

TRANSANAL EXCISIONS FOR RECTAL CANCER - ANOTHER POTENTIAL MULTIDISCIPLINARY TASK?

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Summary

Incidence of rectal cancer in Croatia was 1174 cases in 2012. Most cases were diagnosed at an advanced stage, however there are a few diagnosed in cT1-2N0M0 stage which opens a window for transanal resection. These patients have to be staged meticulously not to disregard possible local spread of disease and nodal involvement. Endorectal ultrasound is not always easily available, therefore MRI is usually the method of choice for preoperative staging. Nevertheless, since the implementation of this mode of treatment advances in neoadjuvant and adjuvant therapy and multidisciplinary approach to treatment have blurred these clear cut indications. In this paper we discuss specificities in selection, treatment and follow up of these patients.

KEY WORDS: *transanal resection, rectal cancer, transanal ultrasound, MRI, indication*

TRANSANAL EKSCIZIJA ZA REKTALNI KARCINOM- MULTIDISCIPLINARNI PRISTUP?

Sažetak

Incidencija karcinoma rektuma u Hrvatskoj je oko 1174 slučajeva u 2012 godini. Većina slučajeva je dijagnosticirana u poodmaklim stadijima bolesti, ipak određen broj se dijagnosticira u cT1-T2N0M0 stadiju što otvara mogućnost za transanalnu eksciziju. Pacijenti kod kojih se predviđa trananalna ekscizija moraju biti u potpunosti slikovno obrađena kako se preoperativno ne bi previdjela proširenja bolest. Endorektalni ultrazvuk nije široko dostupan, tako da se najčešće koristi MR pri odluci o vrsti zahvata. Unatoč dosta jasno definiranim indikacijama za ovaj zahvat, napredak u neoadjuvantom i adjuvantnom pristupu te multidisciplinarnosti liječenja je iste relativizirao. U ovom preglednom radu raspraviti ćemo izbor, vrstu liječenja i praćenja ovih pacijenata.

KLJUČNE RIJEČI: *transanalna resekcija, karcinom rektuma, transanalni ultrazvuk, MR, indikacije*

INTRODUCTION

Incidence of rectal cancer in Croatia is 1174 cases in 2012 (1). Sixty percent of these are diagnosed in stages III/IV which require multidisciplinary approach- treatment sequence based on preoperative staging. Transanal excision for rectal cancer are indicated in early-stage cancers in high-

ly selected patients. The lesions suitable for transanal excision are small lesions (< 3 cm in size), occupying less than a third of a circumference of the rectum, preferably exophytic/polypoid, superficial and non fixed (T₁ and T₂ lesions), low-grade (well or moderately differentiated), non mucinous that are located within 8 cm of the anal verge without radiological evidence of nodal involvement in

the abdomen and pelvis. The advantages of local excision include rapid recovery, minimal effect on sphincter function, and relatively low perioperative morbidity and mortality. It can also eliminate defecation, sexual and urinary dysfunction, and can prevent the need for a permanent stoma. However, one should carefully select patients. Even when following these selection criteria, 3-30% of patients may experience recurrence (2).

EVOLUTION OF THE APPROACH

In 1977, Morson published a paper with a series of 91 patients with complete transanal excision of rectal cancer achieving local recurrence of 3% (3). However, later series did not keep up with low recurrence rates of radical surgery vs. transanal resection 3-6% to 8,2-23% T1 and 13-30% and 7,2% T2 (2). Nevertheless, local excision is increasingly used to treat stage I rectal cancer despite its inferiority to total mesorectal excision, which is the current standard of care. In a study of all rectal cancer patients in the National Cancer Data Base from 1998 through 2010, researchers found that local excision was used to treat 46.5% of those with T1 tumors and 16.8% of those with T2 tumors. For patients with T1 cancer, local excision rates increased from 39.8% in 1998 to 62.0% in 2010. For patients with T2 cancers, rates increased from 12.2% to 21.4% (4,5).

DIAGNOSIS AND LOCATION

According to American Society of Colon and Rectum Surgeons Practice Parameters guidelines for the treatment of rectal carcinoma, digital rectal exam and proctosigmoidoscopy should be performed to establish the distance of the tumor from the anal verge, its mobility and position (6). Digital rectal examinations may characterize lesion as mobile, tethered or fixed. In fact, large and fixed tumors are not eligible for local excision as they often invade deeper layers (7). Colonoscopy should be performed prior to surgery to detect simultaneous polyps or tumors.

