Transanal endoscopic microsurgery in rectal cancer

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CHAPTER 7

The role of endorectal ultrasound in therapeutic decision-making for local versus transabdominal resection of rectal tumors

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INTRODUCTION

Local excision of rectal adenomas (TVA) is a validated treatment modality. Concern has been made regarding local recurrences after local excision, but with the introduction of transanal endoscopic microsurgery (TEM) this risk has become minimal and even larger and more proximal located TVA can be excised. [1-3] In these larger presumed benign rectal lesions, based on preoperative biopsy, definite histopathology reveals a carcinoma in up to 34% of tumors. [4, 5] As a result patients with missed carcinoma need to undergo additional radical surgery by means of total mesorectal excision (TME). Although evidence is lacking, prior TEM procedures may burden immediate radical surgery with possible higher morbidity, including increased risk on a (permanent) stoma. Moreover, this unexpected histopathological finding and the need for additional surgery impede patients' satisfaction. Finally, oncologic outcome in this subgroup of patients is questionable. [6, 7]

Extensive efforts have been made to improve preoperative diagnosis of rectal tumors, with computerized tomography (CT), magnetic resonance imaging (MRI) and endorectal ultrasound (ERUS) as the techniques most commonly used. Each adjunct has its limits, but ERUS seems the most adequate with accuracy rates for tumor infiltration (T-stage) ranging from 64-95%. [8-13]

If ERUS, however, is to be considered essential in preoperative staging, accuracy may not be the only relevant issue. Feasibility of ERUS in all rectal tumors referred for local excision and the additional value of ERUS in therapeutic decision-making are equally important. In this prospective study we investigated the feasibility of ERUS in all TVA referred to our hospital for TEM. Also the additional value of ERUS in diagnosing invasive carcinomas and its role in therapeutic decision making are studied.

PATIENTS AND METHODS

From April 2000 to May 2006 in 264 consecutive patients with 268 tumors preoperative biopsy revealed a TVA. In all tumors ERUS was intended. The group consisted of 128 males and 136 females. Median age was 70 years (range 29-91 years) and median distance from the dentate line to the distal tumor margin was 8 cm (0-20 cm). Fifty-six tumors were located in the lower third of the rectum (0-5 cm), 133 in the middle third (5-10 cm) and 79 in the upper third (10-15 cm). Median tumor area was 12.3 cm^2 (0.25-156 cm^2). In 69 tumors it concerned residual tumor tissue after recent endoscopic treatment or a recurrent tumor.

Two hours prior to ERUS a cleansing enema was given. Patients were placed in lithotomy position and digital rectal examination and rigid rectoscopy were performed. After inspection of the tumor, the tip of the rectoscope was positioned proximal to the upper margin of the tumor and the ERUS–probe was introduced via the rectoscope with the tip of the probe outside the rectoscope. Both were pulled back simultaneously manually. Ultrasound examinations were

documented on videotape. The ultrasound equipment used was a B&K Medical Scanner (Naerum, Denmark) Type 2101 with a type 1850 rotating endosonic probe with a 10 MHz crystal.
If the tumor could not be reached or passed completely during rectoscopy, or if technical problems occurred, such as inability of cleansing the rectum or equipment failure, the tumor was considered not assessable. In assessable tumors all rectal wall layers had to be visualized without artefacts before considering ERUS conclusive. Ultrasound staging was compared with definite histopathological findings.
Statistical analysis was performed using the SPSS® version 11.0 (SPSS, Chicago, Illinois, USA). Continuous variables and percentages were compared between groups using the Mann-Whitney test or Chi-Square test, respectively. A p-value of 0.05 (two-sided) was considered as the limit of significance and 95% confidence intervals (95% CI) are calculated for various percentages. Kappa statistics were calculated to quantify the agreement between ERUS- and histopathological stages.

RESULTS

Of the 268 tumors in this study 231 (86%) were assessable for ERUS. Median distance from the dentate line in not assessable tumors was 11 cm, which was significantly different from assessable tumors, with a median distance of 7 cm ($p < 0.001$). Of the not assessable tumors 62% were located more than 10 cm proximal from the dentate line. There was no difference in median tumor area between assessable and not assessable tumors. Also the percentage of recurrent/residual tumors was not different. (Table 1)
In 16 tumors ERUS was not performed because of a technical failure (patient incontinence n= 8, inability of cleansing the rectum n=4, equipment failure n=4). Twenty-one tumors were not assessable because they could not be reached or passed due to stenosis and angulation in the rectosigmoid, or because the tumor was too voluminous.
In 210 of 231 assessable tumors (91 %) ERUS was considered conclusive. (Table 2) Fifteen of the 21 tumors in which ERUS was not conclusive were residual or recurred after prior endoscopic treatment (71%). Compared to the tumors in which ultrasound staging was considered conclusive, this proportion was significantly higher ($p < 0.001$).
Definite histopathological staging revealed TVA in 166 tumors (79%), T1 rectal carcinoma in 30 (14.3%), T2 rectal carcinoma in 13 (6.2%) and T3 rectal carcinoma in 1 (0.5%). Overall accuracy of ERUS is 84%. (Table 3) ERUS correctly staged 147 tumors as TVA, with a corresponding sensitivity of 89%. (Table 4) ERUS correctly staged 38 tumors as invasive with a corresponding sensitivity of 86%. Positive and negative predictive values were 96% and 67% respectively.
If only TVA are considered indications for local excision, based on preoperative biopsy 44 tumors would have been undertreated with TEM, as definite histopathology revealed a carcinoma (21%; 95% CI: 15-26%). Based on ERUS 6 tumors would have been undertreated (3%;

Table 1. Tumor characteristics regarding feasibility of ERUS.

