Chapter 18
Management of T_2 Rectal Cancer

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Introduction

What's "best" for the cancer, may not always be "best" for the patient. This is particularly true for T_2 rectal cancer; more specifically for *patients* with rectal cancer. More radical treatments may in certain circumstances, result in higher disease free survival, but not in improvements in overall survival, and certainly not a better functional result or enhanced quality of life. In selecting treatment options one must understand multiple important factors regarding the tumor and the patient in whom it resides.

Regarding patient factors: (1) Some patients wish to do "everything possible" to minimize any risk of tumor recurrence, while others want to avoid a colostomy "at all costs". (2) Some patients' anorectal function is poor enough that a radical resection with permanent colostomy will result in the best chance for cure *and* provide the best functional outcome. (3) In others, even a well performed low anterior resection for a mid or proximal tumor will result in an unacceptable deterioration in anal function, and significantly impact quality of life. (4) Finally, in some individuals with significant comorbidities curing the cancer may be an unnecessary goal as life span is already severely limited.

Regarding the tumor: (1) Location is everything; proximal T_2 rectal tumors are very different from distal T_2 tumors. (2) Accurate tumor staging is often difficult prior to surgical resection. Differentiating T_1 from T_2 lesions may be impossible for MRI and difficult for endorectal ultrasound [1, 2]. Even radiologists experienced in MRI evaluation of rectal cancer find it difficult to differentiate between advanced T_2 lesions and early T_3 cancers. (3) Diagnostic imaging, both MRI and endorectal ultrasound, may be little better than "flipping a coin" when predicting metastatic

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lymphadenopathy in association with early rectal cancers. Large lymph nodes may look worrisome but are often benign, while up to 50 % of metastatic lymph nodes are less than 5 mm and missed on both MRI and ultrasound [3, 4].

As one critically evaluates the literature, particularly when comparing radical to local surgical treatment, there is subtle, unintentional selection bias that is ubiquitous, incredibly important, and rarely mentioned. Authors compare patients undergoing local excision for T_2 (lymph node status estimated by inaccurate imaging; with a 50 % false negative rate) N_0, with individuals undergoing radical TME for pathologically staged T_2 N_0 (with microscopic evaluation of regional nodes), commonly in a retrospective analysis. In these studies, authors often implicate occult lymph node metastases as responsible for the local recurrence following local excision. If this is truly the case (which is likely), then many patients in the local excision group are truly T_2 N_+. Therefore, as we compare local with radical resection, it's important to realize a percentage of patients in any "local excision group" have Stage III rectal cancer while essentially none of the patients in the radical resection group are Stage III. As described above, it is often inaccurate staging that leads to increased recurrence in the local excision group rather than inadequate treatment.

Why is the choice between local and radical resection so important, and so often discussed in rectal cancer while it's rarely mentioned and of little clinical importance in colon cancer? The consequences of radical resection in the vast majority of colon cancers is minimal, such that there is no real functional benefit to local excision. In addition, laparotomy or laparoscopy is required for both local and radical resection. Regarding rectal cancer, radical resection requires a transabdominal approach while local excision is accomplished via an endoluminal approach with no cutaneous incision and minimal complications, often as an outpatient procedure. Importantly, the functional consequences of a successful radical resection include significant diminution of anorectal, urinary and sexual function, and a significant percentage of these individuals will require a permanent or temporary stoma [5–9].

In treating rectal cancer of any stage, three modalities are commonly considered; surgery, radiation, and chemotherapy. Some individuals may require all three, each associated with its own unique consequences. As more modalities are used, complications and long term consequences increase. Chemotherapy is a "systemic" treatment designed to decrease systemic recurrence, and is generally associated with systemic consequences. Both surgery and radiation are local therapies, and are predominately associated with local consequences. The combination of radiation and surgery particularly compounds complications and functional consequences.

Patient population	Intervention	Comparators	Outcomes
Patient with T_2N_0 rectal cancer	Local excision with chemoradiation	Radical resection Chemoradiation alone	Oncologic outcomes Functional outcomes

Search Strategy

A literature search was conducted including the following databases: MEDLINE (using PubMed) and the Cochrane Library. Publications not written in English were excluded. Titles and abstracts of retrieved studies were reviewed for relevance and eligibility. Results from the most recent meta-analyses were also included in this review. Full texts of all eligible studies were retrieved and evaluated.

Surgical Decision Making

Extensive literature review revealed very few trials that actually compared local and radical resection for T_2 rectal tumors. In fact, there is only one prospective trial that compared local excision (transanal endoscopic microsurgery) with radial resection following neoadjuvant chemoradiation for T_2N_0 rectal cancer [10]. There are no trials that compare local excision to "watch and wait" following chemoradiation for T_2 lesions. There are several "database" reviews that compare both local and radical resection, but suffer from the traditional shortcomings associated with database queries [11, 12]. Therefore, decision making for patients with T_2N_0 rectal cancer remains difficult and cannot generally be based on level I data. It must come from review of trials that separately evaluate local excision, radical resection, and observation therapy.

