Preoperative Staging Using Transrectal Ultrasound in High and Low Rectal Cancer

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ABSTRACT: **Background:** An accurate preoperative definition of tumor and lymph node status is needed for reaching the correct decision regarding rectal cancer treatment. Transrectal ultrasonography is the most commonly used diagnostic modality for the local staging of rectal cancer.

Objectives: To determine the accuracy of TRUS in the staging of rectal cancer.

Methods: We conducted a retrospective study on 95 patients evaluated by TRUS. The rectum was subdivided into two parts (lower and upper).

Results: Sixty patients underwent radical surgery. Of these, 34 received no preoperative chemo-irradiation owing to μT1, μT2 tumor or the patient's choice (neo-adjuvant treatment was suggested to patients with adenocarcinoma that proved to be μT3). The overall accuracy rate was 80% for T stage. Overstaging was found in 13.3% and understaging in 6.7%.The N-stage was correctly assessed in 70%. The overall accuracy rate for tumors was 73.9% in the lower part and 90.9% in the upper. A trend towards a lower accuracy rate for low-lying tumors compared to high-located rectal tumors was found ($P = 0.532$), which did not reach statistical significance.

Conclusions: TRUS gave better results for T1 and T3 stage rectal tumors but was inaccurate for stage T2, indicating the possible need for local excision in order to base the final treatment for T2 tumors on pathologic staging.

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KEY WORDS: rectum, cancer, ultrasound, staging, histopathology

Rectal cancer is a common cause of death in Europe and the United States [1,2]. Prognosis is directly related to the tumor stage and the presence of lymph node metastases. Current treatment protocols for rectal cancer involve sphincter-saving surgery, transanal surgery, and neoadjuvant chemo-irradiation therapy, or a combination of more than one modality in addition to the longstanding traditional abdominoperineal resection. In order to make the right decision regarding rectal cancer treatment, an accurate preoperative definition of the tumor status (T stage) and lymph node status (N stage) is needed. The extent of tumor spread is generally evaluated by digital examination, transrectal ultrasonography, computed tomography and magnetic resonance imaging [3].

During the last decade TRUS became the most commonly used diagnostic modality for the local staging of rectal cancer. The accuracy rates of TRUS in assessing the depth of rectal wall invasion have ranged from 80% to 95% [1-6]. When assessing lymph nodes, TRUS has demonstrated an accuracy of approximately 58–83% [2-6]. The aims of the present study were to determine the accuracy of TRUS in the staging of rectal cancer compared with histopathologic examination, and to evaluate whether tumor site (in terms of distance from the anal verge) has an influence on the reliability of TRUS.

PATIENTS AND METHODS

In a retrospective study, data were collected on all patients with rectal cancer treated at Assaf Harofeh Medical Center in central Israel between July 2003 and September 2007. Ninety-five patients had a proven biopsy of rectal adenocarcinoma. After a rectal biopsy all 95 patients underwent TRUS using an ultrasound scanner, type Falcon 2101 (B&K Medical, Denmark) with a 10 MHz frequency probe.

All patients were evaluated by colonoscopy, CT of the chest, abdomen and pelvis, chest X-rays and a blood test for tumor markers. The distance of the tumor from the anal verge was measured by rigid rectoscopy. All TRUS examinations were performed by a single investigator (Y.Z.) using Lloyd-Davis stirrups.

During TRUS, rectal wall penetration was assessed using the modification of the TNM classification, based on a five-layer rectal wall model, proposed by Hildebrandt and Feifel [7]. Pathologic lymph nodes were defined as circular or slightly oval-shaped structures, with an echogenicity similar to the tumor, as proposed by Beynon et al. [8]. The surgical specimens were sent for histopathologic examination and the staging was classified according to the pTNM classification. The ultrasound staging was compared with the histopathologic staging of the resected specimen. Furthermore, to establish the tumor site, the rectum was subdivided into two sections – the lower part (0–5 cm from the anal verge) and the upper part (≥ 6 cm). If the tumor was not confined to one level only, the lower point of

TRUS = transrectal ultrasonography

the lesion was determined as the point of reference. The overall accuracy rates of the two levels were analyzed.

Statistical analysis was performed at Tel Aviv University's Department of Statistics, using the Measure of Agreement-Kappa test and Student's *t*-test; $P < 0.05$ was considered statistically significant.

