

The efficacy of endoscopic ultrasonography in local staging of rectal tumors

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Background/aims: The purpose of this study was to research the efficacy and reliability of endoscopic rectal ultrasonography in local staging (T and N stages) of rectal tumors. **Materials and Methods:** This retrospective study was carried out by the Department of Gastroenterology, İzmir Atatürk Training and Research Hospital, which is tertiary level. Thirty-one patients with adenocarcinoma were included in the study. The patients found operable according to computed tomography underwent preoperative local staging by endoscopic ultrasonography. Radial endoscopic ultrasonography and T and N stages were evaluated. **Results:** It was observed that endoscopic rectal ultrasonography had 80.6% accuracy, 93.4% sensitivity, and 96.5% specificity in T stage; 70% accuracy, 70% sensitivity, and 86% specificity in the detection of presence of lymph node; and 76% accuracy, 100% sensitivity, and 22% specificity in the detection of the nature of lymph node. **Conclusions:** In this study, it was observed that endoscopic rectal ultrasonography is an efficient and reliable method in the detection of local lymph node and the depth of invasion of rectal tumors (T staging), although it is not reliable enough to determine the characteristics of lymph nodes.

Key words: Endosonography, rectal neoplasm, neoplasm staging

Rektal tümörlerin lokal evrelemede endoskopik ultrasonografinin etkinliği

Amaç: Çalışmanın amacı, endoskopik rektal ultrasonografinin, rektal tümörlerin lokal evrelemede (T ve N evrelemesi) etkinliğini ve güvenilirliğini araştırmaktır. **Gereç ve Yöntem:** Bu retrospektif çalışma, tersiyer düzeydeki İzmir Atatürk Eğitim ve Araştırma Hastanesi, Gastroenteroloji bölümünde yürütüldü. Adenokarsinom tanılı 31 hasta çalışmaya dahil edildi. Bilgisayarlı tomografiye göre ameliyat edilebilir durumdaki hastalara, endoskopik ultrasonografi ile ameliyat öncesi lokal evreleme yapıldı. Radial endoskopik ultrasonografi ve T ve N evreleri değerlendirildi. **Bulgular:** endoskopik rektal ultrasonografinin T evrede %80,6 doğruluk, %93,4 sensitivite, %96,5 spesifite, ve lenf nodu varlığı tanımlamasında %70 doğruluk, %70 sensitivite, %86 spesifite, ve lenf nodlarının niteliğini tanımlamada %76 doğruluk, %100 sensitivite, %22 spesifite olduğu izlendi. **Sonuç:** Bu çalışmada, endoskopik rektal ultrasonografinin lenf nodu özelliklerini tanımlamada yeterli olmasına rağmen, lokal lenf nodunu, rektal tümörün (T evreleme) invazyon derinliğini tanımlamada etkili ve güvenilir bir metod olduğu gözlemlendi.

Anahtar kelimeler: Endosonografi, rektal neoplazm, neoplazm evreleme

INTRODUCTION

The therapy and prognosis of rectal carcinoma depend on the stage of the tumor during detection. The most common problem faced in postoperative follow-ups is local recurrence. Local recurrence is determined by tumor morphology, depth of the tumor, lymph node metastasis, and surgical techniques (1). Therapeutic strategies to tailor treatment preoperatively thus require precise knowledge of the depth of tumor invasion into the rectal

wall and the presence of regional lymph node and systemic metastasis. Assessment of the invasion depth (T stage) and lymph node involvement (N stage) are vital components of preoperative staging (2). In rectal cancer, the TNM staging is usually performed to guide treatment decisions and prognosis (3). The TNM staging for rectal cancer is dependent on the depth of invasion of the lesion (T), regional lymph node invasion (N), and the pre-

sence of distant metastasis (M). N staging depends on regional lymph node involvement. NX and N0 represent nodes that cannot be assessed or no regional lymph node metastases, respectively. Nodal invasion by rectal cancer is considered locally advanced disease (4).

