Curr Colorectal Cancer Rep (2016) 12:94–102
DOI 10.1007/s11888-016-0315-8

Management of Early (T1 or T2) Rectal Cancer

Benjamin M. Martin[1] · **Kenneth Cardona**[1] · **Patrick S. Sullivan**[1]

Published online: 20 February 2016

Abstract Early stage rectal cancers (T1/T2) are being found more commonly due to increasing compliance with population screening guidelines. Patient selection is the most important element in advising local excision versus standard transabdominal resection with total mesorectal excision (TME). Determining the best strategy for an individual patient relies on accurate histologic assessment (a surrogate of biologic behavior), accurate clinical staging (endorectal ultrasound or MRI), and accurate assessment of patient procedural risk. It is important to review the histology for high-risk features associated with occult lymph node metastasis as this portends a higher local recurrence rate. Since the local recurrence rate following local excision for T2 rectal cancer is high, it has been our practice to offer these patients proctectomy with TME unless the patient has a poor performance status, is unwilling to proceed, or is part of a clinical trial. We limit transanal resection to well-selected patients with T1 lesions without high-risk histologic features (lymphovascular invasion, poor grade, or deep submucosal invasion). Factors such as patient procedural preference and comorbidities may influence this decision but it is on a case by case basis. Local excision can be accomplished with conventional transanal procedures; however, newer techniques such as transanal endoscopic microsurgery (TEM) and transanal minimally invasive surgery (TAMIS) may have less specimen fragmentation and improved R0 resection rates. Neoadjuvant chemoradiation may add further benefit for maximizing local control but is associated with local wound problems including bleeding and infection. Adherence to a strict surveillance program after local excision allows clinicians to salvage recurrence as early as possible. In a multidisciplinary fashion, the surgeon, pathologist, gastroenterologist, and patient need to make informed decisions about risk and benefit when determining the best individualized care for the patient.

Keywords Rectal cancer · Early rectal cancer · T1 rectal cancer · T2 rectal cancer · Transanal excision (TAE) · Transanal endoscopic microsurgery (TEM) · Transanal minimally invasive surgery (TAMIS) · Salvage surgery for rectal cancer

Introduction

With increased population screening, the incidence of early rectal cancers (T1/T2) in the USA has been increasing [1]. Annually, approximately 140,000 new cases of colorectal cancers are diagnosed and of these 30 %, or 40,000 cases, are rectal cancers [2]. Approximately 10 % of these newly diagnosed rectal cancers are early T1 or T2 rectal cancers with 45 % being T1 (4500 cases) and 55 % being T2 (5500 cases) tumors [3, 4•]. Clinicians taking care of patients with newly diagnosed early rectal cancer will be faced with complex decisions on how to best care for these patients. Specifically, is this cohort of patients best served with a transabdominal or transanal resection from an oncologic standpoint?

A transabdominal resection involves a proctectomy with total mesorectal excision (TME) to adequately stage regional lymph nodes. A proctectomy with TME has a higher risk of complications (30–75 %) compared to a transanal local resection. These complications can

This article is part of the Topical Collection on *Localized Colorectal Cancer*

✉ Patrick S. Sullivan
patrick.s.sullivan@emory.edu

[1] Division of Surgical Oncology, Department of Surgery, Winship Cancer Institute, Emory University, 550 Peachtree Street, NE, Atlanta, GA 30308, USA

be quite debilitating for the patient including defecatory (25–75 %), urinary (30–60 %), and sexual dysfunction (23–69 % in males and 19–62 % in females) [5–8]. The standard resection TME has a proven low local and distant recurrence rate (LR and DR) for early stage rectal cancer. Standard resection TME for T1 disease has a reported 2.7–6.0 % LR rate and a 2.6–7.0 % DR rate [9–12]. Standard resection TME for T2 disease has a reported 6.0–14.0 % LR rate and a 4.0–19 % DR rate [9, 11, 12]. Transanal local excision (TAE) is appealing because of less morbidity but at the cost of potential higher LR rates (T1 LR rates of 8.2–21.0 % and T2 LR rates of 13.0–30 %) [9, 11, 12]. Given these data, our group offers local excision only to well-selected T1 lesions without any high-risk histologic features. All other high-risk T1 or deeper rectal cancer patients are offered a standard resection unless part of a clinical trial. There is a national trend towards organ-preserving surgery with transanal resections for early rectal cancer (T1/T2) but is it justified?

The goals of treatment of early rectal cancer include optimizing oncologic control while minimizing treatment-related complications and maximizing quality of life. Patient selection begins with an understanding of the biologic behavior of early rectal cancers to predict potential lymph node spread. Clinicians are unable to precisely predict with 100 % accuracy the biologic behavior and potential lymph node spread of superficial rectal cancers. In addition, neither endorectal ultrasound (ERUS) nor magnetic resonance imaging (MRI) is 100 % accurate in clinically staging early rectal cancer. Patients may be able to avoid standard transabdominal rectal resections (low anterior resection (LAR)/abdominal resection (APR)) if they are carefully well-selected.

Patient Staging and Selection

Patients diagnosed with rectal adenocarcinoma are first clinically staged to ensure no distant metastatic disease with cross-sectional computed tomography (CT) imaging of the chest, abdomen, and pelvis. Once metastatic disease is ruled out, patient selection for local excision begins with a review of the tumor histology (a surrogate of tumor biologic aggressiveness and risk of lymph node spread), local clinical staging, and assessment of patient-related comorbidities that may influence perioperative risk. When considering local excision, it is critical to have accurate imaging to carefully select lesions limited to the superficial rectal wall without evidence of regional lymph node spread. In addition, the histology of the rectal cancer must be reviewed carefully to determine if high-risk features are present which may predict occult lymph node spread and therefore preclude a transanal resection.

