

Local Treatment for Rectal Cancer

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ABSTRACT

The treatment of rectal cancer includes both radical resection and local therapy. Radical resection remains the standard treatment, but is associated with increased morbidity and mortality, as well as the potential need for a temporary and occasionally, a permanent ostomy. The benefits of local treatment include a less invasive procedure with maintenance of bowel function and avoidance of a stoma. However, the efficacy of local treatment is now being challenged as the rates of recurrence after local excision alone appear to be much higher than previously thought. Although the primary goal of an oncologic resection is disease eradication, each case must be individualized to determine an optimal care plan.

KEYWORDS: Rectal cancer, local excision, recurrence, transanal endoscopic microsurgery, radiation therapy, chemotherapy

Objectives: On completion of this article, the reader should be able to summarize the local treatment options for cancer of the rectum and their indications.

BACKGROUND

Local excision for rectal cancer was first described by Lisfranc in 1826.¹ However, consideration of tumor spread away from the primary tumor led Czerny² to advocate removal of the lymphovascular pedicle through a combined abdominal and perineal approach. In the early 1900s, Sir Ernest Miles³ noted a 95% recurrence rate after perineal resection and emphasized the need for clearance of the upward, downward, and lateral lymphatic spread. Thus, in 1908, he first reported the abdominal perineal resection as the ideal treatment for all cancers of the rectum.

The Miles resection was a revolutionary step in the treatment of cancers of the rectum. Although the initial morbidity and mortality was quite high (reported mortality rate of 36.2%), surgical technique as well as perioperative care has greatly improved since the early 20th century.³ While always maintaining that the pri-

mary goal of oncologic surgery is disease eradication, secondary goals (quality of life issues, avoidance of stoma, and preservation of bowel function) can also be explored. With this in mind, the application of sphincter-preserving surgery for even cancers of the very low rectum has now been well described and shown to address both the primary and secondary goals of oncologic surgery effectively.⁴⁻⁶ The advent of surgical stapling devices has improved the ease of performing a low pelvic anastomosis; nevertheless, the increasing use of neoadjuvant therapy raises new and exciting questions for the treatment of rectal cancer.⁶⁻¹² Although the importance of Miles work can never be understated, we have come to realize that not only is each patient unique, but so too are their cancers. Treatment options should therefore be individualized to determine the optimal care plan with consideration to both patient and tumoral factors.

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LOCAL TREATMENT OF RECTAL CANCER

Dating back to the time of Miles, the conservative treatment of rectal cancer has been viewed as a deviation from conventional surgical practice. Local treatment of rectal cancer continues to be a hot topic of debate as surgeons are apprehensive that a limited approach with the avoidance of a colostomy may diminish the opportunity for cure. However, although advances in surgical technique and the incorporation of a multimodality approach to the treatment of rectal cancer have improved sphincter-preservation rates, an abdominal operation is still met with a certain degree of morbidity and mortality. Complications related to radical surgery include cardio-pulmonary compromise and failure, anastomotic leaks and strictures, sexual and urinary dysfunction and functional issues regarding defecation and continence.^{13–17} The incidence of these complications vary greatly; nevertheless, the addition of neoadjuvant therapy significantly increases their prevalence.¹⁸

The decreased morbidity associated with local therapy coupled with the preservation of normal bowel function after local excision makes it a more desirable option, helping to maintain its position in the rectal cancer treatment algorithm as a viable option in the management of select cancers of the rectum. Additionally, as we further our progress in better understanding the clinical behavior of the tumor and the prognostic value of histologic grading and tumor characteristics, the position of local therapy in the treatment of rectal cancer will continue to evolve, securing its place as an alternative to radical surgery.

Patient Selection

The selection process for the appropriate treatment of the patient with rectal cancer involves an individualized, multistep process. This practice considers both patient characteristics and tumor characteristics (Table 1).¹⁹ The goals of oncologic surgery are disease eradication followed by quality of life considerations. Radical resection

Table 1 Selection Criteria for Local Therapy of Rectal Cancer

Patient characteristics
Unfit for major surgery
Refusing major surgery
Small primary cancer with advanced distant metastasis
After neoadjuvant therapy*
Tumor characteristics
Mobile (confined to the bowel wall)
≤ 3 cm in diameter†
Located below the peritoneal reflection†
Well or moderately differentiated

*Currently under investigation.