Some scanning techniques such as computed tomography (CT), magnetic resonance imaging (MRI) and endoscopic rectal ultrasonography (ERUS) are used to stage tumors. In the locoregional evaluation of rectal cancer, CT and MRI have the advantages of acquiring systemic information, whereas ERUS has the advantages of lower cost, easier accessibility, and shorter examination time compared with CT and MRI (5). CT scan is an excellent modality for demonstrating distant metastasis as well as perirectal fat and adjacent organ involvement, but it lacks precision for locoregional staging because of its inability to distinguish between mural layers. EUS can assess the extent of wall invasion, provide good estimates of longitudinal and circumferential extent, and visualize perirectal lymph nodes (to direct fine-needle biopsy); however, liver metastases and distant nodal involvement are not revealed because they are outside the range of the probe. The efficacy rates of these instruments in T staging are ERUS: 80-95%, CT and MRI: 75-85%, and in N staging, they are ERUS: 70-75% and CT: 55-65% (6,7).

The purpose of this study was to research the efficacy and reliability of ERUS in local staging (T and N stages) of rectal tumors.

MATERIALS AND METHODS

Thirty-one consecutive patients with resectable rectal carcinoma were recorded from June 2009 to November 2010. This retrospective study was carried out by the Department of Gastroenterology, İzmir Atatürk Training and Research Hospital, which is tertiary level. Rectal carcinoma was confirmed by histologic analysis of endoscopic biopsy samples, and it was considered that the rectal site extended from the anal verge to the rectosigmoid junction. The patients who previously underwent emergency surgery, chemotherapy or radiotherapy were excluded. The surgical specimen was subjected to full pathologic examination and staged (TNM) in accordance with the guidelines of the American Joint Committee on Cancer. EUS examinations were performed using a Hitachi EUB-7000 Ultrasonography plus Pentax radial 360° probe (7.5-10 MHz) (Pentax FG36UX ultraso-

und scanner; Pentax Precision Instruments, New York, NY). The examinations were conducted on the patient in a left lateral decubitus position. The tip of the probe was covered with a latex balloon filled with degassed water. The probe was introduced past the level of the tumor and then withdrawn slowly. After the lump had been focused for T staging, the rectal wall thickness, its layers, the borders between the layers, the relationship between the layers, perirectal fat planes, and neighboring organs were evaluated. The lymph node evaluation (N staging) was carried out evaluating the lymph nodes in the adjacent perirectal fat planes between the sigmoid colon and anal canal. 10 MHz for T staging and 7.5 MHz for N staging were used.

The ultrasonographic staging corresponded to the TNM classification as follows: (1) T1, tumor confined to mucosa and submucosa; (2) T2, tumor infiltrating the muscularis propria; (3) T3, tumor invading perirectal fat; and (4) T4, tumor infiltrating surrounding organs (8).

The sonographic criteria for identifying involved lymph nodes were as follows: size greater than 5 mm, hypoechoic, sharply demarcated borders, and spherical (rather than ovoid or flat) volume. All lymph nodes were accepted as malignant lymph nodes. All endoscopic examinations were performed by a single endoscopist (A.M.). Histological evaluations were carried out by two pathologists. The patients' parameters were obtained from the endoscopic parameters recorded in the hospital automation and information system, surgical operation records and histology laboratory findings.

Statistical Methods

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each staging technique were calculated, considering the histologic findings. The 95% confidence interval (CI) of the accuracy of the estimates of the T and N stages was calculated by the Wilson score method. The data were analyzed using the Statistical Package for the Social Sciences (SPSS) 17.0 statistical software.

RESULTS

Forty-two patients who were operable (T1-T2) according to MRI and CT results underwent ERUS for this study. Due to the size of the lump, 11 patients were inoperable, and these patients were not included in the study. The ERUS findings and

histological parameters obtained from the surgical materials of the other 31 patients were compared. The surgery day was 17 ± 14 days after ERUS. The average age of the 31 patients was 63.7 ± 11.5 years. Twenty-two of the patients were male. Postoperative histological examination showed that of the 31 patients, 23 (74.1%) were early stage (T 1-2), 12 (29.5%) were locally advanced stage (T3), and four (6.4%) were advanced stage and with adjacent organ invasion. Of the 31 patients, 24 (77.4%) had external (peripheral) lymph nodes. Considering the surgical material, 14 (58.3%) of the lymph nodes were reactive lymph nodes, while 10 (41.7%) were malignant lymph nodes.

When comparing ERUS findings to histological parameters,

T staging

Of 31 patients, 25 (80.6%) had similarities in ERUS and histological T staging. ERUS showed that 5 patients were T1, 14 patients were T2, 9 patients were T3, and 3 patients were T4.