	Assessable tumors N=231	Not assessable tumors N=37
Distance from dentate line in cm§	7 (0-20)	11 (3-18)*
Tumor distribution from dentate line		
0-5 cm	55 (24%)	1 (3%)
5-10 cm	120 (52%)	13 (35%)
10-15 cm	56 (24%)	23 (62%)*
Tumor surface (cm^2)§	14 (0.25-156)	8 (0.25-130)
Number of recurrent/residual tumors at referral (%)	63 (27%)	6 (16%)

§ Values are median (range); * $p < 0.001$.

Table 2. Tumor characteristics regarding possibility of staging with ERUS.

	ERUS conclusive N=210	ERUS not conclusive N=21
Distance from dentate line in cm§	7 (0-15)	8 (0-13)
Tumor distribution from dentate line		
0-5 cm	48	7
5-10 cm	112	8
10-15 cm	50	6
Tumor surface (cm^2)§	12 (0.25-156)	14 (0.25-80)
Number of recurrent/residual tumors at referral (%)	48 (23%)	15 (71%)*

§ Values are median (range); * $p < 0.001$.

95% CI: 1-6%). This reduction in undertreatment is statistically significant ($p < 0.01$). Based on preoperative biopsy no tumor would have been overtreated with TME, whereas based on ERUS 19 ultrasonically presumed T2/T3 carcinomas would have been overtreated (9%; 95% CI: 5-13%). This increase in overtreatment is statistically significant ($p < 0.01$).

If TVA and T1 carcinomas are both considered indications for local excision, based on preoperative biopsy 14 tumors would have been undertreated with TEM (7%; 95% CI: 4-11%). Based on ERUS, 6 ultrasonically presumed tumors suitable for TEM would have been undertreated (3%; 95% CI: 1-6%). This reduction in undertreatment is significant ($p < 0.01$). Based on preoperative biopsy no tumor would have been overtreated with TME, whereas based on ERUS 9 ultrasonically presumed T2/T3 carcinomas would have been overtreated (4%; 95% CI: 2-8%). This increase in overtreatment is significant ($p < 0.01$).

Table 3. Agreement of preoperative ERUS with definite histopathological T-staging.

	Histopathological T-staging				
ERUS T-staging	pTVA	pT1	pT2	pT3	Total
uTVA	147	4	1	1	153
uT1	14	22	4	0	40
uT2	4	2	7	0	13
uT3	1	2	1	0	4
Total	166	30	13	1	210

Overall accuracy 84% (176/210), Kappa coefficient 0.59, sensitivity in diagnosing: TVA 89% (147/166), T1 carcinomas 73% (22/30), T2 carcinomas 54% (7/13).

Table 4. Agreement of ERUS and histopathology in diagnosing tubulovillous adenomas.

	Histopathological staging		
ERUS T-staging	pTVA	pT1/T2/T3	Total
uTVA	147	6	153
uT1/T2/T3	19	38	57
Total	166	44	210

Sensitivity 89% (147/166), Kappa-coefficient 0.68, specificity 86% (38/44), positive predictive value 96% (147/153), negative predictive value 67% (38/57).

Table 5. Agreement of ERUS and histopathological staging in diagnosing TVA and T1 carcinomas.

	Histopathological T-staging		
ERUS T-staging	pTVA/T1	pT2/T3	Total
uTVA/T1	187	6	193
uT2/uT3	9	8	17
Total	196	14	210

Sensitivity 95% (187/196), Kappa-coefficient 0.48, specificity 57% (8/14), positive predictive value 97% (187/193), negative predictive value 47% (8/17).

DISCUSSION

Local excision of rectal TVA is the method of choice. As a tertiary referral centre for TEM, we are frequently encountered with tumors considered suitable for local excision using the TEM technique. TEM has proven to be a safe procedure for TVA, with the possibility to excise larger and more proximal located tumors. [1, 2] In presumed rectal TVA, especially in larger tumors, definite histopathology may reveal a carcinoma. In case a carcinoma was missed with biopsy, immediate radical surgery after local excision might be more difficult with possibly increased morbidity. Moreover, in distal located tumors prior local excision could decrease the possibility on sphincter saving surgery. Finally, oncologic outcome in this subgroup of patients is questionable. [6, 7] For these reasons adequate preoperative staging is of major importance.

