Transanal Endoscopic Microsurgery (TEM) for Rectal Cancer: University Hospital of North Tees Experience

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Abstract Transanal endoscopic microsurgery (TEM) is a minimally invasive technique that is increasingly being used to treat early rectal cancer (T1/T2). We studied the outcomes of TEM for rectal cancer at our institution looking at the indication, recurrence rate, need for further radical surgery, 30-day and 12-month mortality and complication rate. We performed a retrospective analysis of prospectively collected data of cases between 2008 and 2012: 110 TEM procedures were performed during this period: 40 were confirmed rectal cancers and 70 were benign. We analysed the data for the 40 patients with confirmed rectal cancer. Thirty (75 %) of the subjects were male with a mean age of 71 ± 10 years (range 49–90 years) and 19 (48 %) patients were ASA 3 and 4. Nineteen (48 %) of cancers were pT1, eighteen (45 %) were pT2, two (5 %) were pT3 and one was yPT0. Mean specimen size was 66 ± 20 mm (range 33–120 mm) with a mean polyp size of 41 ± 24 mm (range 18–110 mm). The mean cancer size was 24 ± 13 mm (range 2–50 mm). Average distance from the anal verge was 70 ± 37 mm (range 10–150 mm), and the mean operating time was 72 ± 22 min (range 40–120 min), with an average blood loss of 28 ± 15 ml (range 10–50 ml). Median hospital stay was 2 ± 1 days (range 1–7 days). Complete excision (R0) was achieved in 37 (93 %) patients. Minor post-operative complications included urinary retention in two and pyrexia in three patients. There were no 30-day or 12-month mortalities. Mean follow-up was

13 ± 11 months, range (3–40 months). Local recurrence occurred in two (5 %) patients, both underwent redo TEM. Twelve (30 %) patients underwent laparoscopic radical resections (seven AR and five APER) post-TEM. Post-operative histology confirmed pT0N0 in 7/12 patients. Three were lymph node-positive (T0N1), one was pT3N1 and the fifth was pT3N2. TEM is associated with quicker recovery, shorter hospital stay and fewer complications than radical surgery. It is a good alternative to radical surgery in early rectal cancer, especially for high-risk patients. Recurrent tumours can be treated with redo TEM.

Keywords Transanal endoscopic microsurgery · Radical surgery · Rectal cancer · Local resection

Introduction

Transanal endoscopic microsurgery (TEM) was first described by a German surgeon, Gerhard Buess, in 1983 [1]. Originally developed for the excision of benign lesions, TEM is a minimally invasive technique that is increasingly being used to treat both rectal polyps and early rectal cancer [1, 2]. Using special microsurgical instruments, TEM provides an alternative to major rectal surgery for lesions not amenable to endoscopic techniques.

Colorectal cancer is the fifth most common adult cancer worldwide and the third most common in the UK, with over 40,000 new cases every year, almost one third (14,000) are confined to the rectum. Stage I cancers have an up to 90 % five-year survival rates but dropping to even 7 % for stage IV cancers. Despite advancements in chemotherapy and radiotherapy, surgical resection remains the mainstay of treatment throughout the world [3]. Radical rectal resection has a documented mortality rate of 5 %, going up to 25 % in some patient groups [4], in addition to the risks of permanent stoma,

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bladder or sexual dysfunction and poor bowel function. There is no reported mortality from TEM so far, and the 3 % incidence of complication is significantly lower compared to radical resection [5]. TEM requires less operating time, has a lower incidence of bleeding, less post-operative pain, quicker recovery and shorter hospital stay [6, 7]. Recurrence of rectal polyps has been reported to be 4–13 %, and redo-TEM remains an option in such recurrences. TEM is increasingly being used for the excision of lesions in patients who are poor surgical candidate [8–10].