T1 stage: Of 5 patients detected with T1 during ERUS examination, 4 were detected with T1 tumor during the histological examination. In this stage, the rates were as follows: sensitivity: 100%, specificity: 96%, PPV: 80%, NPV: 100%, accuracy: 96%, and kappa: 0.87.

T2 stage: Of 19 patients detected with T2 during histological staging, 15 were detected with T2 tumor during ERUS examination. In this stage, the

rates were as follows: sensitivity: 73%, specificity: 100%, PPV: 100%, NPV: 70%, accuracy: 70%, and kappa: 0.55.

T3 stage: Of 8 patients detected with T3 during ERUS examination, 6 were detected with T3 tumor during the histological examination. In this stage, the rates were as follows: sensitivity: 100%, specificity: 88%, PPV: 66%, NPV: 100%, accuracy: 84%, and kappa: 0.79.

T4 stage: Of 3 patients detected with T4 during ERUS examination, 2 were detected with T4 tumor during the histological examination. In this stage, the rates were as follows: sensitivity: 100%, specificity: 96%, PPV: 66%, NPV: 100%, accuracy: 96%, and kappa: 0.70 (Tables 1, 2).

N staging

Twenty-four patients were detected with lymph node histologically. During ERUS examination, one or more lymph nodes larger than 5 mm were found in 21 (80.7%) of these patients. The average diameter of these lymph nodes was 10.7 ± 4.3 mm. All of the nodes were with sharp borders, round and homogeneous. During the histological examination, malignant lymph nodes were found in 10 (41.7%) of 24 patients. ERUS had 100% PPV, 50% NPV, 70% sensitivity, 86% specificity, 70% accuracy, and 0.64 kappa in the detection of lymph nodes. It had 74% PPV, 100% NPV, 100% sensitivity, 22% specificity, 76% accuracy, and 0.28 kappa in the detection of the characteristics (malignant-reactive) of lymph nodes (Table 3).

Table 1. T stage distribution of ERUS and histology

	Stage T1	Stage T2	Stage T3	Stage T4
Histology	4	19	6	2
ERUS	5	15	8	3

Table 2. The efficiency of ERUS according to T stages

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Kappa
Stage T1	100	96	80	100	96	0.87
Stage T2	73	100	100	70	70	0.55
Stage T3	100	88	66	100	84	0.79
Stage T4	100	96	66	100	96	0.70

PPV: Positive predictive value. NPV: Negative predictive value.

Table 3. The efficiency of ERUS in determining lymph nodes and prediction of nature

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	Kappa
Presence of lymph nodes	70	86	80	100	83	0.64
Type of lymph nodes	100	22	74	100	76	0.28

PPV: Positive predictive value. NPV: Negative predictive value.

When the relationship between T stage and N stage was evaluated histologically,

- locoregional reactive lymph nodes were found in 2 of 4 patients with T1 stage;
- lymph nodes were found in 11 of 19 patients with T2 stage and lymph nodes were malignant in 4 patients;
- lymph nodes were found in all 6 patients with T3 stage and lymph nodes were malignant in 4 patients;
- malignant lymph nodes were found in both patients with T4 stage.

DISCUSSION

It is vital to correctly detect tumor invasion in patients with rectal cancer, to decide the proper treatment, and to correctly predict survival. Survival is lower with advancing disease (9). CT and MRI are rather insufficient for both evaluation and imaging of wall layers. Therefore, CT and MRI cannot be used for detection and staging of early stage tumors (T1-2). However, they are very efficient in the detection of advanced stage disease, distant lymph nodes, and organ metastasis (10). As EUS can clearly show wall layers and perirectal fat planes, it is an effective method in local staging. The meta-analysis of Bipat et al. (11) also found that ERUS was the best technique for assessing local invasion, but they stressed its limitations: operator dependency, no assessment of stenotic tumor, inability to visualize tumors located in the upper rectum (with a rigid probe), inability to detect lymph nodes outside the range of the transducer, and inability to visualize mesorectal fascia. Forty-nine patients were evaluated for the study. However, due to the size and location (sigmoid angle) of the tumor, 31 (73%) of the patients were able to be staged locally. Hence, it is considered that the disadvantages of ERUS are the size and location of a tumor. EUS has been accepted as the standard method for the preoperative staging of rectal cancer, especially for T staging, because of its excellent discrimination of the rectal wall layers (7). Structure and sensitivity of ultrasound probes used in studies, such as radial EUS scope, linear EUS scope, flexible EUS scope, and voice wavelength, may change the efficacy in the detection of T stage as well. When ERUS is flexible and runs at a high megahertz, efficacy in staging increases. In the previous studies, efficacy of transrectal US and ERUS in T stage ranges between 64-90% (12-14). Moreover, efficacy increases

when three-dimensional (3D) EUS software is used (5). The accuracy of EUS in assessing depth of invasion into the rectal wall has been found to vary with tumor stage, with higher accuracy in early (T1) and advanced (T3-T4) lesions than in T2 lesions (16,17).