†May be relative contraindications with use of transanal endoscopic microsurgery (TEM).

with or without neoadjuvant therapy or postoperative chemotherapy remains the most effective proven treatment for most cancers of the rectum. However, not all patients are healthy and are of good operative risk. Patient factors that influence treatment options include associated comorbidities that may make a patient a prohibitive operative risk. Furthermore, a patient may refuse a major abdominal surgery and therefore be considered for local therapy. Finally, patients with small cancers, but advanced distant disease may benefit from local treatment.

The use of local therapy for good-risk patients with curative cancers confined to the rectal wall is currently the focus of considerable discussion. A trend in oncologic surgery, loosely based on the evolving treatment of breast cancer (lumpectomy and radiation), is now being evaluated in a clinical trial.²⁰ Both the role and the results of adding neoadjuvant therapy to the full-thickness local excision of tumors presumed confined to the rectal wall must be scrutinized closely as we reflect on the many recent reports of unexplainably high local recurrence rates after local excision alone.^{21–24}

Tumor Evaluation

Critical in the formulation of an appropriate treatment plan is a systematic evaluation of the patient. After a comprehensive history is obtained with consideration of symptoms, bowel function, continence, and investigation of comorbidities, a thorough physical exam should follow. Special attention should be made to the presence of inguinal lymphadenopathy, abdominal findings, and sphincter integrity and function. The presence of regional lymph node metastasis and the size, position, mobility, configuration, circumference of bowel lumen involved and distance from the anorectal ring are paramount in formulating an ideal treatment plan. The integration of clinical findings with radiographic and laboratory evaluation helps to determine the depth of invasion and presence or absence of distant disease more accurately.

A primary challenge continues to be an adequate preoperative tumor size, node status, metastasis classification (TNM) staging of rectal cancer. Although we have become more precise in preoperatively determining the T-stage and grossly assessing for distant disease, the presence or absence of regional lymph node involvement continues to be inadequately defined. The computed tomography (CT) scan continues to be used to assess for distant disease. However, it was only within the last two decades that endorectal ultrasound (EUS) was shown to be an adequate predictor of T-stage.^{25–27} The predictive value of EUS continues to be a topic of debate; however, it remains the best available preoperative imaging device for staging cancers of the rectum. The T-stage has been proven an adequate predictor for

Table 2 Incidence of Positive Lymph Nodes in Relation to Tumor Characteristics and Pathological Findings

Tumor Characteristic	Positive Lymph Node (%)
Stage	
T1	0–12
T2	12–28
T3	36–67
Size	
< 2 cm	29
< 3 cm	17–31
< 4 cm	33–50
Differentiation	
Well	25
Moderate	33
Poor	77

lymph node metastasis (Table 2). It is generally accepted that T1 cancers are associated with a 0 to 12% risk of nodal involvement. Risk of lymph node metastasis for T2 cancers is 12 to 28% and rises to 36 to 67% for T3 cancers.^{28–33} The relationship between lymph node involvement and the gross morphologic and histologic features of the tumor are currently being defined.

Local treatment options for rectal cancer include electrocoagulation (fulguration/ablation), contact radiotherapy, and local excision with or without neoadjuvant/adjuvant therapy.

Electrocoagulation

First described by Byrne³⁴ in 1889 for the treatment of gynecologic malignancy and popularized by Strauss et al³⁵ in 1935 for rectal cancer, electrocoagulation involves transanal exposure of the tumor and the application of needle-tip bipolar cautery into and through the tumor. The technique involves a general anesthetic and is facilitated with use of a specialized 40-mm operating proctoscope. The cautery tip is applied to the entire surface of the tumor as well as 1 cm around the tumor. The charred tumor is removed with forceps with the tumor bed repeatedly cauterized until no visible tumor remains. With operative times of 60 to 90 minutes, patients are typically discharged home in 24 to 72 hours.

Electrocoagulation and endoscopic laser therapy is an appealing therapy for palliation. However, its use for curative intent remains controversial. Madden and Kandalaf³⁶ reported 5-year survival rates ranging from 52 to 71%. There was renewed interest in electrocoagulation in the 1970s and 1980s after reports from Crile and Turnbull, Wilk and Turnbull, and Salvati and colleagues presented its use for select cancers of the distal rectum and noted similar 5-year survival statistics compared with abdominoperineal resection.^{37–39} Advantages include that it is technically easier to obtain

more proximal and deeper margins than local excision. However, no specimen is obtained for histologic staging and assessment of margins, making its efficacy as a potentially curative procedure difficult to evaluate.