T1/T2 EVALUATION

Most important criteria for selecting patients for transanal excision is extent of rectal wall in-

volvement. Tis means that the process is in the earliest stage (in situ) when it involves only the mucosa- not growing beyond the muscularis mucosa (thin inner muscle layer). T1 stage means that the cancer spread through the muscularis mucosa and extends into the submucosa. In T2 stage cancer has grown through the submucosa and extends into the muscularis propria (thick outer muscle layer).

Endoscopic rectal ultrasound (ERUS) is comparable to magnetic resonance (MR) in estimating the thickness of rectal wall tumor spread. Patel et al. compared T1/T2 sensitivity and specificity of ERUS and MR in 52 patients. Specificity of 100% of ERUS was similar to its sensitivity. Specificity of MRI was similar to that of ERUS (8). In another series, Zorcolo et al. achieved higher accuracy rates in distinguishing early from advanced rectal lesion with 96% sensitivity and 85% specificity, giving accuracy of 94% in 67 patients (9).

Lymphnode involvement

The exclusion criteria for transanal excision is nodal positivity. Assessment of nodal metastases by ERUS is less accurate than that for tumor depth. According to a meta-analysis of 35 studies by Puli et al, which involved more than 2700 patients, the sensitivity of ERUS in diagnosing nodal involvement in rectal cancer was 73.2% and it had a specificity of 75.8% (10).

Turkish study compared the detection of lymph node metastases by MR and ERUS, obtaining an accuracy of 74.50% with phased-array MRI and 76.47% with ERUS. Sensitivity was slightly better with MRI than ERUS (61.76% and 52.94% respectively) (11).

Estimates of lymph node involvement are also based on analysis of pathological specimens after radical excision. Saraste et al. stratified risk of lymph node involvement in early rectal cancer, identifying T2-stage (odds ratio [OR] = 2.0), poor differentiation (OR = 6.5) and vascular infiltration (OR = 4.3) as significant risk-factors for lymph node metastases in the multivariate analysis. The risk stratification index shows the risk for lymph node metastases gradually increasing from 6% to 65% and 11% to 78% in T1 and T2 cancers respectively, when adding these risk factors one by one (12).

According to the review by Maeda et al., the likelihood of lymph node involvement for T1 ranges from 6,3 to 20% and for T2 from 14 to 26% (13).

TECHNIQUE

Transanal resection is suitable for lesions up to 8 cm from the anal verge. Local excision results in a full-thickness specimen including some mesorectal fat with at least 1 cm circumferential mucosal margins. The specimen is usually oriented and fixed on a board by the operator to preserve the orientation and specimen contraction during pathological sample preparation. The defect in the bowel wall is subsequently closed in a transverse manner. Patients perform a full mechanical bowel preparation prior to the surgery. Postoperative recovery is quick, with early start of regular diet and everyday activities and minimal discomfort (14).

Alternative procedure for local excision of rectal cancer is transanal endoscopic excision (TME) which requires more logistics (specialized instruments) than transanal excision. Due to technical requirements and learning curve TEM is not widely available, despite the fact that it is more precise than transanal excision. TEM remains the gold-standard for the resection of rectal adenomas. TEM has a significantly decreased rate of R1 resection compared to traditional transanal excision (2% *vs.* 16%) (15), but achieving an R0 resection did not prevent local recurrence (16). Even when stratifying to low-risk T1 tumors, there is still a 17% local recurrence rate after TEM (16). There was no significant difference in the 5-year recurrence rate between T1 and T2 tumors removed by either of local excision techniques (21% *vs.* 33%, $P=0.07$) (15). Due to the high rate of local recurrence in low-risk patients with even an R0 resection, improving criteria for tumor resection by TEM is of major importance.

OVERALL SURVIVAL AND RECURRENCE RATE

The 5-year survival rate after transanal excision ranges from 65-100% (these figures include some patients with T₂ lesions). The local recurrence rate ranges from 0-40%. Patients with lesions that display unfavorable histologic features but are excised completely may be treated with adjuvant chemo/radiation therapy. Cancer recurrence following transanal excision of early rectal cancer has been studied by Weiser et al., who observed that failures due to transanal excision are mostly due to understaging of local disease (17).