Methods

We performed a retrospective analysis of a prospectively kept database between August 2008 and August 2012. There were 110 TEM procedures performed during this period by two consultant surgeons (TG and DG). Forty were confirmed cancers, and 70 were benign adenomas with varying grades of dysplasia. Forty-two operations were performed in 40 patients with rectal cancers (two redo TEMs). Only patients with confirmed rectal cancer were included in this study. We studied the outcomes like indication for surgery, recurrence rate, further radical surgery, complications and 30-day and 12-month mortality rates.

Operative Technique See picture 1–7

TEM is a minimally invasive technique for the resection of adenomas and early rectal carcinoma unsuitable for colonoscopic or local excision, which will otherwise require major surgical resection in the form of anterior resection or abdominoperineal excision of the rectum. All procedures were performed under general anaesthesia; however, regional anaesthesia can be used. Phosphate enema and prophylactic antibiotics (IV cefuroxime and metronidazole or gentamycin if penicillin-allergic), were routinely used, and antibiotics continued postoperatively if there were signs of infection (raised inflammatory markers and/or pyrexia). The patient is positioned according to the position of lesion (e.g. lithotomy, for posterior lesions or left/right lateral position). Karl Storz TEO system is used (Tubingen, Germany, <https://www.karlstorz.com/cps/rde/xchg/SID-0EB720B4-2F539A4B/karlstorz-en/hs.xsl/15932.htm>). Using a hook diathermy, a full-thickness dissection with at least a 5-mm margin from the edge of the polyp circumferentially was performed in all patients. The defect was closed using Polysorb 3/0 in a continuous fashion and secured using endoclips. All patients were admitted for overnight observation and assigned to a key worker (colorectal nurse specialist) to contact by telephone for advice following discharge.

All patients were discussed at a colorectal multidisciplinary meeting before and after the procedure. Two weeks following the procedure, patients were seen in the outpatient clinic in the presence of the colorectal specialist nurse and were counselled

about the results and further surgery. Postoperatively and following a complete (R0) resection all patients were counselled about the risk of lymph node metastasis. For patients with T1Sm1/2 a risk of <3 % is given, for patients of T1Sm3 a risk of >10 % and for patients of T2 cancers a risk of 20 % lymph node metastasis is explained to them. Radical excision is offered to all patients with T1Sm3 and T2 cancers. A mortality risk of 2–5 % following radical resections plus associated morbidity and the possibility of stoma were also discussed.

For biopsy proven rectal cancer, pre-operative work-up included a full colonoscopy, baseline CEA, full haematological and biochemical profiles, a CT scan of the chest abdomen and pelvis and an MRI of the rectum. If MRI was contraindicated, they underwent an endorectal ultrasound. Follow-up protocol includes clinical examination, sigmoidoscopy every 6 months for the first 2 years, MRI at 6, 12 and 18 months and yearly CT scan for the chest, abdomen and pelvis.

Data were collected from a prospectively collected database kept by the two consultants. Additional data were collected from ICE, PACS, electronic discharge summaries, patients' notes and online pathology system.

Statistical Analysis

The following software were used for statistical analysis: Statistical Package for the Social Sciences, version 19 for Windows (SPSS, Chicago, IL, USA) and Microsoft Excel (Microsoft Corporation, Seattle, USA). Survival curves were generated using the Kaplan–Meier method.

Results

Over a 4-year period, 42 procedures were performed in 40 patients with rectal cancer (T1, T2 and T3). The average age was 71 ± 10 (range 49–90), and 75 % were males [Table 1].

Table 1 Operative characteristics of patients and outcomes

	Mean $\pm$ SD	Range
Age in years	71 $\pm$ 10	49–90
Specimen size (mm)	66 $\pm$ 20	33–120
Polyp size (mm)	41 $\pm$ 24	18–110
Cancer size (mm)	24 $\pm$ 13	2–50
Distance from anal verge (mm)	70 $\pm$ 37	10–150
Circumference	33 %	25 %–75 %
Operative time (min)	72 $\pm$ 22	40–120
Blood loss (mls)	28 $\pm$ 15	10–50
Nearest lateral margin (mm)	6 $\pm$ 4.9	1–25
Deep margin (mm)	3 $\pm$ 2.1	0–10
Length of hospital stay (median days)	2 $\pm$ 1	1–7
Follow up (months)	13 $\pm$ 11	3–40