RESULTS

Of the 95 patients examined by TRUS (42 males and 53 females, median age 66 years, range 33–92 years), 60 patients underwent radical surgery (anterior/low anterior resection in 35, transanal local excision in 15, abdominoperineal resection in 9, and total proctocolectomy with J-pouch in 1). Of the 60 patients, 34 did not undergo preoperative chemo-irradiation therapy because of their disease stage: μT1 in 14 patients, μT2 in 11 patients, and 9 patients with stage μT3 who chose not to have the treatment (neo-adjuvant treatment was suggested to patients with μT3 adenocarcinoma). The remaining 26 patients were treated with preoperative CRT. In 11 of these patients, TRUS was performed not only before but also after completion of CRT. The other 15 patients underwent TRUS only before CRT was given.

For the purposes of our analysis, the patients were divided into two groups: without CRT (group A, 34 patients) and TRUS after CRT (Group B, 11 patients). Patients who underwent TRUS only before CRT were excluded from the study since the purpose of our study was to evaluate the accuracy rate of TRUS.

Evaluating the depth of tumor invasion revealed an overall accuracy rate in both groups of 80% (36 of 45 patients) ($\kappa = 0.583$, $P < 0.01$). TRUS examination correctly staged 13 of 16 patients with T1 tumors (81.2%), 7 of 11 patients with T2 tumors (63.6%), and 16 of 17 patients with T3 tumors (94.1%). No correlation was found comparing TRUS and histopathologic findings in one patient with a T4 tumor. Using TRUS, overstaging was found in 6 of the 45 patients (13.3%) and understaging in 3 (6.7%).

The lymph node status was correctly assessed in 21 of 30 patients (15 of 45 patients underwent transanal local excision), an accuracy rate of 70% ($\kappa = 0.482$, $P < 0.01$) [Table 1]. Positive predictive value was 55.6%, negative predictive value 84.2%, specificity 80% and sensitivity 62.5%.

In the group of patients without CRT (group A), the overall accuracy rate of the depth of tumor invasion was 76.5% (26 of 34 patients) ($\kappa = 0.532$, $P < 0.01$). TRUS correctly staged 12 of 15 patients with T1 tumors (80%), 6 of 10 patients with T2 tumors (60%), and all 9 patients with T3 tumors (100%) [Table 1]. Overstaging was found in 5 of the 34 patients (14.7%) and understaging in 2 (5.9%).

The lymph node status was correctly assessed in 78.9% (15 of 19 patients) [Table 1]. Overstaging was found in 2 of the 19 patients (10.5%) and understaging in 2 (10.5%). In the group of patients in whom TRUS was performed before and after CRT (group B), the overall accuracy rate of the depth of tumor invasion was 90.9% (10 of 11 patients) ($\kappa = 0.750$, $P < 0.01$). TRUS correctly staged the one patient with a T1 tumor (100%), the one patient with a T2 tumor (100%), and seven of eight patients with a T3 tumor (87.5%). No correlation was found when comparing TRUS and histopathologic findings in one patient with a T4 tumor [Table 1]. Overstaging was found in 1 of the 11 patients (9.1%) and understaging in 1 (9.1%).

The lymph node status was correctly assessed in 54.5% (6 of 11 patients) [Table 1]. Overstaging was found in 3 of the 11 patients (27.3%) and understaging in 2 (18.2%). In this group, the rate of tumor downstaging after CRT with respect to the depth of tumor invasion was found in 2 of the 11 patients (18.2%). In one patient, TRUS showed a T3 tumor before CRT and a T1 tumor after CRT, and in another patient a T3 tumor before CRT and a T2 tumor after CRT. In these two patients a correlation was found between TRUS that was performed after CRT and the histopathologic findings. Tumor downstaging rate after CRT with respect to lymph node metastases was found in 4 of the 11 patients (36.4%).

Of the 45 tumors (groups A and B), 23 (51.1%) were located in the distal part and 22 (48.9%) in the proximal part of the rectum. Overall accuracy for tumors situated in the distal part of the rectum was 73.9% (17 of 23 patients) and 90.9% (20 of 22 patients) for tumors in the proximal part of the rectum [Table 2]. Although there was a trend toward a lower accuracy rate for low-lying tumors, this did not reach statistical significance ($P = 0.532$).

