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EFFICACY OF TRUS IN PREOPERATIVE STAGING OF RECTAL CANCER


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Abstract

Background: The aim of this study was to compare the efficacy of TRUS in preoperative local staging of rectal cancer using endosonographic probes with different views (180° vs 360°).

Methods: TRUS was performed in 127 patients with rectal carcinoma by two endoscopists. 71 patients were examined with a 180° endosonographic probe (group A) and 56 patients with a 360° rotating probe (group B). All findings were compared with histopathology report. In order to determine the influence of experience of the endoscopist on TRUS performance, accuracy of T and N staging was compared in the first and second half period of practice.
**Results:** TRUS had a diagnostic overall accuracy of 91.3% for the T category (κ=0.866, SE (k)=0.038, P < 0.0001), and 71.7% for the N category (κ = 0.374, SE (k)=0.082, P < 0.0001). In the group A, TRUS had a diagnostic overall accuracy of 88.7% for the T category (κ = 0.805, SE (k)=0.063, P < 0.0001), and 70.4% for the N category (κ = 0.376, SE (k)=0.101, P < 0.0001). In the group B, TRUS had a diagnostic overall accuracy of 94.6% for the T category (κ = 0.920, SE (k)=0.044, P < 0.0001), and 73.2% for the N category (κ = 0.379, SE (k)=0.131, P = 0.004).

**Conclusion:** The accuracy rate of TRUS in preoperative local staging of rectal cancer is high. Our results imply no significant difference in overall accuracy rates when using endosonographic probes with different views (180° vs 360°).

**Abstrakt**

**Uvod/Cilj:** Ciljovogistraživanja bio je upoređivanjeefikasnosti TRUS u preoperativnojlokalnojprocenistadijumarektalnogkarcinomauzpomočrazličitihendosonograf skihsondi(180° vs 360°).

**Materijalimetode:**Istraživanje je sprovedenona127pacijenata u periodu od 6 godina. 71 pacijent pregledan je uz pomoć180° endosonografske sonde(grupa A) i 56 pacijenatapregledano je uz pomoć 360° rotirajuće sonde(grupa B). Svi nalazi su komparirani sa patohistološkim izveštajima.

**Rezultati:** TRUS je pokazaoukupnudijagnostičkuskonsenzitivnostod 91.3% za T kategoriju(k=0.866, SE (k)=0.038, P < 0.0001), i 71,7% za N kategoriju(κ = 0.374, SE (k)=0.082, P < 0.0001). U grupi A, TRUS je pokazaosenzitivnost od 88.7% za T kategoriju(κ = 0.805, SE (k)=0.063, P < 0.0001), i 70.4% za N kategoriju(κ = 0.376, SE (k)=0.101, P < 0.0001). U grupi B, TRUS je pokazaosenzitivnost od 94.6% za T kategoriju for the T category (κ = 0.920, SE (k)=0.044, P < 0.0001), i 73.2% za N kategoriju(κ = 0.379, SE (k)=0.131, P = 0.004).

**Zaključak:** Efikasnost i tačnost TRUS u preoperativnoj lokalnoj proceni stadijuma rektalnog karcinoma je visoka. Naši rezultati ukazuju da ne postoji značajna razlika u dijagnostici rektalnog karcinoma uz pomoć različitih endosonografskih sondi(180° vs 360°).
INTRODUCTION

Colorectal cancer is the third most common cancer in Europe and the USA and the third commonest cause of cancer related deaths. Over 50% of patients have locally advanced disease that has spread to the lymph nodes and/or the liver at the time of diagnosis [1,2]. The outcome of rectal cancer is dependant on the stage of the tumour. There are several classification systems used to describe the extent of disease. In this study, TRUS tumor stage was assessed by uTNM classification as described by Hildebrandt and Pfeifel[3]. The management of rectal cancer has evolved to become multidisciplinary because it offers the best clinical outcome, although surgery remains the most important treatment of rectal cancer [4,5]. This has greatly increased the importance of accurate preoperative staging in providing information about tumor infiltration and lymph node metastasis in order to make the right decision regarding rectal cancer treatment.