A 10-MHz electronic 2D radial EUS scope and software were used for T stage in this study. Similar to other studies, the efficacy of EUS in the evaluation of T stage was detected as 80.6%. Considering the T stages, subgroup evaluation was carried out in this study. It was detected that efficacy was much higher (96%) especially in the evaluation of T1-T4 stage tumors. However, 70% efficacy in T2 tumor and 84% efficacy in T3 tumor were detected. Three patients with histologically confirmed T2 were evaluated as T3 by ERUS, and a patient with histologically confirmed T3 was evaluated as T4 by ERUS.

One of the most important limitations of ultrasonographic examinations is that they cannot clearly distinguish between a malignant and inflammatory process. Both are monitored as irregular bordered and hypoechoic (15). It is considered that the inaccuracy rate of ultrasonography decreases in T1 lesions when the presence of inflammation is less than in other stages and the hypoechogenic structure of the submucosa layer is clear. In addition, in T4 lesions, disappearance of borders between tissues, depending on invasion in neighboring organs, decreases the inaccuracy rate of ultrasonography. Especially in T3 stages, deformation of the hypoechogenic structure of adipose tissue planes during both inflammation and malignant invasion causes a decrease in diagnostic efficacy. Lymph node metastasis is an essential symptom of lymphovascular invasion. Lymphovascular invasion is related to disease recurrence and poor prognosis (18). In the detection of the characteristics (malignant or benign) of lymph nodes by CT, MRI, and ERUS, structure, size and echogenicity are considered. Most investigators consider a lymph node metastatic if it has round and discrete margins, is uniformly hypoechoic, or has the same echoic pattern as a primary tumor (19,20). However, reactive or fibrotic lymph nodes sometimes may appear hypoechoic, leading to possible confusion between these nodes and typical metastatic lymph nodes. This problem has not yet been solved in standard EUS examinations. 75.8% efficacy and 2.84 likelihood ratio in N stage were detected in a meta-analysis by Srinivas and his colleagues (9),

in which standard 2D rectal US and ERUS studies were evaluated.

In this study, the presence of lymph nodes was defined as round hypoechoic lymph nodes larger than 5 mm. The blood flow pattern in lymph nodes was not evaluated. Of the patients detected with lymph nodes by EUS, 87.5% were detected with lymph nodes histologically. Of the patients detected with malignant lymph nodes by EUS, 66.6% were detected with malignant lymph nodes histologically. However, 43% had reactive lymph nodes. While efficacy in detection of lymph nodes was quite high using standard 2D EUS, efficacy in determination of the characteristics of the lymph nodes was low.

In studies in which cervical lymph nodes were evaluated, it was indicated that peripheral blood supply shows malignant character better and central blood supply shows benign character better with a large hypoechoic round appearance (21,22). As scanning by echo-enhancement was not used in this study, the blood flow pattern in lymph nodes

was not evaluated. US elastography, recently introduced, can evaluate the severity of lymph nodes and estimate their characteristics.

In the study of Giovannini *et al.* (23), sensitivity of US elastography in the detection of malignant lymph nodes was observed as 91.8%. It was also found that lymphovascular invasion was associated closely with advanced primary tumors (T3–T4) and lymph node metastases. In Kim *et al.*'s (19) study by 3D EUS, similar results were obtained.

In conclusion, in this study, it was detected that ERUS is an effective and reliable method in the detection of the depth of invasion of rectal tumors (T staging) and local lymph nodes; however, it is not reliable enough to determine the characteristics of lymph nodes. Moreover, it was noticed that tumor size, aperture of the lumen, and location of the tumor decreased the number of patients who were able to be staged. It is considered that efficacy of ERUS in local staging of tumors may be increased using some supporters such as elastography and mini-probe.

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