Journal of BUON **12:** 23-27, 2007
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REVIEW ARTICLE

Is local excision and chemoradiation an acceptable alternative in the treatment of early rectal cancer?

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Summary

Local excision has a limited but important role in the modern management of patients with rectal tumors. The main criticism of the local treatment of early rectal cancer (T1N0M0 or T2N0M0) is the neglect of any potential metastatic mesorectal lymph nodes.

This article presents the combined experience of several trials and indicates that neoadjuvant preoperative or adjuvant postoperative treatment may reduce the risk of local recurrence in a selected group of patients, and local excision results in overall survival comparable to the most aggressive treatment.

Although the hypothetical improvement in morbidity and quality of life with local excision has not been demonstrated, the advantages of the local excision vs. radical surgery in the oncologic results seem obvious and require prospective randomized studies comparing both types of treatment.

Key words: chemoradiation, early rectal cancer, excision, local recurrence

Introduction

The treatment of rectal cancer has evolved away from the radical abdominoperineal resection to the very low rectal resection with sphincter preservation. Improvements in chemotherapy and radiation therapy along with advances in surgical techniques, especially total mesorectal excision and preservation of the hypogastric nerves, have decreased the local recurrence rate as well the urologic and sexual complications [1,2].

The most popular treatment for patients with small rectal tumors who deny a radical operation has been local resection. The procedure has been described by Lisfranc in 1827 [3] and Lachart-Mummery and Dukes in 1952 [4]. Years later, St. Mark's medical staff reported on their experience and developed a strategy for the use of local excision for early colorectal cancers [5].

After that, local excision of rectal cancer has been performed rarely, due to a potential high risk of local recurrence and concerns about its adequacy as an oncologic operation. So, it has been served as a palliative treatment for patients who were unfit for radical surgery due to advanced age or comorbidities [6].

Recently, data derived from prospective and retrospective studies have shown local recurrence rates varying from 7 to 48%. Of those patients who develop tumor recurrence, 50% are able to undergo surgical salvage with a 5-year disease-free survival of 22-59% [7-9].

The current article focuses in the most recent results from the literature and outlines the usefulness of local excision as a curative treatment in selected patients with rectal cancer who achieved a complete clinical response after neoadjuvant manipulations.

Received 09-10-2006; Accepted 02-12-2006

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Patient selection

Careful patient selection is the most important initial step to achieve the best results from local resection of early rectal cancer. Many factors including tumor stage, histopathology, patient's opinion and comorbidities, and surgeon's impression concerning the tumor behavior, impact the final decision. So each patient represents a unique case due to the variability of the above parameters.

For patients scheduled to undergo a transanal excision, tumor size < 3 cm, infiltration < 30% of the rectal circumference and tumor location < 8 cm from the anal verge, constitute the most important technical information about the feasibility of the technique [10, 11]. The other two important criteria are the extension and the histological behavior of the tumor (well-differentiated T1/T2 and N0 tumors are preferred) [12,13].

Physical examination, endorectal ultrasound (EUS), tumor biopsy, complete colon and rectal evaluation to rule out synchronous carcinomas and polyps, abdominal computed tomography (CT) and magnetic resonance imaging (MRI) to assess the extent of invasion of the primary tumor and to search for metastatic disease, are useful for the preoperative selection of the appropriate patients.

EUS and pelvic phased array coil MRI or endorectal MRI are able to determine the depth of tumor invasion into the rectal wall, the vascular invasion and the presence of perirectal lymph node metastases. The role of these diagnostic tools in the selection of patients for local treatment is essential [14]. EUS is currently the modality of choice for local staging of all rectal carcinomas and mainly for early T1/T2 tumors because of its superior depiction of tumor ingrowth into superficial layers of the rectal wall, with T and N staging accuracy ranging from 69 to 97% and 70 to 75%, respectively. Tumor biopsy must be performed after EUS in order to prevent any interferences with ultrasound from edema, bleeding or inflammation from the biopsy. On the other hand, there is 94% agreement between MRI and pathological assessment of T stage [15].