Transrectal ultrasound (TRUS) introduced by Wild and Reid in 1956, is very accurate imaging modality for the assessment of tumour growth in the bowel wall with the reported overall accuracies for T and N staging between 69%-97% and 58–83%, respectively [6-9]. Moreover, TRUS is inexpensive and quick diagnostic procedure associated with minimal discomfort to the patient.

TRUS probes exist as radial and curved linear array depending on the orientation of the ultrasound transducer. Radial probes produce a 360° picture in a plane vertical to the long axis of the endoscope insertion tube, while a linear array create sector-shaped images horizontal to the long axis of the insertion tube[10]. Assessment of the wall of rectum and nearby structures is best achieved with radial probes with a frequency ranging from 6-16 MHz. Within these probes, two crystals are attached back to back, and can rotate inside the transducer[11].

The aim of the present study was to determine the accuracy of TRUS in rectal cancer staging compared with histopathologic examination using rotating endosonographic probes with different views (180° vs 360°), and to evaluate the influence of experience of the endoscopist on TRUS performance.
MATERIAL AND METHODS

Preoperative TRUS was performed in all patients presented to Clinic of Gastroenterology, Clinical Centre of Serbia with newly diagnosed rectal cancer who had no previous tumor staging evaluation. Patients with previously performed staging (MRI of the pelvis) were excluded. During 6-year period, 127 TRUS examinations were performed for staging of rectal cancer by two endoscopists. 71 TRUS examinations were conducted using biplane endorectal probe with a field of view of 180° (Hitachi EUB 6500 U533), while 56 TRUS examinations were performed using endorectal probe with a full 360° field of view (BK medical 1850). As the operator physically move the 1850 probe while the transducer moves along the entire length of the tumor, and provide an image in the axial direction, the U533 biplane probe provide information both axial and sagittal.

Patient selection regarding the technique of TRUS was performed according to the department where they presented first. Informed consents were obtained from all of the patients prior to the examination. Before the probe was inserted into the rectum, a digital rectal examination was carried-out to identify the size, fixation, morphology and location of the tumor, and to exclude clinically important stenosis to determine whether the anal canal and lower rectum are passable. All patients were evaluated to determine the diagnostic accuracy of depth of transmural tumor invasion and lymph node metastases. TRUS results were correlated with histopathological reports regarded as the gold standard in local staging of rectal carcinoma.

TRUS T stage was assessed by visualising the depth of tumour penetration through five defined layers of echogenicity in the rectal wall as described by Hildebrandt and Pfeifel [12]. All identified lymph nodes were measured, and nodes greater than 5 mm in maximum diameter classified as positive (N+). Nodes smaller than this were assumed to be normal or inflammatory and were defined as N0. Comparison was made between ultrasound staging and histopathologic findings after surgery.

Statistical analysis was performed using the Measure of Agreement-Kappa test for accuracy rates of T and N staging. Comparison of the accuracies within both the T and N
staging results was made using the Fishers Exact Test or Chi-squared test, with a \( p \) value of \(<0.05\) considered to be significant.

In order to determine the influence of experience of the endoscopist on TRUS performance, TRUS performed during this period was divided into two time periods. The first time period was taken as the first half of practice, and the second period was taken as the second half of practice. Accuracy of T- and N-staging was calculated and compared in each time period.

RESULTS

Total of 127 patients were examined by TRUS (90 males and 37 females, median age 63 years, range 26–85 years), and all of them underwent surgery. After surgery, preoperative findings were compared with histopathology findings of the surgical specimen. Following correlations were found comparing TRUS and histopathologic findings: TRUS examination correctly staged 24 of 27 patients with T1 tumors (88.9%), 34 of 37 patients with T2 tumors (91.9%), 56 of 60 patients with T3 tumors (93.3%), and 2 of 3 patients with T4 tumors (66.7%). Overall accuracy rate was 91.3% (116 of 127 patients) (\( k=0.866, SE (k)=0.038, P < 0.0001 \)) [Table 1]. Using TRUS, overstaging was found in 6 of the 127 patients (4.7%) and understaging in 5 (3.9%).