The tables that are compiled below are a result of contemporary literature review in the management of early rectal cancer. Unfortunately, direct comparisons between treatment modalities are rare. The best an informed surgeon can hope for is to review this data and apply it individually to each patient, looking at functional data, oncologic results, stoma and complication rates.

Table 18.1 depicts local recurrence, cancer specific survival, morbidity, and length of follow-up for available techniques. Table 18.2 looks at permanent stoma rates following local excision, radical resection and chemoradiation alone. Table 18.3 looks at response rates, local recurrence and overall survival following "watch and wait" therapy.

Recommendations

There is little debate in the literature regarding treatment of proximal T_2N_0 rectal cancer. All individuals who are medically fit should undergo radical resection, most commonly anterior resection with total (or tumor specific) mesorectal excision, and anastomosis. Current trials suggest this will result in high survival rates, a low incidence of local recurrence, and minimal functional consequences. Neoadjuvant or adjuvant treatment is not necessary.

Table 18.1 Oncologic intervention and results [10–12, 14, 18–24]

Trial	Stage	Intervention	N	Local recurrence (%)	Cancer survival (%)	F/U (months)	Morbidity (%)
LeZoche et al.	T_2N_0	Pre-op chemoXRT & TEM Pre-op chemoXRT & TME	35 35	5.7 2.8	94 94	84	13.8 16.7
Guerrieri et al.	T_2N_0	Pre-op chemXRT and TEM	139	10	92	225	9.2
Chen et al.	T_2N_0	TEM (selective XRT) LAR (selective chemo)	30 30	7.1 0	100 100	18 18	21 20
You et al.	$T_{2–3}N_0$	Pre-op chemo XRT & TEM	60	10	85.9	36	7.5
ACOSOG Z6041	T_2N_0	Pre-op chemoXRT & local excision	79	4	88.2	56	16
You et al.	T_2N_0	LE Radical resection	164 866	22.1 15.1	67.6 76.5	60	5.8 14.6
SEER Database	T_2N_0	LE (selective radiation) Radical resection	332 2,362		81 90.5	60	
Swedish Rectal Cancer Trial	Stage I, II, III	Pre-op XRT & Surgery Surgery alone	454 454	9 26	72 62	156	26 19
German Rectal Cancer Trial	Stage II and III	Pre-op chemXRT & Surgery Surgery & post-op chemoXRT	404 395	7.1 10.1	68.1 67.8	134	36 34
Dutch Rectal Cancer	Stage I, II, III	XRT & Surgery Surgery alone	924 937	5.6 10.9	64.2 63.5	60	

For distal T_2N_0 tumors, local recurrence increases, as do stoma rates, functional consequences and morbidity and mortality. Literature review suggests cancer specific survival, and overall survival are broadly similar for radical resection, local excision with neoadjuvant or adjuvant chemoradiation, or chemoradiation followed by “watch and wait”. Older studies have suggested local recurrence rates are higher

Table 18.2 Stoma rates following various treatment interventions [10, 14, 18–24]

Trial	Intervention	N	Permanent stoma
LeZoche, et al.	Pre-op chemoXRT &TEM Pre-op chemoXRT & TME		0 26
Guerrieri et al.	Pre-op chemoXRT & TEM	139	0
Chen et al.	TEM LAR	30 30	0 0
Yu et al.	TEM	60	0
ACOSOG Z6041	Pre-op chemoXRT & LE	79	9
Swedish Rectal Cancer trial	Preop XRT & Surgery Surgery alone	454 454	55 59
German Rectal Cancer Trial	Pre-op chemoXRT & Surgery Surgery & post-op chemoXRT	404 395	34 30
Dutch Rectal Cancer Trial	Pre-op XRT & surgery Surgery alone	924 937	33 29

Table 18.3 Outcomes following non-operative management of rectal cancer [15, 25–27]

Trial	N	Tumor stage	Clinical complete response (%)	Local recurrence (%)	Follow-up (months)	Disease free survival (%)
Appelt et al	40	Stage I, II, III	73	15.5	24	75
Smith et al. MSKCC	32		22	19	17	88
Maas et al. Netherlands	21	Stage I, II, III	11	4.8	25	93

for local excision when compared to radical resection; however, the majority of these studies evaluated traditional transanal techniques [12]. More recent data, although small case series, have identified equivalent local recurrence rates when comparing TEM to radical resection [13, 14]. More large scale, multicenter trials will be necessary to confirm comparable local recurrence rates. There is clear evidence that local excision alone is inadequate treatment for T_2 rectal cancer, resulting in unacceptable local recurrence rates and subsequent decreases in cancer specific survival [12]. There is currently sufficient data to suggest that traditional transanal excision is technically inferior to advanced techniques for local excision (most data evaluates TEM, but more date is becoming available for TEO, TAMIS, and SILS approaches) [13]. There is no debate that permanent stoma rates, functional (defecatory, urinary, and sexual) consequences, and morbidity and mortality are significantly higher following radical resection.