The main problem of transanal excision for early rectal cancer in a scandinavian study was also the inability to remove all the malignancy. Patients treated with transanal excision had significantly higher rates of local recurrence and inferior survival compared with patients who underwent major surgery. The inferior survival in local excision group, could be because they were older than those who had major surgery (18). Chinese group published comparable results of major surgery and excision in elderly patients and transrectal excision, identifying a subpopulation in which this approach might be preferred (19).

SALVAGE SURGERY

In case of positive resection margins, lymphovascular or perineural invasion, lymph node metastasis or recurrent lesion at follow-up, salvage resection is indicated. Usually, salvage resection is either abdominal perineal resection or TME with coloanal anastomosis (14). On one hand, LTME after TEM is a technically challenging procedure, with a higher risk of APR compared to primary LTME (20). On the other hand, the outcome between patients with rectal cancer undergoing salvage TME after TEM, and those undergoing primary TME were comparable. In selected patients, TEM can therefore be chosen as a primary treatment, since failure of treatment and subsequent conventional resection appears not to compromise the outcome (21).

Borschitz et al. found that patients with high risk T1 tumors, <1 mm margins, tumor fragmentation, or R1 resection had 49 % 10-year survival as compared to 89 % among patients with low-risk tumors and R₀ resection (22).

The discovery of adverse pathologic characteristics after local excision should be followed by immediate radical resection, which may be performed without adverse oncologic outcome compared to primary radical resection. It needs to be stressed, even with intensive surveillance, delaying TME until the clinical appearance of recurrence has been shown leads to significantly worse rates of survival and resectability (23).

FOLLOW UP

Heafner suggested the follow up scheme using CT/MRI with ERUS postoperatively to in-

crease the sensitivity in detecting locoregional recurrences. History and physical examination is performed every 3-6 months for the first 2 years and then annually after. Preoperative CEA is obtained and on subsequent followup visits. Digital rectal exam and proctoscopy or flexible sigmoidoscopy are performed every 3-6 months for 2 years and then yearly after to detect recurrences, alternated with ERUS every 6 months to evaluate for lymph nodes. Every year, CT or MRI are obtained for detecting local or distant recurrences. Most surveillance schedules only extend out to five years, but long-term follow-up after local excision should be pursued (2).

COMBINATION WITH NEOADJUVANT AND ADJUVANT TREATMENT

Neoadjuvant chemoradiation reduces local recurrence rates and downstages primary tumors in patients with rectal cancers (24,25). Tumor downstaging and downsizing has been demonstrated in 51-64% and 26-100% of T2 rectal cancers, respectively (2). However, complete clinical response only translates to a 30-60% pathologically complete response meaning there is minimal disease recurrence.

Lezoche *et al.* noted overall recurrences occurred primarily in the low response and non-responder groups, at rates of 12% after local excision and 10% after radical resection (26). A more aggressive surgical approach is indicated for these patients, as an incomplete response likewise may exist in the regional lymph nodes (27).

In the transanal excision of T2 rectal cancer, neoadjuvant therapy has shown favorable short-term and similar long-term oncological outcomes to radical resection. One should not disregard the increased rate of post-operative complications due to neoadjuvant treatment (most are minor complications (91%) solvable without additional surgery (28).

The use of neoadjuvant therapy for T2 rectal cancer should be used with caution, since radical surgery alone provides an adequate treatment for T2 N0 disease. Possible role of neoadjuvant treatment is to downsize and downstage borderline T2-T3 tumors. Local excision may then be utilized to determine the pathological response to the chemoradiation or as definite treatment. In case of

partial response or remaining tumor tissue, immediate radical resection should be performed (2).

CONCLUSION

Transanal excision for rectal cancer may be a definitive therapy for highly selected early rectal cancers, in combination with chemoradiotherapy for more advanced tumors, or as a palliative procedure for patients unable to undergo transabdominal operation. Development of novel techniques such as transanal endoscopic microsurgery (TEM) did not significantly justify extending rather narrow indications for this type of surgery. In fact, oncologic adequacy of local excision is discussed with caution. There is a lack of prospective, randomized trials and published series vary in terms of patient selection, adjuvant therapy, surgical technique, and length of follow-up.

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