The lymph node status was correctly assessed in 91 of 127 patients, with an accuracy rate of 71.7% (\( \kappa = 0.374, SE (k)=0.082, P < 0.0001 \)) [Table 1]. Understaging was found in 9 of the 127 patients (7.1%) and overstaging in 27 (21.3%).

For the purposes of our analysis, the patients were divided into two groups. First group was examined with a 180° rotating endosonographic probe (group A, 71 patients) and the second group was examined with a 360° rotating endosonographic probe (Group B, 56 patients).

In the group group A, the overall accuracy rate of the depth of tumor invasion was 88.7% (63 of 71 patients) (\( \kappa = 0.805, SE (k)=0.063, P < 0.0001 \)). TRUS correctly staged 5 of 8 patients with T1 tumors (62.5%), 23 of 25 patients with T2 tumors (92%), 35 of 37 patients with T3 tumors (94.6%), and 0 of 1 patient with T4 tumors (0%) [Table 1]. Overstaging was found in 6 of the 71 patients (8.4%) and understaging in 2 (2.8%). In the group group
B, the overall accuracy rate of the depth of tumor invasion was 94.6% (53 of 56 patients) ($\kappa = 0.920, SE (k)=0.044, P < 0.0001$). TRUS correctly staged all 19 patients with T1 tumors (100%), 11 of 12 patients with T2 tumors (91.7%), 21 of 23 patients with T3 tumors (91.3%), and both patients with T4 tumors (100%) [Table 1]. Understaging was found in 3 of the 56 patients (5.3%). There was no statistically significant difference in overall accuracy rate of the depth of tumor invasion between groups (ChiSq=0.736, p=0.391). No correlation was found between groups in accuracy of T2, T3 and T4 staging respectively (Fisher’s test, p=1.00, p=0.634, p=0.333). There was statistically significant difference in accuracy of T1 staging between groups (Fisher’s test, p=0.019).

In group A, the lymph node status was correctly assessed in 50 of 71 patients, with an accuracy rate of 70.4% ($\kappa = 0.376, SE (k)=0.101, P < 0.0001$) [Table 1]. Understaging was found in 3 of the 71 patients (4.2%) and overstaging in 18 (25.3%). In group B, the lymph node status was correctly assessed in 41 of 56 patients, with an accuracy rate of 73.2% ($\kappa = 0.379, SE (k)=0.131, P = 0.004$) [Table 1]. Understaging was found in 6 of the 56 patients (7.1%) and overstaging in 9 (21.3%). There was no statistically significant difference in overall accuracy rate of assessing lymph node status between groups (ChiSq=0.022, p=0.882).

A high accuracy rate was maintained throughout the study period for T staging in both groups. There was a slight improvement in accuracy rate of T staging in group A from 83.3% in the first half of practice to 97.1% in the second half of practice, although the difference was not statistically significant. In group B, a high levels of accuracy in T staging were maintained throughout the study from 92.9% in the first half of practice to 100% in the second half of practice. There was a decrease in accuracy rate of N staging in group A from 81% in the first half of practice to 60% in the second half of practice, although the difference was not statistically significant. In group B, a high levels of accuracy in N staging were maintained throughout the study from 68% in the first half of practice to 79% in the second half of practice.

**DISCUSSION**

At present, a combination of computed tomography (CT), magnetic resonance imaging (MRI) and transrectal ultrasonography (TRUS), is used for the preoperative staging of rectal cancer. The choice of modality depends on local expertise and availability.
For assessing the depth of tumour growth in the bowel wall, TRUS is very accurate with reported overall accuracies for T staging varying between 69% and 97% [9]. On the other hand, CT is the current standard for staging of distant metastasis, and cannot be considered appropriate for local tumor staging[13]. MRI seems to be superior for more locally advanced disease with reported sensitivity between 66% and 92% [14]. Two meta-analyses have shown that sensitivity was affected by the T stage [15,16]. TRUS seems to be more accurate for staging of superficial rectal T1 and T2 tumours, with reported sensitivity of 94%. A report of a large endosonography study in 1184 patients with rectal tumors confirmed these findings with the overall staging accuracy of 69% that is lower than previously reported because of less accurate assessment of local tumor extent in advanced rectal cancer [17]. On the other hand, study conducted in Israel reported that the accuracy of TRUS in local tumor staging was more accurate for T1 (81.2%) and T3 (94.1%) in comparison with T2 (63.6%) [18].

