



Contribution of Endorectal Ultrasound, Magnetic Resonance Imaging and Positron Emission Tomography to Operation Strategy in Rectal Cancer

Endorektal Ultrasonografi, Manyetik Rezonans Görüntüleme ve Pozitron Emisyon Tomografisinin Rektum Kanserinde Ameliyat Stratejisine Katkıları

Yurdakul Deniz Fırat¹, Gökhan Çipe², Coşkun Çakır³, Hüseyin Kazım Bektaşoğlu⁴, Sinan Arıcı¹, Mahmut Müslümanoğlu⁵

¹University of Health Sciences Turkey, Bursa Higher Specialization Training and Research Hospital, Clinic of General Surgery, Bursa, Turkey

²Memorial Hospital, Clinic of General Surgery, İstanbul, Turkey

³University of Health Sciences Turkey, İstanbul Training and Research Hospital, Clinic of General Surgery, İstanbul, Turkey

⁴Bezmialem Vakıf University Faculty of Medicine, Department of General Surgery, İstanbul, Turkey

⁵İstanbul University Faculty of Medicine, Department of General Surgery, İstanbul, Turkey

Abstract

Objective: Colorectal cancer is the most common type of cancer in the gastrointestinal tract. Preoperative staging is important for applying appropriate treatment modalities. The role of endorectal ultrasonography (ERUS), magnetic resonance imaging (MRI) and positron emission-computed tomography (PET-CT) in rectal cancer patients was evaluated.

Method: In this study, between October 2010-April 2012, 30 patients who were diagnosed as rectal cancer clinically and histopathologically were evaluated with ERUS, MRI and PET-CT preoperatively and results were compared with histopathologic findings.

Results: Between October 2010-April 2012, 30 patients who were diagnosed as rectal cancer with biopsy in Bezmialem University Medical Faculty Hospital General Surgery Department were included in this study [20 male (66.6%), 10 female (33.3%) and their ages are 38-75 years old, 21 of them received neoadjuvant treatment and 9 of them did not received]. All patients were evaluated with MRI, ERUS and PET-CT preoperatively. Rectal cancer patients who are primarily operated from rectal adenocarcinoma were included in this study. For T staging, preoperative MRI, ERUS and PET-CT staged 9 (31%), 12 (41%) and 12 (40%) of 30 patients accurately, respectively. For N staging, preoperative MRI, ERUS and PET-CT staged 15 (51%), 16 (55.1%) and 17 (56.6%) of 30 patients accurately, respectively. In comparison to other modalities, PET-

Öz

Amaç: Gastrointestinal sistemin en sık görülen kanserleri kolorektal kanserlerdir. Özellikle rektum kanserli hastalarda operasyon öncesi evreleme büyük önem taşımaktadır. Bunun sebebi ise evrelemeye göre tedavi yönetimindeki değişik olanakların hasta için tercih edilebilmesidir. Evreleme hasta için uygun tedavi yönetimini planlamaya yardımcı olmaktadır. Rektum kanserli hastaların endorektal ultrasonografi (ERUS), manyetik rezonans görüntüleme (MRG) ve pozitron emisyonu-bilgisayarlı tomografi (PET-BT) ile yapılan değerlendirilmelerinin ameliyat stratejisine etkileri araştırıldı.

Yöntem: Bu çalışmada; klinik ve histopatolojik olarak Ekim 2010-Nisan 2012 arasında rektum kanseri tanısı almış 30 olgu preoperatif olarak ERUS, MRG ve PET-BT ile değerlendirilmiş, sonuçlar histopatolojik bulgularla karşılaştırılmıştır.

Bulgular: Ekim 2010-Nisan 2012 tarihleri arasında Bezmialem Üniversitesi Tıp Fakültesi Hastanesi Genel Cerrahi Anabilim Dalında biyopsi ile rektum kanseri tanısı alan 30 hasta çalışmaya alınmıştır. Yirmi hasta erkek (%66,6), 10 hasta kadın (%33,3) idi. Hastaların yaşları 38 ile 78 arasındaydı, 21 hasta neoadjuvan tedavi gördü. Dokuz hasta neoadjuvan tedavi görmedi. Hastaların tümüne preoperatif MRG, PET-BT ve ERUS yapılmıştır. Çalışmaya opere edilen primer rektum adenokanserli hastalar dahil edildi. T evresini değerlendirmede MRG, ERUS ve PET-BT 30



Address for Correspondence: Sinan Arıcı, University of Health Sciences Turkey, Bursa Higher Specialization Training and Research Hospital, Clinic of General Surgery, Bursa, Turkey

E-mail: sinan_arici@yahoo.com **ORCID:** orcid.org/0000-0002-7986-3874 **Received:** 21.08.2020 **Accepted:** 30.11.2020

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Abstract

CT did not yield a significant difference in staging and did not change operation strategy. PET-CT detected distant metastasis in 3 patients. One of them was liver and two of them were lung metastasis. Biopsies from mass predicted as lung metastasis did not result as metastasis. PET-CT has high rates of false positivity to detect distant metastasis. In statistical analysis, significant p-values for evaluation could not be obtained.

Conclusion: Efficacy of routine use of PET-CT on staging, evaluation of T, N and extramesorectal spread could not be shown.

