



Efficacy of transrectal ultrasonography (TRUS) in preoperative staging of rectal cancer

Efikasnost transrektalne ultrasonografije (TRUS) u preoperativnoj proceni stadijuma rektalnog karcinoma

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Abstract

Background/Aim. The outcome of rectal cancer is dependant on the stage of the tumour. There are several classification systems used to describe the extent of the disease. The aim of this study was to compare the efficacy of transrectal ultrasonography (TRUS) in preoperative local staging of rectal cancer using endosonographic probes with different views (180° vs 360°), as well as an influence of experience of an endoscopist on the TRUS performance. **Methods.** TRUS was performed in 127 patients with rectal carcinoma by two endoscopists. Seventy-one 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 a histopathology report. **Results.** TRUS had a diagnostic overall accuracy of 91.3% for the tumor (T) category ($k = 0.866$, SE (k) = 0.038, $p < 0.0001$) and 71.7% for the node (N) category ($\alpha = 0.374$, SE (k) = 0.082, $p < 0.0001$). In the group A, TRUS had a diagnostic overall accuracy of 88.7% for the T category ($\alpha = 0.805$, SE (k) = 0.063, $p < 0.0001$), and 70.4% for the N category ($\alpha = 0.376$, SE (k) = 0.101, $p < 0.0001$). In the group B, TRUS had a diagnostic overall accuracy of 94.6% for the T category ($\alpha = 0.920$, SE (k) = 0.044, $p < 0.0001$), and 73.2% for the N category ($\alpha = 0.379$, SE (k) = 0.131, $p = 0.004$). Experience of the endoscopist had no significant influence on results of preoperative staging of rectal cancer by using TRUS. **Conclusion.** The accuracy rate of TRUS in the preoperative local staging of rectal cancer is high. Our results imply no significant difference in the overall accuracy rates when using endosonographic probes with different views (180° vs 360°). Also, there was no significant influence of endoscopist experience on results obtained.

Key words:

rectal neoplasms; carcinoma; neoplasm staging; preoperative period; ultrasonography; diagnosis, differential.

Apstrakt

Uvod/Cilj: Ishod lečenja rektalnog karcinoma zavisi od stadijuma u kome je otkriven. Postoji više klasifikacionih sistema koji se primenjuju u cilju određivanja proširenosti karcinoma. Cilj ovog istraživanja bio je upoređivanje efikasnosti transrektalne ultrasonografije (TRUS) u preoperativnoj lokalnoj proceni stadijuma rektalnog karcinoma uz pomoć različitih endosonografskih sonda (180° vs. 360°), kao i uticaj iskustva endoskopiste na izvođenje TRUS. **Metode.** Istraživanje je sprovedeno na 127 bolesnika tokom perioda od šest godina. Pregledan je 71 bolesnik uz pomoć 180° endosonografske sonde (grupa A) i 56 bolesnika uz pomoć 360° rotirajuće sonde (grupa B). Svi nalazi su komparirani sa patohistološkim izveštajima. **Rezultati.** TRUS je pokazao ukupnu dijagnostičku senzitivnost od 91,3% za tumor (T) kategoriju ($k = 0.866$, SE (k) = 0.038, $p < 0.0001$), i 71,7% za nodus (N) kategoriju ($\alpha = 0.374$, SE (k) = 0.082, $p < 0.0001$). U grupi A, TRUS je pokazao senzitivnost od 88,7% za T kategoriju ($\alpha = 0.805$, SE (k) = 0.063, $p < 0.0001$), i 70,4% za N kategoriju ($\alpha = 0.376$, SE (k) = 0.101, $p < 0.0001$). U grupi B, TRUS je pokazao senzitivnost od 94,6% za T kategoriju ($\alpha = 0.920$, SE (k) = 0.044, $p < 0.0001$), i 73,2% za N kategoriju ($\alpha = 0.379$, SE (k) = 0.131, $p = 0.004$). Iskustvo endoskopiste u izvođenju TRUS nije imalo značajniji uticaj na preoperativnu procenu stadijuma rektalnog karcinoma. **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 sonda (180° vs. 360°). Takođe, pokazano je da iskustvo endoskopiste u izvođenju TRUS ne utiče značano na procenu stadijuma rektalnog karcinoma.

Ključne reči:

rektum, neoplazme; karcinomi; neoplazme, određivanje stadijuma; preoperativni period; ultrasonografija; dijagnoza, diferencijalna

Introduction

Colorectal cancer is the third most common cancer in Europe and the USA, and the third most common 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, transrectal ultrasonography (TRUS) tumor stage was assessed by the Tumor-Node-Metastasis (TNM) classification as described by Hildebrandt and Pfeifel³.

The management of rectal cancer has evolved to become multidisciplinary because it offers the best clinical outcome, although surgery remains the most important treatment^{4,5}. This greatly increased the importance of the accurate preoperative staging in providing information about tumor infiltration and lymph node metastasis in order to make the right decision regarding rectal cancer treatment.

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 the 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.

The TRUS probes exist as radial and curved linear array depending on the orientation of the ultrasound transducer. The 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 tube¹⁰. 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 transducer¹¹.