Eisenstat and Oliver⁴⁰ reported 81 patients treated with electrocoagulation with curative intent. Thirty-one patients eventually required abdominoperineal resection with the remaining 50 patients experiencing a 5-year survival of 58%. With the procedure requiring a general anesthetic and an overall complication rate of 21%, the benefits over local excision are not readily apparent. Concerns of developing a rectovaginal fistula limit its use in women with anterior lesions. With no pathologic specimen obtained, it is difficult to draw conclusions about its role in the curative treatment of rectal cancer. However, with selection criteria aimed to select out cancers confined to the rectal wall, overall survival data after electrocoagulation does not appear more favorable than local excision while having similar morbidity.

Contact Radiotherapy

Papillon in Lyon, France,⁴¹ advocated the use of endocavitary radiation for the treatment of select rectal cancers. The procedure necessitates the use of a specialized 29-mm proctoscope that allows an X-ray tube to be passed through it and placed in direct contact with the tumor. Suitable tumors must be entirely accessible to the proctoscope and be no larger than 3 by 5 cm in size. Radiation is given in fractions of 2000 to 4000 cGy to a 3 cm in diameter area (two overlapping fields can be treated) every 1 to 4 weeks for a total dose up to 15,000 cGy. It is well tolerated, even by frail patients, and is typically done on an outpatient basis. The advantage of contact radiotherapy to external beam radiation is that a high dose of radiation can be delivered directly to the tumor, minimizing the radiation exposure to healthy tissue.

Several studies have reported very favorable short-term results (cure rates of 75 to 95% for early-stage cancers) with contact radiotherapy.^{42–45} However, concern remains that local control rates vary with length of follow-up. Nevertheless, two studies with a minimum of five-year follow-up have reported locoregional control rates of 92 and 93%,^{46,47} with its use for curative intent being limited primarily to the treatment of small T1 and T2 cancers.

With strict selection criteria and prolonged follow-up, Papillon and Berard⁴⁶ reported a 73.8% 5-year survival rate in 310 patients treated with endocavitary radiation with or without iridium-192. Local failure occurred in 4.5% and nodal failure in only 3.8%. However, other studies have failed to support this, with rates of local recurrence ranging from 18 to 30%.^{48,49} The role of supplementary iridium-192, advocated by Papillon

and Gerard, but not routinely used by others, remains unclear. However, it may be responsible for the improvement in local control seen in Lyon. Although contact radiotherapy appears as a safe option for the treatment of select early rectal cancers and it has a wider application than electrocoagulation, it remains limited to the few institutions that have the appropriate equipment.

Local Excision

Local excision can only cure tumors confined to the rectal wall and can be accomplished by a transanal approach, a Kraske transsacral approach, or a York-Mason transsphincteric procedure. The advantage of local excision over other local therapies is that an intact specimen is obtained for further pathologic evaluation. Disadvantages include suboptimal access and visualization as well as limited treatment of the nodal basin.

After appropriate bowel preparation suitable for a colon resection, the procedure is typically performed under general anesthesia, although spinal and local anesthesia has been reported. The patient is adequately positioned with the tumor in the six-o'clock position. Various retractors have been utilized with visualization being enhanced with the use of lighted retractors. The tissue surrounding the tumor can be infiltrated with an epinephrine-containing solution to assist with hemostasis. The dissection is facilitated by placement of stay sutures 2 cm lateral to the tumor. An alternative is to place a suture proximal to the tumor, which can later be used to close the defect. The excision is performed with electrocautery in a full-thickness fashion with 1-cm margins around the tumor. After irrigation with a tumoricidal agent, the defect may be closed primarily or left open. The specimen should then be marked with regards to left, right, cephalad, and caudal margins. Patients can usually be discharged home by postoperative day 1 and maintained on a soft diet with a stool softener prescribed as needed.

Whereas the primary goal for any oncologic resection is disease eradication, local excision is appealing over other local therapies in that a complete and intact specimen is obtained for pathologic evaluation to assure complete excision of the primary tumor. Furthermore, local excision is associated with minimal morbidity and mortality, while preserving bowel continuity as well as bowel, bladder, and sexual function. Local excision continues to be readily accepted as an alternative to radical resection for patients unfit to undergo major abdominal surgery. However, its role in the treatment of healthy patients remains unclear. With the continued improvement of imaging devices (EUS, CT, magnetic resonance imaging [MRI]), patients can be more accurately staged preoperatively with hope of better selecting out tumors suitable for local excision.

Early results of local recurrence after local excision were quite favorable. Gall and Hermanek⁵⁰ reported a local recurrence rate of less than 10% after local excision of T1 and T2 tumors. Willet and colleagues⁵¹ reported a local recurrence rate of 4% and overall recurrence rate of 13% after local excision compared with an overall recurrence rate of 9% after abdominoperineal resection. However, follow-up was limited to 48 months.