Review of Tumor Histology

Patient selection with thorough review of rectal tumor histology can be useful to avoid over- and under-treatment of tumors. Histological assessment is the best predictor of biologic behavior and possible lymph node metastases. By identifying high-risk features, clinicians can assess risk of recurrence (local or distant) if a transanal resection is performed. In a systemic review, Bosch et al. identified important features in rectal cancer biopsy specimens that are associated with regional lymph node metastases and they include poor histologic differentiation (relative risk 4.8), lymphatic invasion (RR 5.2), submucosal invasion ≥1 mm (RR 5.2), and budding (RR 5.1) defined as the presence of isolated single cells or small cluster of cells scattered in the stroma at the invasive tumor margin [4•]. Additional histologic features associated with lymph node metastasis include perineural invasion (PNI), mucinous features, and signet ring cells [13–15]. Ideally, in the near future, gene expression and molecular markers would be used to identify a tumor's risk of lymph node metastasis. Currently, there are no validated molecular markers available for routine clinical use, although methylation status of select targeted genes seems to be a promising area to predict lymph node metastatic potential of T1 rectal cancers [16].

The depth and width of submucosal invasion of early rectal cancer has been correlated with potential micro-metastatic lymph node spread. The Haggitt classification has been used to determine the depth of submusocal invasion in a pedunculated colon polyp, and this depth is correlated with the risk of lymph node spread (0—carcinoma confined to the mucosa, 1—head, 2—neck, 3—stalk, and 4—submucosa of underlying colonic wall) [17]. Haggitt class "4" lesions are associated with an increased risk of lymph node metastasis (6.2 %) [18]. For non-pedunculated lesions, the Kikuchi classification is used to divide the submucosa into three parts: sm1 (superficial), sm2 (middle), and sm3 (deep) for T1 cancers. The risk of lymphatic spread of T1 lesions has been correlated to the degree of submucosal invasion with the risk of lymph node spread being 2, 8, and 23 %, respectively, for each level [19]. A submucosal width of invasion of more than 5 mm has also been associated with an increased risk of lymph node metastasis [20–22]. Currently, the National Comprehensive Cancer Network (NCCN) guidelines identifies high-risk features for T1 rectal lesions to include poorly differentiated tumors, positive margins, lymphovascular invasion, or sm3 invasion [23].

Clinical Staging

Paramount to patient selection is accurate clinical staging of the rectal cancer. Local excision can be considered when the tumor has superficial invasion without evidence of lymph node metastases or metastatic disease. Computed tomography (CT) imaging of the liver and lungs is performed to rule out

potential sites of metastatic disease; however, it lacks the resolution to accurately stage rectal cancer in the pelvis.

To assess if a patient would benefit from local excision, the lesion must first be assessed with digital rectal examination (DRE) and proctoscopic examination. The objective is to determine the size (cm), mobility (freely mobile, tethered, or fixed), circumference (%), distance from the anal verge (cm), and location within the rectum (anterior, posterior, or lateral). Although flexible endoscopy is typically used to diagnose rectal cancer, its accuracy to determine the precise location in the rectum has been questioned. Piscatelli et al. reviewed the endoscopic, pathologic, and operative reports of 236 patients with colon and rectal cancer and found that in 49 cases (21 %) the endoscopic location was inaccurate. In addition, this study found that in 12 cases, errors in endoscopic localization resulted in a change of operative approach [24]. These errors in localization can be corrected with the use of rigid proctoscopy to evaluate lesions within 20 cm of the anal verge. Of note, complete colonoscopy is necessary to rule out the presence of synchronous colorectal tumors that may occur in 2-4 % of cases [25].

Endorectal ultrasound (ERUS) and pelvic MRI are both superior to CT in accurately staging rectal cancer [26]. Both imaging modalities are used to assess tumor depth of penetration into the rectal wall (T stage) and evaluate for possible mesorectal lymph node involvement (N stage). Neither modality is 100 % accurate for staging rectal cancer. Both have strengths and weaknesses but instead of being mutually exclusive they can be complementary in assessing depth of invasion and possible lymph node involvement.

In general, ERUS has the ability to depict the layers of the bowel wall better than pelvic MRI and is therefore thought to be the imaging modality of choice for early stage rectal cancer. Based on work by Solomon et al., the sensitivity and specificity of tumor depth for ERUS is 97 and 87 %, respectively [27]. The specificity of pelvic MRI for tumor depth is lower at 75 % but accuracy can be enhanced with the use of phased array multichannel coils [26, 28]. Thus, ERUS is the best imaging modality in staging superficial lesions and in discriminating between T1 and T2 lesions, whereas pelvic MRI is the modality of choice for staging T2 or greater rectal tumors [29••]. Pelvic MRI has the additional benefit of improved visualization of pelvic anatomy including the mesorectum and circumferential radial margin (CRM), mesorectal lymph nodes, lymph nodes outside the mesorectum along the lateral pelvic side wall, and the tumor's relationship to the anal sphincter and pelvic floor.

Both MRI and ERUS lack sensitivity and specificity of mesorectal lymph node metastasis. Lymph node size is not an accurate predictor of lymph node metastasis, as ≥50 % of lymph nodes less than 5 mm have evidence of metastasis [30, 31]. Lymph node morphology including round shape, heterogeneous signal intensity, and irregular borders can be used to increase the sensitivity and specificity of lymph node metastasis [32]. The sensitivity and specificity of pelvic MRI for detecting mesorectal lymph node metastasis is 77 and 71 %, respectively [26].

Patient Factors

Patients at high risk of surgical complications may be better served with less invasive procedures even if the local recurrence rate or risk of lymph node metastasis is higher. Patients with poor performance status may have greater threats to survival, making local excision a much more attractive alternative to TME. Patient education and involvement in decision-making regarding local excision versus transabdominal TME for early stage rectal cancer enables the patient to be part of the decision-making process. In a multidisciplinary fashion, the treating surgeon, medical oncologist, gastroenterologist, and pathologist should carefully weigh the risk and benefits.