Fifteen (38 %) patients were ASA III and four (10 %) were ASA IV, the remainder 52 % were ASA 1 and 2. Nineteen (48 %) of cancers were pT1, 18 (45 %) were pT2, two (5 %) were pT3, and one patient (2 %) had a complete pathological response (ypT0) after a long course pre-operative chemoradiotherapy [Table 2]. Mean specimen size was 66 ± 20 mm (range 33–120 mm), mean polyp size including cancer was 41 ± 24 (range 18–110), mean cancer size was only 24 ± 13 mm (range 2–50 mm). Average distance from the anal verge was 70 ± 37 mm (range 10–150 mm). Mean operating time was 72 ± 22 min (range 40–120 min), with an average blood loss of 28 ± 15 ml (range 10–50 ml). Median hospital stay was 2 ± 1 days (range 1–7 days). Average follow-up was 13 ± 10 , range (3–40 months) [Table 1]. Complete excision (R0) was achieved in 37 (93 %) patients [Table 2]. Three patients had incomplete excision, two of them developed local recurrence. Patient one had involved margins (pT2R1); after counselling, she refused radical surgery and underwent redo TEM, post-operative histology confirmed pT2N1R0, she only agreed to oral chemotherapy. Similar scenario occurred in patient two, in whom post-TEM histology confirmed involved margins (pT1Sm2R1), he developed local recurrence at 18 months, redo TEM showed involved margins (pT3R1); after further counselling, he had APER (pT0pN1R0), followed by post-operative chemotherapy. Patient three post-TEM histology was pT1Sm3R1; again, the patient declined radical surgery and agreed to radiotherapy.

Minor post-operative complications included urinary retention in two and pyrexia in three patients. There were no 30-day or 12-month mortalities, but there were three non-TEM-related deaths, one from known metastatic lung cancer, one from massive pulmonary embolus at 30 months, and the third

patient died at 12 months from non-TEM-related causes. Local recurrence occurred in two (5 %) patients, both underwent redo TEMs.

Twelve (30 %) patients underwent laparoscopic radical resections (seven anterior resection [AR] and five abdominoperineal excision of the rectum [APER]) post-TEM. Post-operative histology confirmed pT0N0 in 7/12 patients. Three were lymph node-positive (T0N1), one was pT3N1 and the fifth was pT3N2, [Table 3].

Discussion

Rectal cancer surgery was revolutionised by the concept of total mesorectal excision (TME), which coupled with advances in adjuvant and neoadjuvant therapies, and has been instrumental in achieving excellent oncological outcomes after resections. However, radical surgical resection carries a significant risk of morbidity and mortality. The quality of life is also affected with urinary and sexual dysfunction, as well as the need for a stoma or poor bowel function if the sphincters are preserved.

The idea of local excisions is not new. However, historical data on transanal excisions showed unacceptably high local recurrence rates (LR) (0–28.8 %) [11–15].

TEM is a minimally invasive technique that has the advantage of better visualisation and allowing clear margins with the additional benefits of a reduced length of hospital stay, less operative blood loss, shorter operation time and less use of opiate analgesia [16].

Although initially used for benign lesions, it has been increasingly accepted for T1 rectal cancers. Most reports show significantly better oncological outcomes when compared to the mainly historical reports of transanal local excision with local recurrence rate ranging from 0–11 % for T1 tumours. Our local recurrence rate of 5 % after a median follow-up of 1 year compares favourably [Fig. 1, Table 4].

The introduction of the National Bowel Cancer Screening Programme, UK, in 2006 has led to the earlier detection of rectal cancers, and this has highlighted the need for less aggressive treatment modality options to treat these early cancers.

