

Review Article

Transanal resection of rectal cancer: a review

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ABSTRACT

As an alternative to conventional resection of rectal tumors with low morbidity, the transanal approach has become popular and in-demand. It's been almost 30 years since the techniques for transanal resection have been evolving steadily. The revolution started with the advent of transanal endoscopic microsurgery in the 80's. Later, the introduction of transanal minimally invasive surgery improved the access and visibility for surgeons across the world. Concerns have been raised about recurrence rates of cancers with transanal approach and success of subsequent salvage operations. This review is an attempt to concisely describe the available techniques, their results and also to bring about a consensus as to whether it is worth to give our patients an option of transanal resection of rectal cancer.

Keywords: Early rectal cancer, Local excision, Rectal polyp, Early rectal cancer, Transanal excision, Transanal endoscopic microsurgery, Transanal minimally invasive surgery

INTRODUCTION

Each year there are over 34,000 new cases of colorectal cancer (CRC) in the UK. Similar numbers of men and women are affected, usually over the age of 45 years. Early stage cancer is associated with higher (~90%) 5-year survival. Early stage CRC is defined as lesions limited to the bowel wall with no disease extension beyond the submucosa (T1) or the muscularis mucosa (T2). Furthermore, there is no evidence of lymph node spread (N0).

Even though total mesorectal excision (TME) is considered standard surgical management for resectable rectal cancer, its value in early rectal cancer is becoming questionable. The aim of this procedure is to achieve adequate tumor clearance through the removal of the primary tumor including the mesorectum with the associated regional lymph nodes.¹⁻³ TME or radical surgery is the primary surgery that offers excellent rates of local control and therefore, excellent long-term

survival. Patients who undergo radical surgery for stage I and II rectal cancer can expect excellent long-term results which approach 4.5% 5-year local recurrence rates and 90% 5-year disease free survival (DFS) rates.⁴ However, the morbidity is high (30-68%) with a mortality that approaches 7%.^{1,4-6} Radical surgery is often followed by significant complications including anastomotic leakage, sepsis, permanent or temporary stoma, perineal wound complications, and urinary, sexual and bowel dysfunction that may diminish quality of life.^{1,2,4-8}

Given these significant complications, there has been increased interest in the local treatment of early rectal cancer, as some patients may be cured by avoidance of radical surgery and its concomitant disadvantages. Local excision (LE) of early rectal cancer is an attractive alternative to radical surgery for several reasons. First, the surgery is less invasive and associated with less postoperative pain and a shorter length of stay. The surgery preserves normal bowel function without the use of a stoma. There is less associated perioperative

morbidity. Furthermore, newer methods known as transanal endoscopic microsurgery (TEM) or transanal minimally invasive surgery (TAMIS) have been introduced that provide better visualization of tumors in the mid and upper rectum. Although local disc excision of the primary tumour, plus an adequate margin of normal tissue, allows for preservation of the rectum. But, omitting total mesorectal excision risks leaving behind microscopic lymph node metastases, a potential cause of local failure. The probability of tumour spread to mesorectal nodes and the rate of local failure following LE can be estimated using predictive histopathological biomarkers in the locally excised specimen like the St. Marks Lymph Node Positivity (LNP) Score. The aim of this review is to guide the reader in the understanding of the current debates in the management of early stage rectal cancer. This review will include a discussion of patient selection, surgical techniques, and expected oncological outcomes following treatment.

METHODS

A systematic search was carried out in PubMed and the 2017 Guidelines of Association of Coloproctology of Great Britain and Ireland. Studies done on management of small and early rectal cancers were identified and evaluated. Keywords used were “early rectal cancer, transanal excision, transanal endoscopic microsurgery, transanal minimally invasive surgery, local excision, rectal polyp”. The way patients are selected, how each of the procedures are done, the oncological outcomes of each procedure, adjuvant and neo-adjuvant therapies, surveillance and follow up were studied and reviewed.