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

Methods

Preoperative TRUS was performed in all patients presented to the Clinic of Gastroenterology, Clinical Centre of Serbia, Belgrade 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 the staging of rectal cancer by two endoscopists. Seventy-one TRUS examinations were conducted using a biplane endorectal probe with a field of view of 180° (Hitachi EUB 6500 U533), while 56 TRUS examinations were performed using the 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 provides an image in the axial direction, the U533 biplane probe provides information both axial and sagittal.

The 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. The TRUS results were correlated with the histopathological reports regarded as the gold standard in local staging of rectal carcinoma.

The TRUS T stage was assessed by visualising the depth of the tumour penetration through five defined layers of echogenicity in the rectal wall as described by Hildebrandt et al.¹². All identified lymph nodes were measured and nodes greater than 5 mm in the maximum diameter were classified as positive (N+). The nodes smaller than this were assumed to be normal or inflammatory and were defined as N0. Comparison was made between the 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 χ^2 -test, with a *p* value of < 0.05 considered to be significant.

In order to determine the influence of experience of the endoscopist on the 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

The 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.

Comparing TRUS and histopathologic findings the following correlations were found: the TRUS examination correctly staged 24 (88.9%) of 27 patients with T1 tumors, 34 (91.9%) of 37 patients with T2 tumors, 56 (93.3%) of 60 patients with T3 tumors, and 2 (66.7%) of 3 patients with T4 tumors. 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 (4.7%) and understaging in 5 (3.9%) of 127 patients.

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 (7.1%) and overstaging in 27 (21.3%) of the 127 patients.

Table 1

Comparison of transrectal ultrasonography versus histopathologic findings

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

T – tumor; N – node.

For the purpose 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 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 (62.5%) of 8 patients with T1 tumors, 23 (92%) of 25 patients with T2 tumors, 35 (94.6%) of 37 patients with T3 tumors, and 0 (0%) of 1 patient with T4 tumors (Table 1). Overstaging was found in 6 (8.4%) and understaging in 2 (2.8%) of the 71 patients. 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 (100%) patients with T1 tumors, 11 (91.7%) of 12 patients with T2 tumors, 21 (91.3%) of 23 patients with T3 tumors and both (100%) patients with T4 tumors (Table 1). Understaging was found in 3 (5.3%) of 56 patients. There was no statistically significant difference in the overall accuracy rate of the depth of tumor invasion between groups ($\chi^2 = 0.736$, $p = 0.391$). No correlation was found between the groups in accuracy of the T2, T3 and T4 staging, respectively (Fisher's test, $p = 1.00$, $p = 0.634$, $p = 0.333$). There was a statistically significant difference in accuracy of the T1 staging between the groups (Fisher's test, $p = 0.019$).

In the group A, the lymph node status was correctly assessed in 50 of 71 patients, with the accuracy rate of 70.4% ($\kappa = 0.376$, SE (k) = 0.101, $p < 0.0001$) (Table 1). Understaging was found in 3 (4.2%) and overstaging in 18 (25.3%) of 71 patients. In the group B, the lymph node status was correctly assessed in 41 of 56 patients, with the accuracy rate of 73.2% ($\kappa = 0.379$, SE (k) = 0.131, $p = 0.004$) (Table 1). Understaging was found in 6 (7.1%) and overstaging in 9 (21.3%) of 56 patients. There was no statistically significant difference in the overall accuracy rate of assessing lymph node status between the groups ($\chi^2 = 0.022$, $p = 0.882$).

A high accuracy rate was maintained throughout the study period for the T staging in both groups. There was a slight improvement in the accuracy rate of the T staging in the 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 the group B, a high level of accuracy in the 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 the accuracy rate of the N staging in the 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 the group B, a high level of accuracy in the N staging was 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 TRUS, is used for the preoperative staging of rectal cancer. A 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 the 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 the local tumor staging¹³. MRI seems to be superior for more locally advanced disease with reported sensitivity between 66% and 92%¹⁴. Two meta-analyses showed 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 1,184 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 the local tumor extent in advanced rectal cancer¹⁷. On the other hand, study conducted in Israel reported that the accuracy of TRUS in the 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%, and understaging in 3.9% of 127 patients. Thus, our results are comparable to those reported in relevant literature¹⁹. A reason for good results of this study is the level of experience of the endoscopists. Both operators were highly experienced endosonographers that demonstrated superior performance, underscoring the existing learning curve for mastering endoscopic ultrasonography. The improvement with experience was shown by Orrom et al.²⁰, who found that the staging accuracy of rectal cancer increased from 58% in the initial 12 examinations to 88% for the subsequent 24 procedures. In our study, a high levels of accuracy in the 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 a selection of a high risk patients which are candidates for preoperative chemoradiotherapy, and still represents a diagnostic problem. Meta-analysis of 6 included studies showed that TRUS was only slightly superior to non-contrast 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%. The 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 a lymph node status was 71.7% which was similar to the previously reported results. There was no significant difference between the groups in the overall accuracy rates of assessing the lymph node status. It seems that 360° view is not superior to 180° view in better visualization of perirectal lymph nodes.

A high accuracy rate for the N staging in this study (with a cut-off of 5 mm for positive nodes) was somewhat surprising as we were aware that almost 30–40% of the involved nodes were of 4 mm 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 the 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 the patients were not deliberately selected, as the type of TRUS was determined according to the unit where a patient was first presented.

Conclusion

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

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