A meta-analysis of studies comparing conventional radical surgery with TEM for T1 rectal cancers found that TEM was associated with a significantly shorter hospital stay and fewer post-operative complications. It concluded that TEM is a safe, feasible and effective option for T1 rectal cancer. Although they did find a higher rate of LR after TEM (12.0 % compared with 0.5 % for conventional surgery), this did not translate into a statistically significant difference in the 5-year survival [6].

Similarly, another meta-analysis found TEM to be superior to standard resection with respect to morbidity, but less effective in obtaining negative margins and associated with higher rates of LR [17]. Resection of rectum by conventional surgery,

Table 2 Post-TEM stage and grade

Stage post-TEM	Number of patients	Comments
T0	1	ypT0: complete pathological response LCRT, pre-op pT3N1
T1	19	Sm1=4 Sm2=5 Sm3=9 pT1N1=1
T2	18	pT2N0=17 pT2N1=1
T3	2	pT3=2
R0	37	
R1	3	
Grade 1	5	Well differentiated
Grade2	32	Moderately differentiated
Grade 3	3	Poorly differentiated
Total patients	40	

Table 3 Outcome of TEM patients who had radical surgery

Patient age (years)	TEM histology, lymph nodes status	Radical surgery histology, lymph nodes status	TEM LOS (days)	Radical surgery LOS, (days)	TEM complications	Radical surgery complications	Radical surgery type
68	pT1N1R0	pT0pN0R0, 0/16	2	7	None	None	APER
62	pT1Sm3R0, VI ^a	pT0pN0R0, 0/6	1	38	none	Stoma necrosis, laparotomy, chest problems, ICU	APER
63	pT1Sm3R0	pT0pN1R0, 1/10 (micrometastasis)	2	5	None	None	AR
62	pT1Sm3R0	pT0pN0R0, 0/5	2	5	None	?	AR
62	pT1Sm3R0	pT0N0R0, 0/13	1	4	None	AR syndrome, ultra low AR with pouch	AR
67	pT1Sm3 R0	pT0N1R0, 1/11	2	6	None	None	AR
70	pT1Sm3R0	pT3N1R0, 2/12	2	8	None	UTI	AR
68	pT2R0	pT0pN0R0, 0/9	1	4	None	None	APER
63	pT2R0	pT0N0R0, 0/14	1	9	None	Pyrexia, ileus	APER
67	pT2R0	pT3N2R0, 5/14	1	3	None	None	AR
57	pT2R0	pT0N0R0, 0/40	3	10	None	Pneumonia	AR
77	pT3R1	pT0pN1R0, 1/13	6	4	None	None	APER

APER abdominoperineal resection, AR anterior resection of the rectum

^a Vascular invasion

in case of unfavourable pathology after TEM, is an option used in our institute successfully.

TEM has been shown not to have any long-term effect on anorectal function or quality of life (QOL) [18, 19]. The ageing population in the UK is presenting us with management dilemmas for early rectal cancer when conventional surgical

resection has been shown to have significantly higher risks of post-operative morbidity and mortality in the elderly [20]. There does appear to be definite role for TEM in older patients where the risk of radical surgery does not favour it. Our patients had a mean age of 71, and a significant proportion (48 %) had an ASA of III or IV.

Fig. 1 Kaplan–Meier curve for disease-free survival

Table 4 Local recurrence rates according to studies

	Year	Patient no.	Local recurrence rate (%)
Buess et al.	1988	12	0
Buess et al.	1992	25	4
Windle et al.	1996	24	4.2
Smith et al.	1996	30	10
Langer et al.	2001	16	12.5
Demartines et al.	2001	9	8.3
Lee et al.	2003	52	4.1
Stipa et al.	2006	23	8.6
Floyd et al.	2006	53	7.5
Baatrup et al.	2008	72	6
Ramirez et al.	2011	54	7
Yu et al.	2011	38	2.6
Araujo et al.	2012	50	8
Morino et al., (T1/T2) ^a	2011	48	10
Steinhagen et al. ^b	2011	33	9
Gill et al	2012	40	5