PATIENT SELECTION

Appropriate patient selection coupled with full thickness excision is very important for a good outcome. In carefully selected patients local recurrence rates have been reported to be <4% and local excision can be curative, with similar oncological outcomes to radical surgery.⁹

There are several factors that need to be considered in a patient for local excision, viz: differentiation, the presence of lymphovascular invasion (LVI), the location in the rectum, the size, and the clinical stage. Other factors that are important to consider prior to performing surgery for rectal cancer are the characteristics of the patient that may put him or her at a higher surgical risk.

On digital rectal examination, a fixed tumor is indicative of advanced disease. Proctoscopy determines the tumor size, extent of rectal circumference involvement, and distance from anal verge. Tumors larger than 4cm or involving more than 50% of the rectal circumference are often excluded from local excision for technical reasons.

Clinical staging of early rectal cancer is a controversy. Preoperative tumor and lymph node staging can be a

challenge. Modern imaging modalities of endorectal ultrasound (ERUS) and magnetic resonance imaging (MRI) have been used to detect depth of tumor invasion and lymph nodes metastases in rectal cancer.^{2,9} However, ERUS is considered superior to MRI for assessment T staging in early rectal cancer if done by an expert.

The reported sensitivity and specificity of ERUS for depth of tumor invasion, perirectal tissue invasion and lymph node involvement is 94%, 90% and 67%, and 86%, 75% and 78%, respectively. Sensitivity of MRI for tumor invasion was similar to ERUS, specificity of the later was significantly better than MRI.¹⁰ The major disadvantage of ERUS is the variability in the interpretation of the study due to its dependence on one individual to perform and read the study accurately. MRI has a sensitivity and specificity for T staging ranging from 85% to 100% and from 91% to 98%, respectively.^{11,12} MRI is also superior at mesorectal lymph node staging with similar sensitivity and specificity as T staging. Both imaging modalities will not determine the absence of occult nodal metastases with complete certainty, and some authors suggest that both modalities can be used in combination to increase the likelihood of accurate local staging.

Assessment of histology after endoscopic biopsy of a rectal tumor may help in determining tumors at a higher risk of lymphatic spread. Indicators of tumor behaviour include histological grade, mucinous tumors, signet cell tumors, and the presence of LVI or perineural invasion (PNI) (Table A).^{13,14} Mucinous adenocarcinoma is defined by the findings of >50% of the tumor volume composed of extracellular mucin.

Traditionally, only rectal cancer below 8cm was considered a candidate for LE. This was due to the limitation of the surgeons' ability to reach higher and the lack of proper visualization of the rectal tumor. With advances in technology and instrumentation, tumors that are higher up can be reached with good visualization. Newer methods including TEM and TAMIS may allow access up to 15cm in the rectum. It is important that the patient is aware that these procedures will most likely result in a perforation of the bowel above the retroperitoneum and into the peritoneal cavity which will require repair. The details of these procedures are discussed further in this review. Extended indications for LE have been reported.

As of now, patients with a clinical stage \geq T2 rectal adenocarcinoma should undergo radical surgery. Patients with an advanced rectal cancer who are not candidates for radical surgery due to high operative risk or those who refuse to undergo radical surgery may be considered for neoadjuvant therapy followed by local excision of residual disease. Moreover, the use of local excision in patients with early rectal cancer treated with neoadjuvant therapy has been studied in clinical trials with mixed results.¹⁵⁻¹⁷

Currently, there is limited data supporting local excision or “wait and watch” in those patients with a complete clinical response following neoadjuvant therapy as an alternative to radical surgery.^{4,6,9}

Table 1: (ACPGBI 2017 MDT guidelines) suggested criteria for LE.

Anatomic
Tumor <4 cm
Tumor <50% of bowel circumference
Tumor within 8 cm dentate line
Tumor freely mobile
Imaging (ERUS/MRI)
Tumor limited to submucosa (T1)
No lymph node involvement (N0)
Histology
Well to moderately differentiated (sm1 or sm2)
Absence of LVI or PNI
No mucinous or signet cell component

SURGICAL METHODS OF LOCAL EXCISION (LE)

Transanal excision (TAE)

The use of standard equipment and direct visualization has been a routine treatment option for many years. Routinely TAE is mostly limited to tumors of less than 4 cm in diameter that lie within 8 cm of the anal verge. The lesions located in middle and upper rectum are usually not accessible with this technique because of their distance from the anal verge, and attempted excisions suffer from poor surgical exposure, confinement of the operating field, and uncertainty of the surgical clearance margin achieved.