Now with prolonged follow-up, rates of local recurrence after local excision appear significantly higher than previously reported. In fact, the rates of local recurrence recently reported by several institutions cannot be explained simply by lack of treatment to the nodal basin. With the risk of lymph node positivity being 0 to 12% for T1 cancers and 12 to 28% for T2 cancers, the simple excision of a primary rectal cancer without treatment of the nodal basin *should* be associated with a risk of local recurrence of up to 12% for T1 cancers and as high as 28% for T2 cancers. However, several recent studies report disturbingly high rates of local recurrence with local excision.²¹⁻²⁴

The University of Minnesota was among the first to bring into question the true rates of local recurrence after full-thickness local excision. Mellgren and colleagues²² reported on 108 patients undergoing local excision for T1 ($N=69$) and T2 ($N=39$) cancers over a 10-year period. They found an 18% local recurrence rate for T1 cancers and a 47% local recurrence rate for T2 cancers at 5 years. Of note, these were all patients with clear pathologic margins. Over the same period, the local recurrence rate after radical resection was 0% for T1 cancers and 6% for T2 cancers. Finally, overall recurrence (local and/or distant disease) was also higher in the local excision group (21% for T1 and 47% for T2 cancers) than after radical resection (9% for T1 and 16% for T2 cancers).

A study from the Cleveland Clinic Foundation looking at recurrence after transanal excision for T1 cancers of the rectum reported similar findings. With a median follow-up of 55 months, Madbouly et al²¹ found a 23% local recurrence rate (17% local and 6% local and distant) in 52 patients treated with local excision alone for T1 rectal cancer. With prolonged follow-up, other studies have reported similar findings.^{23,24}

It is unclear the cause of this higher than expected rate of local recurrence. However, it is likely that both tumoral and technical factors may play a role. In an attempt to counteract this unexpectedly high rate of local recurrence, increased interest in improving technical aspects of the operation (growing use of transanal endoscopic microsurgery [TEM]) and additional treatment to the nodal basin and tumor margins (addition of neoadjuvant therapy) are being explored.

Transanal Endoscopic Microsurgery

To combat the technical challenges of transanal excision and facilitate endoluminal dissection, Buess and Raestrup⁵² developed transanal endoscopic microsurgery (TEM) in Tübingen, Germany, with its first clinical application in Cologne, Germany, in 1983. The equipment was developed by Wolf Surgical Instruments Company (Vernon Hills, IL) and is now available through Wolf and Storz (Karl Storz & Co., Tuttlingen, Germany). The operating rectoscope is 40 mm in diameter and is available in lengths of 12 and 20 cm. The distal end is angled 45 degrees and delivers a light from an external source; rectal insufflation is accomplished with CO₂. A double-ball joint attached to the operative table allows for stability and easy adjustment. The sealing system prevents gas leakage, while allowing for instrument introduction through three operative ports.

Patient preparation is similar to transanal excision with special care noting the exact position of the tumor. Postoperative care is also similar to that of local excision, although I typically admit the patient for 48 hours and maintain him or her on a liquid diet if the abdominal cavity is entered. The advantages of TEM include superior visualization with an insufflated and magnified view of the rectum as seen from above the tumor, precise full-thickness dissection with improved lymph node harvest and ability to excise larger tumors, and better access to tumors in the mid and upper rectum as well as the distal colon. Disadvantages include cost of the equipment and the learning curve associated with the use of this highly specialized piece of equipment.

With follow-up limited to 2 years, Buess and colleagues⁵³ reported a 4% (2 out of 46) local recurrence rate for T1 tumors, while Floyd and Saclarides⁵⁴ reported 2 recurrences in 75 patients (3%), both of which were salvaged by radical resections. The first prospective randomized study comparing TEM to anterior resection in patients with T1 cancers of the rectum was reported in 1996. Winde and colleagues⁵⁵ evaluated 24 patients undergoing TEM and 26 patients undergoing anterior resection with a mean follow-up of 45 months. There were no differences in the survival curves between the groups. In a comprehensive review of 58 reports, Middleton et al⁵⁶ found local recurrence to be significantly less, 6 versus 22%, following TEM when compared with traditional transanal excision while also noting a lower complication rate, 10 versus 17%.