The final decision about the surgical approach will be based on the pathology results: patients with poorly differentiated carcinomas with lymphatic or vascular invasion, thus bearing a high probability of lymph node involvement and distant metastases, are not candidates for local excision.

What type of local treatment?

Many different opinions exist in the literature, especially in the management of small T1 tumors. The differences may include the choice of the surgical procedure as transanal excision, transsacral excision (Krashke's procedure), transanal endoscopic microsurgery and transsphincteric excision, and variations of other treatments such as chemotherapy, radiation and chemoradiation before or after the excision of the tumor [6,11-13].

1. *Local excision*

Local transanal excision of an early rectal tumor with a surgical margin of 1 cm is the worst choice. The important consequence from this approach is the high rates of local recurrence which varies from 4 to 18% for T1 tumors and from 27 to 47% for T2 tumors.

Three complete studies after 2000 confirm that these results refer to the biology of the excised tumors. An explanation why the local failure remains high is the occult lymphatic spreading which occurs approximately in 10-20% of T1 tumors, and in 25-35% of T2 tumors [7-9]. Another mechanism is the tumor cell entrapment phenomenon into the surgical excision sites, suture lines or traumatic surfaces.

The 5-year survival rates from the present studies appear to be favorable for T1 or T2 tumors, varying from 65 to 100%. Two factors may explain this result. First, the long term follow-up of these patients, which means that the survival remains high in the first 5 years but drops at 10 years (92 % vs. 75%). The second factor of this high survival rate is that more than 50% of patients with local recurrence undergo curative salvage surgery and adjuvant treatment [15].

Recently the study from Paty et al. [8] demonstrated also that microscopic involvement of the surgical margins was not associated with local recurrence because this finding is regarded as an indication for either immediate radical resection or delivery of adjuvant radiotherapy. This finding explains the heterogeneity of the results in the use of local excision alone as curative treatment for rectal cancer. The main criticism of the local excision alone is the neglect of any potential metastatic mesorectal lymph nodes. This concern has been supported by the findings that in most series the rate of local recurrence parallels the expected incidence of lymph node metastases.

Because of these data local excision alone may be avoided as curative treatment.

2. *Preoperative chemoradiation followed by local excision*

This is the newest approach but with limited

literature data in the last 4 years. Currently the American College of Surgeons Oncology Group designed a prospective trial to study preoperative chemoradiation followed by local excision for T1 and T2 rectal cancers. This protocol (ACOSOGZ6041) is a phase II trial in order to determine the rate of disease- free survival in a selected group of patients with early rectal cancer. It collects tissue samples from early rectal cancer before chemoradiation, investigates the toxicity associated with chemoradiation, and assesses the proportion of early rectal cancers that respond to chemoradiation. The patient selection criteria include patients with biopsy-proven adenocarcinoma of the rectum, with tumor distal margin located within 8 cm from the anal verge, stage T2N0 by EUS and patients with no history of pelvic irradiation or distant metastases. Most recent data from a phase II study from Europe with preoperative oxaliplatin, capecitabine and external beam radiotherapy (RadOxCape study) in rectal cancers demonstrates a feasible downstaging in T3-T4/ or N+ rectal tumors [16].

This strategy has several potential advantages comparatively to postoperative chemoradiotherapy [17-19]. Preoperative radiotherapy reduces tumor cells entrapment in the surgical site at the time of local resection and on the other hand the better oxygenation of the tumor due to the intact blood supply may increase radiation sensitivity. Another advantage is the clinical monitoring of the tumor response to therapy. If a tumor is unresponsive or it is only partially downstaged, most investigators recommend abdominoperineal resection as appropriate treatment. Complete or near complete responders may be managed with local excision.

In Table 1, 4 studies from 2001 until 2005 demonstrate a 5-year survival rate of 50-90%, with a recurrence rate varying between 10-20% and a pathologic complete response rate of 65-85% [16,17,19,20].

Postoperative complications include rectal stricture, incontinence, rectovaginal fistulas, radiation cystitis and tenesmus.

The goal of performing a local excision for early rectal cancer after preoperative neoadjuvant treatment is to eradicate tumors with low morbidity and mortality, while avoiding a permanent colostomy and retaining good bowel, bladder, and sexual function. Additional studies of preoperative chemoradiation and local resection are warranted.