As a standard, patients need to be assessed preoperatively which includes digital exam and proctoscopy to confirm location and mobility. Any lesion that looks suspicious should be subjected to transrectal ultrasound and/or magnetic resonance imaging for staging. Positioning of the patient is left to the preference of the operating surgeon, but orientation of the lesion is usually the deciding factor, with preference taken to operating downward. To aid in visualization, the anus is retracted with a Lone Star®.¹⁸ Traction sutures can be placed distal to the lesion to improve mobility and visualization. The chosen excision margin is typically marked out with electrocautery in a circumferential pattern around the lesion. For tumors that harbor malignant potential, a 1-cm margin is typically employed. After full-thickness excision is done, the specimen is oriented on a needle board and sent to pathology. After irrigation, the defect can be either left open or closed transversely with absorbable sutures.

Most common complications that can occur with conventional TAE may include retention of urine,

delayed haemorrhage, urinary tract infection, infections of the perirectal and ischioirectal space, and fecal impactions.

If patients receive radiation prior to resection, rectal pain is the most common complication (8%).¹⁹ The major disadvantage for TAE is the poorer surgical outcomes. Moore and others have demonstrated that newer procedures such as TEM yields clear margins more frequently than with the traditional TAE (90% vs. 71%) and significant less chance of tumor fragmentation, 94% vs. 65% respectively.²⁰ Intraoperative suboptimal visualization has been hypothesized as the cause for the increase risk of positive margins and tumor fragmentation following TAE.

Transanal endoscopic microsurgery (TEM)

TEM procedures are usually performed under general anaesthesia and a Foley catheter is used to decompress the bladder. Bowel preparation is done by phosphate enema in most patients. Rigid sigmoidoscopy is done to localise the tumor preoperatively in the clinic setting to determine the quadrant location of the lesion and to plan for operative positioning of the patient to allow the lesion of interest to sit at the 6-o'clock position. Prone jack knife position for patients with anterior lesions (legs spread apart and secured to arm boards) while those with a posterior lesion are positioned in lithotomy. Laterally located lesions are best approached with patients in the appropriate lateral decubitus position.²¹

Anus is gently dilated and rectum is inspected under manual air insufflation. The rectoscope is then attached to the operating table using the Martin's arm. Optics and operative instruments are introduced and the endosurgical unit is activated providing insufflation, suction, irrigation and pressure monitoring. Using cautery, the surgeon first makes the desired margin of clearance. This margin should be 5 mm from the macroscopic tumor edge for benign lesions and 10 mm in cases of invasive carcinoma. For adenomas located within the intraperitoneal portion of the rectum, a careful mucosectomy is performed to prevent entry into the peritoneum with the ensuing loss of rectal distention. For extraperitoneally located adenomas and for all invasive carcinomas, full thickness resection is standard. Circumferential adenomas in the lower and middle rectum can be resected as complete full thickness segments followed by an end-to-end anastomosis. Invasive carcinoma in the posterior or lateral position may be resected with some perirectal fat, which can often yield 1 or 2 adjacent lymph nodes, which can be examined for metastatic spread.

The resection bed for lesions below the peritoneal reflection may be left open or closed using a running suture with 3-0 polydioxanone suture (PDS) on a small-half (SH) needle. Closure of all intraperitoneal defects is mandatory and should be performed in 2 layers with separate closure of the peritoneum if entered.

