report on 2 patients treated using the EPMR technique [15]. Similarly, in the 3-year follow-up mortality was also zero in our study group and we had 1 case of intraoperative perforation, treated endoscopically with two additional sutures, which led to an uneventful

postoperative course. Perforation of the rectum wall was probably due to a scar after TEM operation of a tumor localized in the posterior wall. Moreover, we observed one case of sexual dysfunction (see below) and 1 case of hematoma formation in the postoperative period which was resolved without any additional treatment. No patient developed ischemic complications, which demonstrates that the blood supply was not significantly impaired after posterior mesorectum excision.

The EPMR also appears to be a feasible technique for harvesting a representative number of LN. In the series of Tarantino *et al.* the median number of resected LN was 7 (range: 1–22). Among them 5 patients had positive LN [9]. In the report of Koeninger *et al.* histopathological workup revealed only one tumor-free LN in the first resected specimen. However, in the second case they found metastatic involvement in one out of six excised LN [15]. In the study by Wu*et al.*, assessing local recurrence rates of patients with high risk T1 rectal cancer (RC) after TEM, 15.4% of patients had mesorectal LN involvement (T1 RC patient reoperated after TEM within 4 weeks with unfavorable histopathological factors) [16]. In our study group, the average number of harvested LN was also 6.9 (range: 4–11) with no case of metastases. Moreover, it is also important to mention that more than half of LN in the mesorectum are small LN (< 5 mm in size) which are not possible to detect using present imaging modalities. In the study by Yun-Feng Yao *et al.*, small LN detection increased the accuracy of N staging by 20%. As far as location and number of the involved LN is concerned, both in the middle and low located RC they were higher in the distal mesorectum than in the proximal. Furthermore, in the case of RC located < 6 cm from the anal verge there were no metastases in the LN in the upper mesorectum area. This could also be an important fact in the discussion on the extent of excision of EPMR, which includes mesorectum up to the level of the arteria rectalis superior [17].

In the study by Doorneborsch *et al.* tumor size (> 3 cm) alone or in combination with submucosal invasion depth or tumor budding appeared to be a predictive factor for locoregional failure. In our study, 5 patients had a tumor larger than 30 mm, usually connected with submucosal invasion assessed as stage 2 or 3. None of the patients had LN metastases, or lymphatic or blood vessel invasion. Also, in the follow-up none of them developed recurrence [18].

Conclusions

Endoscopic posterior mesorectal resection in combination with TEM does not influence basic anorectal functions in the long-term follow-up. However, it requires further evaluation using a larger study group.

It is a safe and feasible procedure. It also makes it possible to harvest a representative number of LN, which thereby makes this technique not only a diagnostic tool but also a treatment modality. Whether this approach can really be oncologically radical will remain unclear until the results of further studies on a larger group with a longer follow-up are published.

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