3. *Local excision followed by postoperative chemoradiation*

The aim of this strategy is to destroy residual microscopic disease in the surgical field and within the pelvis. The combined experience of several institutional protocols indicates that postoperative chemoradiation reduces the risk of local recurrence in these patients (Table 2) [8,21-23].

These data demonstrate overall survival rates of 67-80% and overall recurrence rates of 26-48%. T stage is the most important factor to predict final survival outcome and recurrence. Well-selected T1 tumors will have better cure rate than T3, and excision with clear margins is critical for good results [24].

The most important question is if the treatment with local excision and postoperative radiotherapy can achieve cure rates comparable to radical surgery for high-risk T1 and T2 tumors.

Recent data demonstrate that the local recurrence rates, varying from 10 to 35% with this approach, are higher than those reported for radical surgery [7,25], and appear to be better compared with patients treated by local excision alone [6]. Due to this uncertainty radical surgery remains the treatment of choice for high risk T1 or T2 tumors.

Salvage surgery after failed local excision for early rectal cancer

The most important question which arises after failed local excision in rectal cancer is whether sal-

Table 1. Preoperative chemoradiation followed by local excision

Study	*Patients, n (T stage)*	*Preoperative treatment*	*5-year survival (%)*	*10-year survival (%)*
Kim et al, 2000 [20]	23 (T2: 5, T3: 18)	4500 cGy + 5FU	50	20
Lechoche et al, 2002 [19]	35 (T2)	5040 cGy	90	12
Schell et al, 2002 [17]	11 (T3)	4500 cGy + 5FU	67	17
Machiels et al, 2005 [16]	40 (T3)	5040 cGy + oxaliplatin + capecitabine	NR	NR

5FU: 5-fluorouracil, NR: not reported

Table 2. Local excision followed by postoperative chemoradiation

Study	*Patients, n*	*Tumor stage (T1/2/3)*	*5-year survival (%)*	*10-year survival (%)*
Russel et al, 2000 [21]	51	13/25/13	56	14
Mendenhall et al, 2001 [23]	67	N.R	80	14
Benson et al, 2001 [22]	68	24/36/8	67	32
Paty et al, 2002 [8]	31	7/24/0	NR	22

N.R: not reported

vage surgery can provide local control and cure rates equal to initial radical surgery. Local recurrence is often considered amenable to salvage radical surgery, and some authors have reported high survival rates after salvage surgery [26,27].

Table 3 demonstrates data on surgical salvage. Approximately 50% of patients with recurrence are able to undergo salvage surgery [7,8,21,22,27-29].

The long-term outcome for patients undergoing salvage surgery is controversial. Most authors agree that the pathologic stage of the recurrent tumor was more advanced than the stage of the primary tumor and the treatment protocol calls for preoperative chemoradiation before salvage surgery, especially in patients who did not previously receive radiation treatment [27,28,30].

Baron et al. [31] compared the results of patients who underwent salvage radical surgery for recurrent rectal cancer after local excision vs. patients who underwent immediate radical surgery after local treatment for tumors with adverse features. They reported a disease-free survival rate of 55.5% for patients who underwent salvage surgery vs. 94% for those with immediate surgery.

From these data, our suggestion is for aggressive initial surgery for patients whose initial tumors show invasion of the muscularis propria, positive margins, poor differentiation or lymphovascular invasion.

Table 3. Salvage resection studies

Study	*Tumor resected (%)*	*5-year survival after salvage resection (%)*
Chakravarti et al, 1999 [29]	50	56
Russel et al, 2000 [21]	64	28
Mellgren et al, 2000 [27]	88	50
Benson et al, 2001 [22]	45	55
Paty et al, 2002 [8]	50	41
Friel et al, 2002 [27]	100	59

Conclusion - future perspectives

From the available data, local excision is a treatment dependent on patients' selection. When excision is followed by chemoradiation cure rates and local control appear improved, but excision with clear margins is still essential. Preoperative chemoradiation may be more efficacious but more studies with longer follow-up are needed to define case selection and outcome.

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