Surgical Management

Surgery offers the best chance of cure for patients with early stage rectal cancer. When deciding upon the surgical approach, one must take into account tumor stage, size, location, risk of recurrence, need for neoadjuvant/adjuvant therapy, and patient-related factors. Population-based studies show that local excision is increasingly being used in the United States for the management of early rectal cancers (T1 and T2). This trend from 1989 to 2003 has been quite remarkable. Local excision for T1 tumors has increased from 26.6 to 43.7 % and for T2 tumors from 5.8 to 16.8 % [12]. Is this trend justified or are we putting patients at risk? One must balance the decreased morbidity of local excision techniques with oncologic control and long-term outcomes (Table 1).

Table 1 Criteria for local excision of early rectal cancer [1, 29••]

- Appropriate preoperative staging with pelvic MRI and/or ERUS
- Tumors with high-grade dysplasia or early invasion (T1)
- Well to moderately differentiated histology
- Absence of lymphatic, vascular, and perineural invasion
- ≤1 mm of submucosal invasion
- No mucinous or signet ring cell components
- Tumor diameter <4 cm
- Tumor involving <40 % of the rectal wall circumference
- Poor performance status or patient unwillingness to undergo standard resection
- Compliance with postoperative surveillance

Local Excision

Transanal Excision (TAE)

TAE is the most commonly used local excision technique and is well-suited for tumors within 6–10 cm of the anal verge. The objective is a full-thickness excision of the rectal cancer with a lateral margin of 1 cm and a histologically negative deep margin. We give patients both mechanical and oral antibiotic bowel prep the day before, and intravenous antibiotics are given to cover intestinal flora prior to the procedure. The procedure is performed under general anesthesia or under monitored anesthesia care (MAC) with local or regional (spinal) anesthesia. The patient is positioned in lithotomy for tumors involving the posterior rectal wall; otherwise, the prone jack knife positioned is preferred for other tumor location sites (i.e., anterior wall). The Lone Star retractor greatly facilitates exposure during which fragmentation of the specimen should be avoided. Care must be taken when removing anterior tumors near the posterior vagina to prevent inadvertent injury leading to potential rectovaginal fistula. Orientation of the specimen can be done prior to histologic assessment by pinning the specimen. Patients are typically discharged the same day on a low-residue diet. The patient is then seen in clinic 2 weeks post-resection to assess for complications, review pathology, and determine future strategy and surveillance.

The benefits of TAE are clearly in the reduced incidence of complications, including reductions in anorectal, bladder, and sexual dysfunction. The most frequent postoperative complications are rectal bleeding (6 %), rectal stenosis (5.5 %), urinary retention (1.5 %), and fecal incontinence (0.5 %) [33, 34]. A retrospective review by Ptok et al. of 479 patients with T1 rectal cancers found significantly fewer postoperative complications in patients undergoing local excision via TAE or transanal endoscopic microsurgery (TEM) versus transabdominal resection (8 vs. 25 %, respectively) [35].

The disadvantage of TAE is the potential high rate of recurrence if optimal local excision is not performed. In the Norway Rectal Cancer Study Group, 291 patients with T1 rectal cancer treated with transabdominal resection ($n=256$) or TAE (n = 35) were prospectively followed for 6 years. Patients treated with TAE had a significantly higher 5-year local recurrence rate (12 vs. 6 % $p=0.01$) and lower 5-year survival rate (70 vs. 80 % $p=0.04$). However, it is important to note that 34 % of the TAE patients had either a macroscopically positive specimen margin or a margin <1 mm [36]. Alternatively, the Cancer and Leukemia Group B study prospectively evaluated 59 patients with T1 disease who underwent TAE with a follow-up of 4 years. All specimens had negative margins and no lymphovascular invasion (LVI). The local recurrence was 3.4 %, highlighting the importance TAE technique and patient selection [37].

Transanal Endoscopic Microsurgery (TEM)

TEM was first described by Beuss in 1984 as a minimally invasive technique that facilitates local excision of rectal adenocarcinoma between 4 and 15 cm from the anal verge, higher than can be accessible with the conventional TAE approach [38, 39]. The TEM platform consists of a beveled rectoscope that creates an airtight seal for standard $C0_2$ insufflation to 15 mmHg. The patient is positioned so that the tumor is in the dependent position. Using laparoscopic instruments, the specimen can be excised using the same principles employed during TAE. Within the upper rectum, one must be careful to prevent intraperitoneal perforation which has been reported to occur 4.3 % of the time [40]. This may require conversion to a transabdominal procedure if there is any concern about the integrity of the transanal closure or concern about any other visceral injury. Lesions within 6 cm of the anal verge are best removed via TAE due to difficulties maintaining CO_2 insufflation. Further limitations include equipment expense and technical expertise. Patients are typically discharge the same or next day. The most frequent postoperative complications are rectal bleeding (27 %), urinary tract infection (21 %), suture line dehiscence (14 %), and fecal incontinence (1 %) [40]. TEM has also been associated with low short-term anorectal dysfunction [41].

When compared to TAE, TEM has been shown to decrease local recurrence rates. In a retrospective review by Moore et al. of patients undergoing TEM ($n=82$) vs. TAE (n = 89) for early rectal cancer, local recurrence was 5 % after TEM versus 27 % after TAE ($p=<0.01$). TEM was much more likely to produce a non-fragmented specimen (94 vs. 65 % $p<0.001$) in this series. Complication rates between the two groups were statistically similar [42]. For T1 tumors, TEM has a 5-year local recurrence rate comparable to transabdominal resection (4.1 vs. 0 % $p=0.95$). However, local recurrence for T2 tumors was significantly higher (19.5 vs. 9.4 % $p=0.04$) [43]. The local recurrence rate and disease-free survival for T2 lesions would favor a transabdominal resection with TME.