^a T1=0 %, T2=22.7 %

^b In situ=2 %, T2=1 %

The evidence on selection criteria for TEM is especially poor, and the literature shows that larger tumours (>3 cm) in combination with submucosal invasion depth are significant predictive factors for locoregional failure after TEM for T1 rectal cancer [19, 21]. The evidence for oncological safety of TEM for T2 tumours is conflicting. A prospective randomised study of TEM versus TME after neoadjuvant chemoradiotherapy for T2 tumours with 50 patients in each group showed an LR of 8 % with TME surgery compared with 6 % with TEM after a median follow-up of 9.6 years. There was no difference in disease free survival & overall survival. There were also the expected advantages with TEM like shorter operating time, less blood loss, reduced transfusion requirements and no stomas [22].

However, Lee and colleagues demonstrated a significantly higher 5-year local recurrence rate following TEM compared with radical excision for T2 lesions (19.5 vs. 9.4 %, $p=0.035$). In this study, no neoadjuvant or adjuvant therapies were used [23].

The indications for TEM are being broadened when used in conjunction with neoadjuvant therapy. Current standard practice in the UK is to advise patients to undergo radical surgery if pre-operative staging shows a T2 lesion. However, this approach is being challenged and a UK-based multicentre randomised control trial TREC: transanal endoscopic microsurgery (TEM) and radiotherapy in early rectal cancer is currently recruiting. The study randomises T1-2N0M0 'early' rectal cancer to radical TME surgery (current gold standard) or short course pre-operative radiotherapy (SCPRT) with delayed local excision. This is close to the real life scenario in

the UK, where patients with T2 tumours would not have neoadjuvant chemoradiotherapy [24].

Our patients did not have any neoadjuvant therapies as this is not the standard practice for early rectal cancers in the UK except one who had a pre-operative stage pT3N1 rectal cancer. Following a LCRT, he had a complete pathological response ypT0, post-TEM histology was T0 [Table 2].

Excellent results have been reported when TEM is performed after neoadjuvant chemoradiotherapy, especially if there is a complete pathological response (CR). These patients have a low risk of LR. A retrospective review of local excision in 68 patients who had complete pathological response after neoadjuvant CRT showed no evidence of LR after a median follow-up of 87 months [25].

Accurate pre-operative staging is obviously essential. In our unit, we employ pre-operative pelvic MRI scan for local staging in all patients with rectal cancer, as well as a CT scan of the chest, abdomen and pelvis to look for evidence of distant disease. In the past, we were not using endorectal ultrasound (ERUS) as a routine in all patients; but now, we have added this for all patients to improve local staging done by MRI scan. A recent audit of the UK TEM database which comprises a prospectively collected data on nearly 500 patients, showed that ERUS was used in only third of the patients who underwent TEM for early rectal cancer. Moreover, ERUS inaccurately staged rectal cancer in 44.8 % of patients [26]. However, their data did show that the negative predictive value of EUS for transmural penetration, which is the question of most clinical relevance, was 0.97, a point highlighted by commentaries on this article by Halligan S [27].

In our series, 12 patients proceeded to early salvage surgery. The most common reason for this was advanced pathology [Table 4]. We do not routinely offer TEM if the pre-operative stage is >T1 or if nodal disease is detected. If the post-TEM histology is more advanced than T1Sm2, then the patient is counselled and salvage surgery offered. Studies have shown salvage surgery post-TEM to be safe in advanced and recurrent disease [28, 29]. In our series, all salvage surgery was performed laparoscopically with no conversions. However, Morino et al., in the study of 17 patients found that laparoscopic TME surgery after TEM is challenging and is associated with a significantly higher rate of APER [30].

Limitation of the Study The limitation of the study is its retrospective nature, and also, it is limited by the small number of participants; however, most of the data in TEMs are small numbers, and the largest study contained 150 patients.

Conclusion

TEM is associated with quicker recovery, shorter hospital stay and fewer complications than radical surgery. It is a good

alternative to radical surgery in early rectal cancer, especially for high-risk patients. Recurrent tumours can be treated with redo TEMs.

Conflict of Interest All the authors had no conflict of interest.

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