Table 1. Comparison of transrectal ultrasonography versus pathologic findings

	T1 tumor n (%)	T2 tumor n (%)	T3 tumor n (%)	T4 tumor n (%)	Overall n (%)	N stage n (%)
Group A: Without CRT	12/15 (80)	6/10 (60)	9/9 (100)	–	26/34 (76.5)	15/19 (78.9)
Group B: Post-CRT	1/1 (100)	1/1 (100)	7/8 (87.5)	0/1	10/11 (90.9)	6/11 (54.5)
Group A + B	13/16 (81.2)	7/11 (63.6)	16/17 (94.1)	0/1	36/45 (80)	21/30 (70)

CRT = chemo-irradiation, N stage = lymph node status

Table 2. Accuracy of transrectal ultrasonography according to tumor site in patients with pre- and post-CRT TRUS

Lower part (0–5 cm) n (%)	Upper part (≥ 6 cm) n (%)
17/23 (73.9)	20/22 (90.9)

DISCUSSION

To select the optimal treatment modality for patients with rectal cancer, accurate preoperative staging is necessary since it will

CRT = chemo-irradiation therapy

benefit the patients in terms of cure and quality of life. Depth of rectal wall tumor invasion and pararectal lymph node involvement have become important parameters when determining the type of treatment. An early small rectal cancer confined to the mucosa and submucosa can be excised locally by the transanal approach [9]; preoperative CRT is recommended for advanced rectal cancer for tumor downstaging, which may enable sphincter-saving procedures. The accuracy of TRUS in the evaluation of the depth of tumor invasion and regional lymph node involvement was found to be superior to or equivalent to that of digital examination, computed tomography and magnetic resonance imaging [3-6]. The accuracy rates of TRUS in determining the depth of tumor invasion and regional lymph node involvement have been reported to be 80–95% and 58–83%, respectively [1-6]. CT accuracy was found to range from 53% to 94% for depth of penetration and from 54% to 70% for lymph node metastases. MRI accuracy ranged from 66% to 92% for depth of penetration and from 60% to 90% for lymph node metastases [10]. In our study, the overall accuracy rate in determining the depth of tumor invasion and regional lymph node involvement was 80% and 70%, respectively. Overstaging was found in 13.3% of the 45 patients, and understaging in 6.7%. Thus, our results are comparable to those reported in the literature.

There is some controversy regarding the interpretation of the images obtained from TRUS. Our experience suggests that the accuracy of TRUS in assessing the depth of rectal wall invasion varies with tumor stage. It is more accurate for T1 (81.2%) and advanced tumors that penetrate the perirectal fat (94.1% accuracy rate for T3 tumors).

The endosonographic diagnosis of T2 tumors, which was only 63.6% in our series, was worse than previously reported but better than that reported (41% in T2) by Sailer and co-authors [11]. The low accuracy rate of TRUS in the diagnosis of T2 tumors emphasizes the need to base the final treatment, after transanal local excision, on the pathologic and not the ultrasound staging [12,13]. It is also difficult to diagnose a T4 lesion because of the short focal length of the transducer.

The high rate of tumor overstaging (13.3% in our study) was mostly due to tissue edema or an inflammatory reaction that cannot be easily differentiated from the tumor by TRUS. Understaging of the tumor was probably due to microscopic invasion, which cannot be detected by TRUS [14,15].

Whether tumor location, in terms of rectal level, has an impact on the endosonographic assessment of wall invasion is not yet settled. Sentovich and collaborators [16] reported a significantly better result for tumors within 6 cm of the anal verge. This is in contradiction to the study conducted by Herzog et al. [5] who found a significantly poorer accuracy rate for tumors of the distal third.

Our experience suggests that the accuracy rate of TRUS in assessing the depth of rectal wall invasion is higher for proximal than distal rectal tumors, but this is not statistically significant. A possible reason for the lower accuracy rate of tumor staging in the lower part of the rectum is the difficulty in reaching all sites of the ampulla recti with a rigid probe. Furthermore, the typical endosonographic five-layer structure of the rectal wall, as described by Hildebrand and Feifel [11], is somewhat less well defined at the level just above the anal canal.

In conclusion, the accuracy rate of TRUS examination in determining the depth of tumor wall penetration and regional lymph node involvement is high. TRUS gave better results for T1 and T3 rectal tumors and was relatively inaccurate for stage T2. The low accuracy rate of TRUS in the diagnosis of T2 tumors emphasizes the need to base the final treatment, after local excision, on the pathologic and not the ultrasound staging.

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