Transanal Minimally Invasive Surgery (TAMIS)

Transanal minimally invasive surgery (TAMIS) was designed, and first reported in 2010, as an alternative to the TEM platform that was more cost-effective and allowed for smoother adoption [44•]. Single-incision laparoscopic (SILS) ports, most commonly the GelPOINT®, are utilized to perform the procedure with conventional laparoscopic instrumentation including the use of a 30°, 10-mm high-definition laparoscopic camera [45]. Patients are positioned in dorsal lithotomy, and the lubricated SILS port is introduced into the anal canal for establishment of pneumorectum to 15 mmHg. A full-thickness resection of the neoplasm with 1-cm margins is then performed as previously described. Limitations encountered

with TEM also apply to this technique including difficulties obtaining pneumorectum when attempting to remove distal rectal lesions close to the anal verge and potential intraperitoneal perforation when excising upper rectal lesions.

In a systematic review by Martin-Perez et al., the rate of a positive margin after resection of a malignant polyp was 4.4 %. In the same study, complications following TAMIS were reported at 7.4 %. The laparoscopic or open conversion rate following 390 excisions for benign and malignant lesions was reported at 2.3 %. Intraperitoneal perforation occurred in 1 % of cases of which a few cases were managed with primary transanal closure of the defect [46]. The TAMIS platform is currently being modified to accommodate the Da Vinci© robotic system for local resection and transanal TME [47].

Transabdominal Resection

Standard transabdominal resection has the best proven oncologic outcomes and is the gold standard to which all other procedures should be compared. When feasible, sphincter-sparing resections such as a LAR with TME and colonanal anastomosis should be performed. APR remains the treatment of choice for the surgical treatment of low-lying rectal malignancy when sphincter preservation would result in threatened margins.

It is well understood that morbidity is substantially lower following local excision when compared to transabdominal resection methods. However, how do oncologic outcomes compare? In the aforementioned study by You et al., the authors were able to use the National Cancer Database (NCDB) which represents a more accurate representation of clinical practice across the country rather than single-center experiences. The 5-year local recurrence and 5-year distant recurrence rates for T1 lesions resected transanally were 8.2 and 3.6 %, compared to 4.3 and 2.6 % for patients who had a standard TME resection. For patients with T2 lesions, the 5-year local recurrence and 5-year distant recurrence rates for T2 lesions resected transanally were 22.1 and 7.7 %, compared to 15.1 and 5.0 % for transabdominal TME. The overall 5-year survival was no different for T1 lesions excised locally or with standard resection (77.4 vs. 81.7 %; $p = 0.09$, respectively). However, the 5-year overall survival for T2 lesions resected transanally was statistically lower than transabdominal standard resection (67.6 vs. 76.5 %; $p = 0.01$, respectively) [12]. Many other single-center studies support these findings but are variable depending upon patient selection criteria for local excision (Table 2) [43, 48, 49]. It is our practice to offer all T2 rectal cancer patients a transabdominal resection with TME unless the patient has a poor performance status, is unwilling to undergo a TME, or the patient is part of a clinical trial.

Local Excision Following Neoadjuvant Therapy

Neoadjuvant therapy prior to local excision has been proposed for select T1/T2 early rectal cancers due to evidence of complete tumor regression in 10–30 % of patients [50, 51]. The American College of Surgeons Oncology Group (ACOSOG) Z6041 phase II trial aimed to evaluate short-term outcomes after neoadjuvant long-course chemoradiation (CRT) therapy for T2N0 rectal cancer. Among the 77 patients completing the protocol, pathologic complete response (pCR) rates were seen in 44 % and tumor down staging occurred in 64 % of the patients [52]. The estimated 3-year disease-free survival for the group was 88.2 %, with a local recurrence rate of 4 % and distant recurrence rate of 6 % [53••]. This study demonstrates a low local failure rate in T2 patients after neoadjuvant CRT and local excision. This approach may offer an organ-preserving alternative in carefully selected T2N0 patients who refuse or who are too high risk for standard resection.

Local recurrence highly correlates with the pathologic response following neoadjuvant treatment. A review of multiple retrospective studies with a median follow-up between 24 and 55 months demonstrate no local recurrence if local resection revealed a pathological complete response (pCR), a local recurrence of 2 % for ypT1 tumors, and 6–20 % local recurrence for ypT2 tumors [54].

It should be noted that chemoradiation-related toxicity is not trivial. In the ACOSOG Z6041 study, 39 % of enrolled patients developed chemoradiation-related grade ≥3 toxicities [52]. Marks et al. retrospectively reviewed short-term outcomes in 43 patients undergoing long-course CRT followed by TEM and 19 patients undergoing TEM alone. Morbidity rates were substantially higher after CRT (33 vs. 5.3 %, $p < 0.05$), specifically wound healing related to suture line dehiscence (25.6 %) [55]. Ten patients with wound separation required long-term antibiotics, and two patients had major wound separation—one patient required additional surgery for a diverting stoma. Although there is a significant increase in wound complications, most are not major and therefore should not prohibit transanal resection after neoadjuvant radiation treatment.

Surveillance

Surveillance after local excision is crucial in identifying early recurrence so that salvage surgery can potentially be performed. Surveillance guidelines published by the National Comprehensive Cancer Network (NCCN) include the following: (1) complete history and physical exam, including digital rectal exam, every 3–6 months for 2 years; (2) carcinogenic embryonic antigen level every 3–6 months for 2 years; (3)

Table 2 Review of outcomes following local excision vs. transabdominal resection for T1 rectal adenocarcinoma