The conversion rate from TEM to radical surgery from an abdominal approach has been reported to be 4.3% in one large series of 693 patients.²² The most common complications reported are hemorrhage, urinary tract infection, and suture line dehiscence. Bleeding and perforation can become life threatening especially in multimorbid or elderly patients. They frequently require reoperations and extend hospital stays.²³⁻²⁵ The reported incidence of fecal incontinence developing after insertion of the resectoscope is 1% and this is generally temporary.²²

Disadvantages of TEMS include limited clinical role to small tumors between 5 to 15cms and steep learning curve. Barendse et al, demonstrated by observing four different providers resect 693 lesions with TEM that a significant learning curve was associated with lowering conversion rates, peritoneal entrance, and procedure time.²² This same study also demonstrated that in patients undergoing TEM after the surgeon had performed at least 35 procedures, the risk of recurrence for malignant lesions declined by 10% as compared to those individuals undergoing surgery in the first 1-35 procedures.

Transanal minimally invasive surgery (TAMIS)

2009 was the year when TAMIS was introduced for the first time. It came as a substitute to the TEMS. TAMIS procedure uses the single incision laparoscopy surgery (SILS) ports. With this port, conventional laparoscopic instrumentation including the camera can be used to perform the procedure. In preparation for surgery, systemic antibiotics are administered, and all anticoagulant use is discontinued. Bowel preparation is routinely not required. Anaesthesia is provided with either spinal or general and the patient is placed in the dorsal lithotomy position (Table B). A SILS port after lubrication is inserted into the anal canal and pneumorectum is established with a standard laparoscopic CO₂ insufflator. Laparoscopic camera lens (preferably using a 5-mm 30 degree or 45 degree lens) and instruments such as graspers, thermal energy devices, and needle drives are introduced through the SILS port to assist the operator in performing a full thickness resection of the neoplasm with 1 cm margins. The remaining rectal defect is closed in the transverse direction and the specimen oriented for pathological review. If the tumor is above the peritoneal reflection, the abdominal cavity may be perforated and this may require laparotomy to repair.²⁶ Postoperatively, patients are expected to have an overnight hospital stay and quick recovery with early resumption of normal diet and activities. Several investigators are designing the TAMIS platform so that the procedure can be performed with the assistance of the Da Vinci® robot. Complications following the TAMIS procedure are infrequent with an overall rate of 7.4%.¹⁷ The conversion rate in 390 cases performed for both benign and malignant lesions was 2.3%.¹⁷ Inadvertent peritoneal entry during TAMIS was reported in 1% of cases and in some cases, the closure of the rectum was

successful transanally.¹⁷ In malignant polyps, the rate of positive margins was 4.4% and the rate of tumor fragmentation was 4.1%.¹⁷

Table 2: Comparison of techniques for LE.

Variables	TAE	TEM	TAMIS
Tumor distance in the rectum (from dentate line)	Up to 8 cm	>4 cm-up to 15 cm	Up to 15 cm
Bowel preparation	Phosphate enema	Phosphate enema	Phosphate enema
Patients position	Tumor dependent	Tumor dependent	Lithotomy
Anaesthesia	Spinal or general	General	General
Instrument	Rigid	Rigid	Flexible
Cost	Low cost	Expensive	Low cost
Learning curve	Moderate learning curve	Steep learning curve	Shallow learning curve
View	~180 degree view	220 degree view	360 degree view

ONCOLOGICAL OUTCOMES FROM LE

Pigot et al, demonstrated that in large rectal tumor up to 6 cm, the risk or recurrence of benign polyps was 10%.²⁷ If a malignancy was identified, the risk of recurrence was 20%. Pigot further speculated that the results from TAE can be explained by inadequate intraoperative exposure and suggested that the newer and improved techniques of LE may improve outcomes.²⁷

Many published literatures have confirmed that TEMS or TAMIS are better than TAE with regards to margin of resection and tumor fragmentation. Baatrup et al, examined his series of 143 consecutive TEM resections for rectal cancer. Of the patients that were pathological stage T1 tumors, the local recurrence rate was 12%.²⁸ They also found that the significant predictors for survival in his group of patients were tumor size and patient age. They strongly urged that tumors greater than 3 cm should not be removed by LE. There were no local recurrences noted in patients with pathological stage T1 tumors and the overall survival rate was 86% at 193 months. Moore et al, in 2007 reported a retrospective comparison of TEM to TAE for rectal cancer.²⁰ In this study, 171 patients (82 with TEM) were analyzed. This study included equal number of patients in each group with T2 and T3 tumors. Patients undergoing TEM had an overall lower recurrence rate (8%) when compared to patients undergoing TAE (24%) but this did not reach statistical significance.