As with conventional local excision, proper case selection is critical. Although TEM is technically challenging, the proper use of the equipment allows enhanced visualization and superior access to tumors of the rectum and distal colon that facilitates a "hands-off" dissection. With appropriate training, TEM will likely help overcome any technical limitations of conventional local excision that may, in part, be associated with increased rates of local recurrence.

The Role of Radiation and Chemotherapy in a Multimodality Treatment Plan with Emphasis on Full-Thickness Local Excision

All cancers are at risk of recurring. To improve the rates of local recurrence after local excision further, the addition of radiation and chemotherapy to the treatment regimen is being further explored. Under ideal circumstances, a T1 cancer treated with local excision alone has up to a 12% risk of local recurrence due to lack of treating the nodal basin. With histologic evaluation revealing good prognostic indicators (well differentiated, no lymphovascular invasion), this risk may be as low as 2 to 4%. Although it is well known that the role of adjuvant therapy is not to make up for poor surgery, its use to enhance the oncologic outcome as part of a multimodality approach emphasizing an appropriate local excision is an intriguing concept that needs to be better defined.

Local Excision and Postoperative Radiation Therapy

Although limited data are available, the morbidity associated with postoperative radiotherapy after local excision appears significant. Rich and colleagues⁵⁷ reported a 23% (6 of 26 patients) rate of proctitis that was directly related to the dose of radiation delivered. The development of rectovaginal fistula after completion of radiation therapy has also been reported.⁵⁸

Neoadjuvant Therapy

The use of preoperative radiation therapy for rectal cancer was first well described by Stuart Quan and colleagues⁵⁹ in 1960. Gerald Marks et al⁶⁰ first reported the application of full-thickness local excision after preoperative radiotherapy in 1984. The addition of chemotherapy as a radiosensitizer followed by local excision with TEM offers to be an appealing prospect to address both the technical issues of conventional local excision as well as the tumoral aspects that contribute to high local recurrence rates.

Although the importance of a complete clinical response remains a hot topic of debate, the increasing rates of complete pathologic response, now generally greater than 30%, cannot be ignored and will likely compel clinicians to continually appraise its role as part of the treatment algorithm for the local management of rectal cancers. With the ongoing advancements in the field of medical oncology, it is likely that rates of complete pathologic response will continue to rise. While its incorporation into a multimodality treatment plan including local excision is currently being studied,²⁰ others have used neoadjuvant therapy as a sole treatment option when a complete clinical response is noted.

Habr-Gama and colleagues⁶¹ in Sao Paulo, Brazil reported their findings after the routine use of

neoadjuvant therapy prior to planned surgical resection in 265 patients with cancer of the distal rectum. Seventy-one patients (26.8%) were noted to have complete clinical response and were followed closely (no immediate surgical intervention) under a strict institutional protocol necessitating monthly follow-up with biopsies when feasible. Of the 194 patients with an incomplete clinical response, all underwent radical resection with 22 (8.3%) showing complete pathologic response. Five-year overall and disease-free survival was 100% and 92% in the observation group and 88% and 83% in the radical resection group, respectively. The prospect of potentially curing over 35% of rectal cancers with adjuvant therapy alone could help revolutionize the way certain rectal cancers are treated, drawing similarities to Norman Nigro's⁶² revolutionary work with anal cancer in 1973. This is all the more notable when the ongoing evolution of chemotherapy is taken into consideration as we will likely continue to see higher rates of both complete clinical and pathologic response.

There are now widespread reports of significant complete clinical and pathologic response rates. To date, however, the long-term follow-up results noted by Habr-Gama and colleagues⁶¹ have not been duplicated by other studies. Although the concept of avoiding surgery and its attendant morbidity and mortality is appealing, this modality is best reserved for patients that are prohibitive surgical risks or as part of a clinical trial as we await what will likely be exciting new results in the multimodality approach for the treatment of rectal cancer.

CONCLUSION

Local therapy will remain a desirable option in the treatment of rectal cancer as it is associated with decreased morbidity and mortality compared with radical resection. It will remain an appealing alternative to patients as it is associated with a better functional outcome and the avoidance of a stoma. However, as we enter this new and exciting realm in the treatment of rectal cancer and evaluate and continually assess the various treatment modalities available, it is now as clear as ever that we must exercise extreme caution when selecting the appropriate patient and the appropriate cancer suitable for local therapy. With all cancers at risk of recurring, patient selection and counseling should focus on the acceptable treatment options for a particular patient with deep consideration given to the risk of recurrence associated with the treatment option proposed. As we continue our search for an adequate predictor of nodal involvement and further our appreciation of tumor biology, emphasis should remain on appropriate patient selection and excellent surgical technique.

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