Study	Patients (n)	Local recurrence (%)	Distant recurrence (%)	Disease-free survival (%)	Overall survival (%)	Median follow-up (months)
Transanal excision (TAE)						
Garcia-Aguilar et al. 2000 [9]	55	16.0	4.0	77.0	82.0	52
Paty et al. 2002 [11]	74	17.0	–	–	74.0	120
Nascimbeni et al. 2004 [19]	70	6.6	14.2	66.6	72.4	54
Endreseth et al. 2005 [36]	35	12.0	0	64.0	70.0	60
Bentrem et al. 2005 [63]	151	15.0	12.0	93.0	89.0	48
Madbouly et al. 2005 [64]	52	23.0	12.0	70.0	75.0	55
Ptok et al. 2007 [35]	85	6.0	4.0	91.4	83.6	44
You et al. 2007 [12]	601	8.2	3.6	93.2	77.4	60
Nash et al. 2009 [10]	137	19.0	19.0	83.0	69.0	59
Transanal endoscopic microsurgery (TEM)						
De Graaf et al. 2009 [65]	80	24.0	0	90.0	75.0	42
Palma et al. 2009 [66]	34	5.9	5.9	82.4	88.2	86.5
Doornebosch et al. 2010 [67]	88	21.0	8.0	–	–	36
Transanal minimally invasive surgery (TAMIS)						
Albert et al. 2013 [68•]	16	6.25	–	–	–	20
Transabdominal resection						
Nascimbeni et al. 2004 [19]	74	2.8	6.9	83.6	90.4	–
Endreseth et al. 2005 [36]	256	6.0	7.0	77.0	80.0	60
Bentrem et al. 2005 [63]	168	3.0	3.0	97.0	93.0	58
Ptok et al. 2007 [35]	359	2.0	4.0	92.3	91.5	–
You et al. 2007 [12]	493	4.3	2.6	97.2	81.7	60
Nash et al. 2009 [10]	145	2.7	–	96.0	85.0	77
De Graaf et al. 2009 [65]	75	0	8.0	87.0	77.0	84
Palma et al. 2009 [66]	17	0	0	82.4	82.4	93

computed tomography of the chest, abdomen, and pelvis annually for 3 years; (4) colonoscopy at 1 year and thereafter depending upon findings; and (5) proctoscopy every 6 months for 5 years. The addition of ERUS and pelvic MRI has been advocated for postoperative surveillance to increase the detection of local regional recurrences. A standardized surveillance schedule does not currently exist for these modalities. In addition to the above recommendations, it is our practice to follow patients with alternating ERUS and pelvic MRI every 6 months [56–58]. Follow-up should continue long-term, especially for patients who have had radiotherapy which has been shown to delay recurrence [59].

Salvage for Recurrence

Patterns of recurrence following TAE for early stage rectal cancer have been reported. Friel et al. reviewed 29 patients with recurrent rectal cancer following TAE. The mean time between local excision and salvage surgery was 26 months. Recurrence involved the rectal wall in 90 % of patients and was purely extra-rectal in 10 % [60]. After TAE for T1 rectal lesions, Garcia-Aguilar et al. reported an 18 % recurrence rate at 54 months. Eighty percent were local recurrences in the pelvis, 10 % were distant recurrences, and 10 % were both local and distal recurrences [9]. Finally, studies have suggested that local recurrence following local excision of early stage rectal cancer may be confined to the mesorectal fascia as opposed to the pelvic sidewall following transabdominal TME, making salvage surgery technically more feasible in this patient cohort [57].

While prospective data is lacking, retrospective studies have shown that outcomes of salvage surgery for recurrence after prior local excision of early rectal cancers are not equivalent to patients initially treated with standard TME resection. Friel et al. noted a 24.1 % (7/29) positive microscopic margin (R1) or unclear margin in patients recurring after initial transanal resection of T1/T2 rectal cancer. Eighty percent of patients who recur after local excision have resectable disease [11]. You et al. report an 80 % R0 resection rate following salvage surgery for recurrence after prior local resection. This required multivisceral resection in 33 %, total pelvic

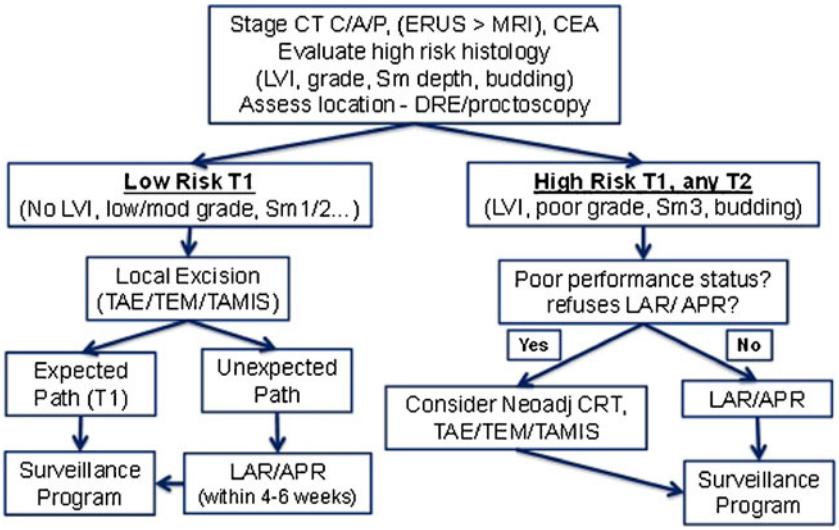

Fig. 1 Early rectal cancer treatment algorithm. *ERUS* endorectal ultrasound, *CEA* carcinoembryonic antigen, *LVI* lymphovascular invasion, *Sm* submucosal, *DRE* digital rectal examination

exenteration in 5 %, and metastasectomy in 25 % of patients [61]. Of those who undergo salvage surgery, the 5-year disease-free survival is 50–60 % [60–62].

Stage migration due to discordant preoperative and final pathologic staging may necessitate immediate "salvage" surgery, and this should be part of the preoperative discussion and counseling of the patient. A positive margin following local excision carries a high risk of recurrence and these patients should be offered further treatment. Hahnloser et al performed immediate (<30 days) transabdominal resection (APR = 24, low anterior resection = 28) on 37 patients after local excision due to reasons including a positive margin, LVI, and nodal disease. Similar 10-year overall survival and cancer-free survival were noted for T1N0-1 ($n = 37$) study patients (62 and 90 %) compared to a standard resection case match-cohort (72 and 84 %, respectively $p = 0.04$)). They concluded that local excision followed by transabdominal salvage surgery within 30 days does not adversely affect long-term survival. Several other studies have reported similar findings [1].