When comparing the results of LE to radical surgery, local recurrence rates tend to be higher for both T1 (8.2-23%) and T2 adenocarcinomas (13-30%) undergoing LE when compared to radical surgery for T1-T2 disease (3-7.2%).^{19,29-31} In patients undergoing LE for T1-T2 disease the disease free survival (DFS) at 5 years following LE was 55-93%.^{19,29} This was comparable to patients undergoing radical surgery whose DFS at 5 years was 77-97%.^{29,32} The inability to demonstrate improved survival following radical surgery may be due to the retrospective analysis that occurred in many of these studies and the lack of adequate follow up. Only recently has there been an emphasis on appropriate follow up following LE. In addition, Nash et al emphasizes from his review of this topic that when he analyzed the patients he followed after LE, there was a survival difference seen between LE and radical surgery and this difference was the result of longer follow up.³³ They noted a significantly increased rate of cancer related death at 4-8 years following LE when compared to radical surgery. They recommend that all patients undergoing LE be committed to long term follow-up.

Whether LE compromises the oncological outcome with the risk of recurrence and local failure remains unknown. Lymph node metastasis occurs in 0-12% in T1 and 10-22% in T2 rectal cancer, however, as local lymph nodes are not sampled using TEM, it is reliant on preoperative staging and histopathological features of the tumor to direct further adjuvant treatment.^{3,34,35} Comparing different LE techniques; the negative margin is most likely achieved with TEM compared to TAE. Furthermore, the local recurrence rate is lower with TEM compared to TAE.²⁰ This is likely the direct result of improved visibility that is achieved with TEM. Whether or not these differences ultimately affect DFS is yet to be determined.

RADICAL RESECTION IMMEDIATELY AFTER LE

Differences in the sensitivity and specificity of the preoperative staging modalities, it is not uncommon for a preoperatively staged T1N0 rectal cancer to have a final pathological stage of T2 or T3. Moreover; a positive margin following LE carries a high risk of recurrence.³⁵

One method of managing unfavorable pathology is to offer the patient immediate radical surgery. Hahnloser et al, reported his experience at Mayo clinic with immediate radical resection after LE of rectal cancer.³⁶ In this series, 52 patients underwent radical surgery within 30 days after LE were matched with 90 patients with a T2-3N0-1 primary as a radical surgery control group. The indications for radical re-resection were: cancerous polyp, positive margins, LVI, advanced stage, nodal disease and residual cancer. The five-year overall survival for the study cases vs. the control case was (79% vs. 91%), respectively and the ten-year survival was (65% vs. 78%), respectively with no statistical significant. Several

studies have reported that the oncologic outcomes in patients treated by immediate radical surgery after LE for unfavourable histologic findings are comparable to that of radical surgery performed as a primary treatment.^{2,20,36,37} However, there is no consensus on the timing of radical surgery or on the use of radiotherapy before radical surgery.⁹

EFFICACY OF PELVIC RADIOTHERAPY COMBINED WITH LOCAL EXCISION

Combination of pre-operative radiotherapy and local excision is appealing as:

- Radiotherapy may effectively treat microscopic mesorectal nodal metastases.
- Tumour down sizing should facilitate local excision with clear margins.
- Tumour down staging is measured objectively rather than relying upon clinical examination.
- Histopathological non-responders are converted to radical surgery.

There is currently very little evidence to guide the use of down staging radiotherapy and local excision as curative treatment for early rectal tumours. Two small prospective studies have been conducted, the first comparing radical versus local excision following down staging CRT, the second evaluated efficacy of long and short course neoadjuvant radiotherapy schedules prior to delayed local excision.^{38,39}

A meta-analysis of seven studies of CRT and local excision to treat 237 cT2-T3 rectal tumours, reported pCR rates of 22%⁴⁰ with no local recurrences seen in this group. A further 19% of tumours were staged ypT1, 36% ypT2 and 14% ypT3 with local recurrence rates of 2%, 7% and 12% respectively.