Of all frequently used staging modalities in rectal tumors ERUS is the most promising, as accuracy concerning tumor invasion depth is higher compared to CT scanning and at least as

accurate as MRI. [8-10] The additional value of ERUS in preoperative staging, compared to other modalities, is expressed by the power to discriminate TVA from invasive carcinomas. ERUS was already shown to be able to correctly establish a cancer diagnosis in 81% of the missed carcinomas at biopsy. [14] These results are of major importance as treatment options, local excision versus radical surgery, are to be discussed with every patient. In rectal carcinomas TME is the gold standard. Although evidence is sparse, in T1 rectal carcinomas the role of TEM has been re-appraised. [15, 16] If both TVA and T1 rectal carcinomas are considered suitable candidates for local excision, ERUS might be of additional value in discriminating these two from more invasive carcinomas. However, especially in larger and more proximal tumors ERUS may be more difficult and if ERUS is considered a useful preoperative adjunct, feasibility in all rectal tumors has to be investigated. One study suggested that in 13% of all rectal tumors ERUS was not feasible. The percentage of not assessable tumors increased from 11% in distal tumors (0-4 cm above anocutaneous line) to 34% in proximal located tumors (12-16 cm above anocutaneous line). However, uniformity regarding the technique of ERUS lacked. Moreover, physicians were allowed not to perform ERUS if considered without additional value. This resulted in 63% of all rectal tumors in which ERUS was not performed. Moreover, only 10% of all tumors in which ERUS was performed were located proximal in the rectum. In our series in all tumors referred for local excision by means of TEM, ERUS was intended. In 86% of all tumors ERUS was technically feasible. If not feasible, distance from the dentate line proved to be a significant contributing factor. Proper interpretation of ERUS imaging was possible in 78% of all tumors. The only significant factor negatively influencing interpretation of ERUS imaging was residual or recurrent disease, especially after recent (endoscopic) manipulation ($p < 0.001$). Several authors already stated that tumor biopsy or (endoscopic) manipulation prior to ERUS should be avoided if on clinical grounds local excision is considered suitable. [11] This could lower the proportion of patients in which ERUS is not conclusive.

Because of the possibility to excise larger tumors with TEM in a large proportion of presumed adenomas a carcinoma is found. In our series in 21% of tumors an unexpected carcinoma was found, which is comparable to other series. [4, 5] The role of ERUS in preoperative evaluation of presumed TVA is significant. In a relatively large review ERUS correctly established a cancer diagnosis in 81% of preoperative (biopsy) misdiagnosed TVA. The need for additional surgery and other associated problems caused by misdiagnosis could be decreased from 24 to five percent. [14] These results are confirmed in our study, with 86% of missed carcinomas on biopsy corrected with ERUS. In TVA sensitivity rates of 89% and specificity rates of 86% can be achieved. The main advantage of ERUS in presumed adenomas is the high positive predictive value of 96%, meaning if ERUS confirms the tumor as TVA only in four percent an invasive carcinoma is found at definite histopathological staging.

The question which rectal tumors are suitable for local excision using the TEM technique is still unanswered. In rectal cancer TME is the gold standard, but evidence, although anecdotic, is growing that T1 rectal carcinomas may be candidates for TEM. [15-18] This means distinction

between TVA and T1 carcinomas may be of less priority but the difference between T1 and more invasive carcinomas is essential. Sailer et al. stated if TVA and T1 carcinomas are considered one ultrasonic entity, ERUS reaches a sensitivity of 81% and a specificity of 98%.[11] They concluded ERUS is helpful in therapeutic decision-making between local excision and radical surgery. In our series sensitivity in diagnosing TVA and T1 carcinomas was 95%. In 14 tumors (7%) a T2 or more invasive carcinoma was found at definite histopathology. Preoperative biopsy found none of these carcinomas, whereas ERUS correctly classified eight of these tumors as uT2/uT3. If ERUS findings would have been used as adjunct in therapeutic decision-making, 57% of missed T2 and T3 carcinomas on biopsy could have been spared prior local excision. This absolute risk reduction in undertreatment, 7 versus 3 per cent, was statistically significant ($p < 0.01$). However, ERUS classified nine tumors as not suitable for local excision (uT2 or higher), which proved to be adenomas (five) or T1 carcinomas (four). This increase in possible overtreatment, 0 versus 4 per cent, was also statistically significant ($p < 0.01$). This overstaging is also found in other series and is a major drawback of ERUS. [11]

In conclusion, based upon this study ERUS is technically feasible in almost all rectal tumors in which preoperative biopsy shows tubulovillous adenoma. Proper ERUS interpretation is possible in 78% of all presumed rectal TVA. ERUS can discriminate between adenomas and invasive carcinomas and has, next to biopsy findings, a substantial additional value in recognizing TVA suitable for local excision. If a carcinoma is suggested with ERUS, one has to discuss treatment options, local excision versus radical surgery, with every patient. This study has shown that if T1 rectal carcinomas are considered suitable candidates for TEM, ERUS has a major additional value in preoperative staging.

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