Conclusion

Appropriate patient selection is the most important factor in determining if transanal resection is the best treatment strategy for patients with early stage rectal cancers. Patient selection involves careful assessment of high-risk histology, clinical staging (ERUS/MRI), and consideration of patient-related factors. We limit transanal resection to only well-selected T1 lesions without high-risk pathologic features (well-differentiated, no lymphovascular invasion, submucosal depth of invasion ≤1 mm) and clinically staged with ERUS as T1. It is our practice to limit transanal resection of T2 lesions to patients with poor performance status, patients who refuse standard TME resection, or patients participating in a clinical trial. Newer techniques such as TEM and TAMIS may decrease local recurrence rates by decreasing fragmentation and increasing R0 resections (Fig. 1).

Compliance with Ethical Standards

Conflict of Interest Benjamin M. Martin, Kenneth Cardona, and Patrick S. Sullivan declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

References

Papers of particular interest, published recently, have been highlighted as:
- • Of importance
- •• Of major importance

1. Althumairi AA, Gearhart SL. Local excision for early rectal cancer: transanal endoscopic microsurgery and beyond. J Gastrointest Oncol. 2015;6(3):296–306.
2. Stamos MJ, Murrell Z. Management of early rectal T1 and T2 cancers. Clin Cancer Res. 2007;13(22 Pt 2):6885s–9s.
3. American Cancer Society. Colorectal cancer facts and figures 2014-2016.
4.• Bosch SL, Teerenstra S, de Wilt JHW, Cunningham C, Nagtegaal ID. Predicting lymph node metastasis in pT1 colorectal cancer: a systematic review of risk factors providing rationale for therapy decisions. Endoscopy. 2013;45(10):827–34. **This article evaluates the relative risk of lymph node metastasis with high risk histologic features**.
5. Elmessiry MM, Van Koughnett JA, Maya A, DaSilva G, Wexner SD, Bejarano P, et al. Local excision of T1 and T2 rectal cancer: proceed with caution. Colorectal Dis. 2014;16(9):703–9.