Transanal endoscopic microsurgery (TEM) and Radiotherapy in early rectal cancer (TREC) is a randomised Phase II feasibility study to compare radical TME surgery versus short course preoperative radiotherapy with delayed local excision for treatment for early rectal cancer. Results of this trial are expected soon.

Currently, the standard of care for T2 rectal adenocarcinoma is radical surgery to ensure accurate staging and decrease the risk of local recurrence but with the promising results of pathological complete response; extended indications for LE have been considered as a middle ground between radical surgery and observation in good responders.

LE FOLLOWING NEOADJUVANT THERAPY

Very good response to neoadjuvant chemo-radiotherapy for rectal cancer has been observed with complete tumor regression even for advance clinical stages in 10 % to 30% of patients.^{37,41,42} These finding have translated into

a significant reduction in local recurrence rates from 12% to 4%.⁴³ In patients with pathological complete response (pCR), the risk of lymph node involvement is 1.8% compared to 24-52% in those who didn't have pCR.⁹ Furthermore, patients with a pCR tend to have favorable long-term outcomes, including better overall survival and lower recurrence rates.^{9,44,45} This had led some clinician to question the need for radical surgery with its associated morbidity in those who have a clinically complete response (cCR) confirmed by endoscopic exam.

STAR-TREC, a new multi-centre international trail, has commenced recruiting patients into three arms of which one may be observed without any surgical intervention and compared with patients who either may undergo radical TME or LE following completion of neoadjuvant treatment.⁴⁶

ADJUVANT THERAPY FOLLOWING LE

In an attempts to improve the oncological outcome and decrease recurrence; adjuvant therapy has been given following LE. To examine the efficacy of this approach, Sasaki et al, conducted a clinical trial to determine the efficacy of adjuvant chemoradiotherapy combined with local excision in the treatment of T1 to T2 low rectal cancer.⁴⁷

The completion rate for full-dose chemoradiotherapy was 86%.^{43,48} Serious, nontransient treatment-related complications were not reported. With a median follow-up of 7.3 years after local excision, the 5-year disease-free survival rate was 94% for the 53 patients with T1 lesions and 75% for the 4 patients with T2 lesions. There were 2 local recurrences during the entire observation period. Anal function after local excision and chemoradiation were kept at almost the same levels as observed before treatment. The addition of chemoradiotherapy to local excision of T1 rectal adenocarcinomas with poor prognostic features including deep submucosal invasion and lymphovascular invasion could improve on less favorable historic oncologic outcomes of local excision alone in this high-risk group for lymph node metastasis.

SURVEILLANCE FOLLOWING LE

Assuming that LE may not have achieved cure, initial follow up is usually intense and similar to the protocol followed for endoscopic resection of a malignant polyp. Optimal surveillance following LE should consider endoscopic assessment at 3-6 monthly intervals along with MRI pelvis at 3-6 monthly intervals and CT to detect distant metastases at 12 monthly intervals for 3-5 years.⁴⁹

CONCLUSION

LE for small and early rectal cancer is becoming a popular option because it comes with reduced morbidity

and mortality as compared to radical surgery, but the selection of patients is a key point to get good results. It is also appropriate for those who otherwise would be unfit or unwilling to undergo a more aggressive surgical approach. Oncologic outcomes of LE are not as good as radical surgery, but newer literature suggests the TEM and TAMIS may achieve better resection of the primary lesion with lower margin positivity rates and hence potentially reduce the risk of recurrence. However, the risk of recurrence in patients with node positive disease remains. Newer trials may reveal role of neo-adjuvant treatment in eliminating such risk in patients who would prefer to opt for rectal preserving surgery. Any locally excised tumor, regardless of approach, merits meticulous follow-up and surveillance for local and distant recurrence.

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