In our study, the overall accuracy rate in determining the depth of tumor invasion was 91.3%. Accuracy rates for T1 and T2 tumours were 88.9% and 91.9% respectively. The highest accuracy rate was for T3 (93.3%). Overstaging was found in 4.7% of 127 patients, and understaging in 3.9%. Thus, our results are comparable to those reported in the literature[19]. A reason for good results of this study is the level of experience of the endoscopist. Both operators were highly experienced endosonographers that demonstrated superior performance, underscoring the learning curve that exists for mastering endoscopic ultrasonography. The improvement with experience was shown by Orrom et al., who found that the staging accuracy of rectal cancer increased from 58% in the initial 12 examinations to 88% for the subsequent 24 procedures [20]. In our study, a high levels of accuracy in T staging were maintained throughout the study in both groups, from 83.3% in the first half of practice to 97.1% in the second half of practice, and from 92.9% to 100% respectively.

Assessment of pararectal lymph node involvement is essential for selection of high risk patients which are candidates for preoperative chemoradiotherapy, and is still a diagnostic problem. Meta-analysis of six included studies showed that TRUS was only slightly superior to noncontrast enhanced MRI and CT in identifying lymph node metastasis with reported accuracy rate from 58–83% [8, 21]. CT cannot accurately distinguish between malignant and benign lymph nodes with nodal staging accuracy between 54% and 70%. MRI accuracy was found to range from 60% to 90% for lymph node metastases [14, 22-25]. In our study, the overall accuracy rate of assessing lymph node status was 71.7% which
was similar to previously reported results. There was no significant difference between groups in overall accuracy rates of assessing lymph node status. It seems that 360° view is not superior to 180° view in better visualization of perirectal lymph nodes.

High accuracy rate for N staging in this study (with a cut-off of 5 mm for positive nodes) was somewhat surprising as we are aware that almost 30-40% of involved nodes are of 4mm diameter or less. However, this should be viewed through the prism of a high level of false negative and false positive rates reported in the study. There was a tendency for overstaging nodes in both groups.

We are aware that this study has potential drawbacks. Only patients without previous staging were included in the study, so this could be a source of selection bias. A lack of randomization is the most important drawback since patients were not randomized for the technique of TRUS. Although it may be a potential source of error, we believe that this issue could not significantly influence results since patients were not deliberately selected, as the type of TRUS was determined according to the unit where patient was first presented.

**CONCLUSION**

In conclusion, the accuracy rate of TRUS in preoperative local staging of rectal carcinoma and regional lymph node involvement is high. Our results imply no significant difference in overall accuracy rates of assessing local and lymph node status when using endosonographic probes with different views (180° vs 360°) with the exception of accuracy in T1 staging where 360° was superior to 180°.
Table 1. Comparison of transrectal ultrasonography versus pathohistologic findings

<table>
<thead>
<tr>
<th>Group</th>
<th>T1 tumor n (%)</th>
<th>T2 tumor n (%)</th>
<th>T3 tumor n (%)</th>
<th>T4 tumor n (%)</th>
<th>Overall n (%)</th>
<th>N stage n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A: 180°</td>
<td>5/8 (62.5)</td>
<td>23/25 (92)</td>
<td>35/37 (94.6)</td>
<td>0/1</td>
<td>63/71 (88.7)</td>
<td>50/71 (70.4)</td>
</tr>
<tr>
<td>B: 360°</td>
<td>19/19 (100)</td>
<td>11/12 (91.7)</td>
<td>21/23 (91.3)</td>
<td>2/2 (100)</td>
<td>53/56 (94.6)</td>
<td>41/56 (73.2)</td>
</tr>
<tr>
<td>A + B</td>
<td>24/27 (88.9)</td>
<td>34/37 (91.9)</td>
<td>56/60 (93.3)</td>
<td>2/3 (66.7)</td>
<td>116/127 (91.3)</td>
<td>91/127 (71.7)</td>
</tr>
</tbody>
</table>

REFERENCES