6. Nelson H, Sargent DJ. Refining multimodal therapy for rectal cancer. N Engl J Med. 2001;345(9):690–2.
7. Banerjee AK. Sexual dysfunction after surgery for rectal cancer. Lancet. 1999;353(9168):1900–2.
8. Ho VP, Lee Y, Stein SL, Temple LK. Sexual function after treatment for rectal cancer: a review. Dis Colon Rectum. 2011;54(1): 113–25.
9. Garcia-Aguilar J, Mellgren A, Sirivongs P, Buie D, Madoff RD, Rothenberger DA. Local excision of rectal cancer without adjuvant therapy: a word of caution. Ann Surg. 2000;231(3):345–51.
10. Nash GM, Weiser MR, Guillem JG, Temple LK, Shia J, Gonen M, et al. Long-term survival after transanal excision of T1 rectal cancer. Dis Colon Rectum. 2009;52(4):577–82.
11. Paty PB, Nash GM, Baron P, Zakowski M, Minsky BD, Blumberg D, et al. Long-term results of local excision for rectal cancer. Ann Surg. 2002;236(4):522–9. discussion 9-30.
12. You YN, Baxter NN, Stewart A, Nelson H. Is the increasing rate of local excision for stage I rectal cancer in the United States justified?: a nationwide cohort study from the National Cancer Database. Ann Surg. 2007;245(5):726–33.
13. Blenkinsopp WK, Stewart-Brown S, Blesovsky L, Kearney G, Fielding LP. Histopathology reporting in large bowel cancer. J Clin Pathol. 1981;34(5):509–13.
14. Stitzenberg KB, Sanoff HK, Penn DC, Meyers MO, Tepper JE. Practice patterns and long-term survival for early-stage rectal cancer. J Clin Oncol. 2013;31(34):4276–82.
15. Glasgow SC, Bleier JI, Burgart LJ, Finne CO, Lowry AC. Meta-analysis of histopathological features of primary colorectal cancers that predict lymph node metastases. J Gastrointest Surg. 2012;16(5):1019–28.
16. Leong KJ, Beggs A, James J, Morton DG, Matthews GM, Bach SP. Biomarker-based treatment selection in early-stage rectal cancer to promote organ preservation. Brit J Surg. 2014;101(10):1299–309.
17. Haggitt RC, Glotzbach RE, Soffer EE, Wruble LD. Prognostic factors in colorectal carcinomas arising in adenomas: implications for lesions removed by endoscopic polypectomy. Gastroenterology. 1985;89(2):328–36.
18. Matsuda T, Fukuzawa M, Uraoka T, Nishi M, Yamaguchi Y, Kobayashi N, et al. Risk of lymph node metastasis in patients with pedunculated type early invasive colorectal cancer: a retrospective multicenter study. Cancer Sci. 2011;102(9):1693–7.
19. Nascimbeni R, Burgart LJ, Nivatvongs S, Larson DR. Risk of lymph node metastasis in T1 carcinoma of the colon and rectum. Dis Colon Rectum. 2002;45(2):200–6.
20. Okabe S, Shia J, Nash G, Wong WD, Guillem JG, Weiser MR, et al. Lymph node metastasis in T1 adenocarcinoma of the colon and rectum. J Gastrointest Surg. 2004;8(8):1032–9. discussion 9-40.
21. Suzuki T, Sadahiro S, Mukoyama S, Ishikawa K, Yasuda S, Tajima T, et al. Risk of lymph node and distant metastases in patients with early invasive colorectal cancer classified as Haggitt's level 4 invasion: image analysis of submucosal layer invasion. Dis Colon Rectum. 2003;46(2):203–8.
22. Ueno H, Mochizuki H, Hashiguchi Y, Shimazaki H, Aida S, Hase K, et al. Risk factors for an adverse outcome in early invasive colorectal carcinoma. Gastroenterology. 2004;127(2):385–94.
23. Network NCC. Rectal Cancer (Version 1.2016). Available from: http://www.nccn.org/professionals/physician_gls/pdf/rectal.pdf.
24. Piscatelli N, Hyman N, Osler T. Localizing colorectal cancer by colonoscopy. Arch Surg. 2005;140(10):932–5.
25. Isler JT, Brown PC, Lewis FG, Billingham RP. The role of preoperative colonoscopy in colorectal cancer. Dis Colon Rectum. 1987;30(6):435–9.
26. Al-Sukhni E, Milot L, Fruitman M, Beyene J, Victor JC, Schmocker S, et al. Diagnostic accuracy of MRI for assessment of T category, lymph node metastases, and circumferential resection margin involvement in patients with rectal cancer: a systematic review and meta-analysis. Ann Surg Oncol. 2012;19(7): 2212–23.
27. Solomon MJ, McLeod RS. Endoluminal transrectal ultrasonography: accuracy, reliability, and validity. Dis Colon Rectum. 1993;36(2):200–5.
28. Jhaveri KS, Hosseini-Nik H. MRI of rectal cancer: an overview and update on recent advances. AJR Am J Roentgenol. 2015;205(1): W42–55.
29.•• Morino M, Risio M, Bach S, Beets-Tan R, Bujko K, Panis Y, et al. Early rectal cancer: the European Association for Endoscopic Surgery (EAES) clinical consensus conference. Surg Endosc. 2015;29(4):755–73. **The first consensus guidelines and evidence for the management of early rectal cancer. Clearly reviews the criteria and evidence for management decisions of early rectal cancer (T1/T2)**.
30. Andreola S, Leo E, Belli F, Bufalino R, Tomasic G, Lavarino C, et al. Manual dissection of adenocarcinoma of the lower third of the rectum specimens for detection of lymph node metastases smaller than 5 mm. Cancer. 1996;77(4):607–12.
31. Kotanagi H, Fukuoka T, Shibata Y, Yoshioka T, Aizawa O, Saito Y, et al. The size of regional lymph-nodes does not correlate with the presence or absence of metastasis in lymph-nodes in rectal-cancer. J Surg Oncol. 1993;54(4):252–4.
32. Brown G, Richards CJ, Bourne MW, Newcombe RG, Radcliffe AG, Dallimore NS, et al. Morphologic predictors of lymph node status in rectal cancer with use of high-spatial-resolution MR imaging with histopathologic comparison. Radiology. 2003;227(2):371–7.
33. Pigot F, Bouchard D, Mortaji M, Castinel A, Juguet F, Chaume JC, et al. Local excision of large rectal villous adenomas—long-term results. Dis Colon Rectum. 2003;46(10):1345–50.
34. Piccinini EE, Ugolini G, Rosati G, Conti A. Transanal local resection for benign and malignant rectal tumors. Int J Colorectal Dis. 1995;10(2):112–6.
35. Ptok H, Marusch F, Meyer F, Schubert D, Koeckerling F, Gastinger I, et al. Oncological outcome of local vs radical resection of low-risk pT1 rectal cancer. Arch Surg. 2007;142(7):649–55.
36. Endreseth BH, Myrvold HE, Romundstad P, Hestvik UE, Bjerkeset T, Wibe A, et al. Transanal excision vs. major surgery for T1 rectal cancer. Dis Colon Rectum. 2005;48(7):1380–8.
37. Steele Jr GD, Herndon JE, Bleday R, Russell A, Benson 3rd A, Hussain M, et al. Sphincter-sparing treatment for distal rectal adenocarcinoma. Ann Surg Oncol. 1999;6(5):433–41.
38. Buess G, Hutterer F, Theiss J, Bobel M, Isselhard W, Pichlmaier H. A system for a transanal endoscopic rectum operation. Chirurg. 1984;55(10):677–80.
39. Buess G, Mentges B, Manncke K, Starlinger M, Becker HD. Technique and results of transanal endoscopic microsurgery in early rectal cancer. Am J Surg. 1992;163(1):63–9. discussion 9-70.
40. Barendse RM, Dijkgraaf MG, Rolf UR, Bijnen AB, Consten ECJ, Hoff C, et al. Colorectal surgeons' learning curve of transanal endoscopic microsurgery. Surg Endosc Other Intervent Tech. 2013;27(10):3591–602.
41. Kennedy ML, Lubowski DZ, King DW. Transanal endoscopic microsurgery excision: is anorectal function compromised? Dis Colon Rectum. 2002;45(5):601–4.
42. Moore JS, Cataldo PA, Osler T, Hyman NH. Transanal endoscopic microsurgery is more effective than traditional transanal excision for resection of rectal masses. Dis Colon Rectum. 2008;51(7): 1026–30. discussion 30-1.
43. Lee W, Lee D, Choi S, Chun H. Transanal endoscopic microsurgery and radical surgery for T1 and T2 rectal cancer. Surg Endosc. 2003;17(8):1283–7.
44.• Atallah S, Albert M, Larach S. Transanal minimally invasive surgery: a giant leap forward. Surg Endosc. 2010;24(9):2200–5. **This**

manuscript describes the first large series of transanal minimally invasive surgery (TAMIS).