Regarding "watch and wait" observational therapy following chemoradiation, oncologic outcomes are similar to radical resection for the select group of patients with a complete clinical response [15, 16]. These are observational trials, predominately from one center. There are no prospective randomized data available. There are no trials comparing observational therapy with local excision.

Based on this literature review, treatment must be individualized. The main benefits associated with radical resection are accurate pathologic staging, the avoidance of chemotherapy and radiation, and possibly lower rates of local recurrence. These benefits come at the cost of higher complication rates, greater functional consequences, and higher permanent stoma rates.

The benefits of local excision are obvious; avoidance of laparotomy or laparoscopy, outpatient surgery, minimal morbidity and mortality, fewer functional consequences, and avoidance of a permanent stoma. However, local excision requires neoadjuvant chemoradiation and may be associated with higher rates of local recurrence. In addition, accurate pathologic staging cannot be achieved.

Author's Approach

It can't be emphasized enough that treatment for T_2N_0 rectal cancer must be individualized. A detailed history identifying a patient's desires, fears, physical, and social limitations is essential for developing a treatment plan. As previously stated, I separate proximal and distal T_2N_0 rectal cancer into two distinct treatment groups. All medically fit patients with proximal lesions undergo radical resection without neoadjuvant therapy.

For distal lesions, decision making is more complex. Enrollment in open clinical trials is offered if appropriate. After discussion, if patients are most concerned about tumor recurrence and need to have definitive evidence regarding mesorectal lymph node spread, they undergo radical resection (either LAR or APR depending upon tumor location). Perineal dissection for all APRs is performed prone with a cylindral excision [17]. For patients more concerned about anorectal function, a multimodality approach is used. Pathology is reviewed, patients with poor differentiation or lymphovascular invasion identified on biopsy (this is uncommon) are counseled that radical resection is preferred.

For others, treatment begins with neoadjuvant chemoradiation (after discussions in a rectal cancer multidisciplinary tumor conference). Five fluorouracil based chemotherapy, *without* oxaliplatin, combined with 5040 rads over 5 weeks is most common. Patients are then evaluated 4 weeks following completion of chemoradiation with physical examination and flexible sigmoidoscopy. Photographs of the tumor site are taken and stored electronically. If there is significant tumor response, patients undergo 2–4 more cycles of chemotherapy and then subsequent repeat endoscopic evaluation of the tumor. If there is little or no treatment response, radical resection is recommended. If no tumor is identified or if the tumor continues to decrease in size, patients complete 4 months of chemotherapy. After completion of the entire neoadjuvant regimen, patients have another endoscopic rectal evaluation, and CT chest, abdomen and pelvis. Provided there is no metastatic disease, patients will either undergo TEM or careful observation. TEM was used for all patients in the past but recovery is very slow with significant delays in wound healing if local excision is performed following radiation [18]. Now only patients with actual or a question of a small residual rectal tumor undergo TEM. Patients with a cCR are

individualized to observation vs TEM depending upon patient and physician preference. This is an area of cancer management that is changing rapidly and will likely change significantly in the next decade.

For individuals who have little or no response to neoadjuvant therapy, local excision is not an option. These patients are at *very high risk* for local recurrence following TEM and radical resection is recommended. Only patients that are medically unfit or refuse radical resection are considered for TEM, and are at risk to fail this treatment plan.

Conclusions

T_2N_0 rectal cancer comprises a heterogeneous group of patients with varied worries, goals, and expectations. In addition, risk of recurrence, both local or systemic, may be influenced by factors beyond TNM Stage, such as lymphovascular invasion, degree of differentiation, and response to neoadjuvant therapy. Importantly, multiple treatment options exist, each with different risks of recurrence and with different effects on post treatment quality of life. Current surgical literature is inadequate to provide an absolute "standard" treatment regimen at the present time Therefore, treatment must be tailored to match the patient's personal needs (desire to avoid a colostomy, concerns regarding anorectal, urinary, and sexual function, and need to know accurate lymph node status) in addition to curing the cancer. This can only be successfully accomplished by taking the time to thoroughly learn the patient's goals and to assess subtle tumor factors in order to assure the treatment is not worse than the disease.

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