45. Gill S, Stetler JL, Patel A, Shaffer VO, Srinivasan J, Staley C, et al. Transanal minimally invasive surgery (TAMIS): standardizing a reproducible procedure. J Gastrointest Surg. 2015;19(8):1528–36.
46. Martin-Perez B, Andrade-Ribeiro GD, Hunter L, Atallah S. A systematic review of transanal minimally invasive surgery (TAMIS) from 2010 to 2013. Tech Coloproctol. 2014;18(9):775–88.
47. Atallah S, Martin-Perez B, Pinan J, Quinteros F, Schoonyoung H, Albert M, et al. Robotic transanal total mesorectal excision: a pilot study. Tech Coloproctol. 2014;18(11):1047–53.
48. Wu Y, Wu YY, Li S, Zhu BS, Zhao K, Yang XD, et al. TEM and conventional rectal surgery for T1 rectal cancer: a meta-analysis. Hepatogastroenterology. 2011;58(106):364–8.
49. Heintz A, Morschel M, Junginger T. Comparison of results after transanal endoscopic microsurgery and radical resection for T1 carcinoma of the rectum. Surg Endosc. 1998;12(9):1145–8.
50. Habr-Gama A, de Souza PM, Ribeiro Jr U, Nadalin W, Gansl R, Sousa Jr AH, et al. Low rectal cancer: impact of radiation and chemotherapy on surgical treatment. Dis Colon Rectum. 1998;41(9):1087–96.
51. Hiotis SP, Weber SM, Cohen AM, Minsky BD, Paty PB, Guillem JG, et al. Assessing the predictive value of clinical complete response to neoadjuvant therapy for rectal cancer: an analysis of 488 patients. J Am Coll Surg. 2002;194(2):131–5. discussion 5-6.
52. Garcia-Aguilar J, Shi Q, Thomas Jr CR, Chan E, Cataldo P, Marcet J, et al. A phase II trial of neoadjuvant chemoradiation and local excision for T2N0 rectal cancer: preliminary results of the ACOSOG Z6041 trial. Ann Surg Oncol. 2012;19(2):384–91.
53.•• Garcia-Aguilar J, Renfro LA, Chow OS, Shi Q, Carrero XW, Lynn PB, et al. Organ preservation for clinical T2N0 distal rectal cancer using neoadjuvant chemoradiotherapy and local excision (ACOSOG Z6041): results of an open-label, single-arm, multi-institutional, phase 2 trial. Lancet Oncol. 2015;16(15):1537–46. **Phase 2 trial evaluating the use of neoadjuvant therapy in stage I (T2N0) rectal cancer patients. This trial is the first well done trial evaluating long-term outcomes after neoadjuvant therapy for T2N0 rectal cancers**.
54. Borschitz T, Wachtlin D, Mohler M, Schmidberger H, Junginger T. Neoadjuvant chemoradiation and local excision for T2-3 rectal cancer. Ann Surg Oncol. 2008;15(3):712–20.
55. Marks JH, Valsdottir EB, DeNittis A, Yarandi SS, Newman DA, Nweze I, et al. Transanal endoscopic microsurgery for the treatment of rectal cancer: comparison of wound complication rates with and without neoadjuvant radiation therapy. Surg Endosc. 2009;23(5):1081–7.
56. Heafner TA, Glasgow SC. A critical review of the role of local excision in the treatment of early (T1 and T2) rectal tumors. J Gastrointest Oncol. 2014;5(5):345–52.
57. Tytherleigh MG, Warren BF, Mortensen NJ. Management of early rectal cancer. Br J Surg. 2008;95(4):409–23.
58. Ramirez JM, Mortensen NJ, Takeuchi N, Humphreys MM. Endoluminal ultrasonography in the follow-up of patients with rectal cancer. Br J Surg. 1994;81(5):692–4.
59. Chakravarti A, Compton CC, Shellito PC, Wood WC, Landry J, Machuta SR, et al. Long-term follow-up of patients with rectal cancer managed by local excision with and without adjuvant irradiation. Ann Surg. 1999;230(1):49–54.
60. Friel CM, Cromwell JW, Marra C, Madoff RD, Rothenberger DA, Garcia-Aguilar J. Salvage radical surgery after failed local excision for early rectal cancer. Dis Colon Rectum. 2002;45(7):875–9.
61. You YN, Roses RE, Chang GJ, Rodriguez-Bigas MA, Feig BW, Slack R, et al. Multimodality salvage of recurrent disease after local excision for rectal cancer. Dis Colon Rectum. 2012;55(12):1213–9.
62. Weiser MR, Landmann RG, Wong WD, Shia J, Guillem JG, Temple LK, et al. Surgical salvage of recurrent rectal cancer after transanal excision. Dis Colon Rectum. 2005;48(6):1169–75.
63. Bentrem DJ, Okabe S, Wong WD, Guillem JG, Weiser MR, Temple LK, et al. T1 adenocarcinoma of the rectum: transanal excision or radical surgery? Ann Surg. 2005;242(4):472–7. discussion 7-9.
64. Madbouly KM, Remzi FH, Erkek BA, Senagore AJ, Baeslach CM, Khandwala F, et al. Recurrence after transanal excision of T1 rectal cancer: should we be concerned? Dis Colon Rectum. 2005;48(4):711–9. discussion 9-21.
65. de Graaf EJ, Doornebosch PG, Tetteroo GW, Geldof H, Hop WC. Transanal endoscopic microsurgery is feasible for adenomas throughout the entire rectum: a prospective study. Dis Colon Rectum. 2009;52(6):1107–13.
66. Palma P, Horisberger K, Joos A, Rothenhoefer S, Willeke F, Post S. Local excision of early rectal cancer: is transanal endoscopic microsurgery an alternative to radical surgery? Revista espanola de enfermedades digestivas. 2009;101(3):172–8.
67. Doornebosch PG, Ferenschild FT, de Wilt JH, Dawson I, Tetteroo GW, de Graaf EJ. Treatment of recurrence after transanal endoscopic microsurgery (TEM) for T1 rectal cancer. Dis Colon Rectum. 2010;53(9):1234–9.
68.• Albert MR, Atallah SB, deBeche-Adams TC, Izfar S, Larach SW. Transanal minimally invasive surgery (TAMIS) for local excision of benign neoplasms and early-stage rectal cancer: efficacy and outcomes in the first 50 patients. Dis Colon Rectum. 2013;56(3):301–7. **The authors describe a series of 50 TAMIS patients and their outcomes**.