Keywords: Imaging methods, PET-CT, rectum cancer

Öz

hastadan sırasıyla 9 (%31), 12 (%41) ve 12 (%40) hastada doğru evreledi. N evresini değerlendirmede MRG, ERUS ve PET-BT 30 hastadan sırasıyla 15 (%51), 16 (%55,1) ve 17 (%56,6) hastada doğru evreledi. PET-BT'nin diğer görüntüleme yöntemleri ile karşılaştırıldığında evrelemede anlamlı bir farklılık oluşturmadığı ve ameliyat stratejisini değiştirmedeği görülmüştür. PET-BT ile üç hastada uzak metastaz saptandı. Bunlardan biri karaciğer, ikisi akciğer metastazı idi. Akciğer metastazı düşünülen kitlelerden alınan biyopsilerde metastaz saptanmadı. PET-BT'nin uzak metastazı saptamada yüksek yanlış pozitiflik oranı olduğu görülmüştür. İstatiksel analizde değerlendirme sonucu için anlamlı p-değerleri saptanmamıştır.

Sonuç: PET-BT'nin rektum kanseri evrelemesinde T, N ve ekstremitözektal yayılım değerlendirilmesinde rutin olarak kullanılmasının faydası gösterilememiştir.

Anahtar kelimeler: Görüntüleme yöntemleri, PET-BT, rektum kanseri

Introduction

The most common cancer of the gastrointestinal tract is colorectal cancer. Colorectal cancer is the fourth most common type of cancer (1). Preoperative staging is important in patients with rectal cancer since treatment is planned according to the management of the patient's initial application stage. The main purpose of treatment management is to prolong survival, to prevent distant metastasis, and to reduce local recurrence. Physical examination, endoscopic examination, double contrast colon radiography and histopathological methods are used in the diagnosis of rectal cancer. With these methods, rectal cancers can be diagnosed, but distant metastasis, bowel wall involvement, depth and lymph node spread cannot be determined for staging of the disease (2,3). A variety of imaging methods are used to investigate tumor localization and distant organ involvement in patients with histopathological diagnosis of rectal cancer.

In this study, 30 patients with clinically and histopathologically proved diagnosis of rectal cancer were staged by ERUS, MRI and PET-CT. These methods were compared with postoperative histopathological staging and their role in the diagnosis and staging of rectal cancer and the determination of surgical strategy were evaluated.

Materials and Methods

A prospective randomized clinical trial was planned and local ethics committee approval was obtained. All patients included in the study were informed succinctly and informed consent forms were signed. Between October 2010 and April 2012, a total of 42 patients with a diagnosis of rectal cancer by endoscopic biopsy were assigned to

the Department of General Surgery, Bezmialem Vakıf University Medical Faculty, and 30 patients were randomly included in the study (20 males, 10 females, age range: 38-78 years, mean age: 60 years). Patients who had recurrence, an additional pathology that would prevent surgery or who did not accept the operation were excluded from the study. After diagnosis, all patients were staged with pelvic MRI, PET-CT and ERUS imaging. Twenty-one (70%) patients underwent surgery after neoadjuvant therapy and 9 (30%) were treated with primary surgery. In patients receiving neoadjuvant therapy, after 4-6 weeks of treatment, regression levels were evaluated by MRI and ERUS weekly according to Dworak regression staging (4).

Statistical Analysis

Statistical analysis of this study was done using GraphPad Prisma V.3 program. In-group and inter-group evaluations other than descriptive methods (mean, standard deviation, median) were performed through the Fisher Exact test, Friedman chi-square test, and Wilcoxon test with Bonferoni correction.

Results

Examination by PET-CT: One patient had T1, 13 had T2, 12 had T3, 3 had T4, 22 had N0 and 8 had N1. PET-CT showed rectal cancers in all patients except one patient. For T staging: it gave the accurate staging in 12 patients (40%), down stage in 10 patients (33.3%) and up stage in 8 (26.6%) patients. For N staging: it gave the accurate staging in 17 patients (56.6%), up staging (36.6%) in 11 patients, and down staging in 6 patients (20%). PET-CT showed distant metastasis in 3 patients. Two of these were in the lungs and one in the liver. Lung biopsies of patients with

lung metastasis were benign in PET-CT imaging. Liver metastasectomy was evaluated correctly. The PET-CT imaging technique correctly staged 1 (33%) patient with distant metastasis.

Examination by ERUS: Five patients were classified as T0, 3 as T1, 7 as T2, 13 as T3 and 1 as T4. ERUS imaging was not performed for one post-neoadjuvant patient, so this patient was excluded from the evaluation. The ERUS imaging technique gave 12 (41%) accurate staging, 6 (20%) over staging and 11 (38%) down staging for the T parameter. In N staging with ERUS: Twenty-nine patients (55%) were N0 and 13 (44%) were N1. The ERUS imaging technique gave 16 (55%) accurate staging, 6 (20%) over staging and 7 (24%) down staging for the N parameter. Three patients had lateral pelvic lymph nodes. One of these patients underwent lateral pelvic lymph node dissection and all four resected lymph nodes were negative.

Examination by MRI: 3 (10%) patients were T1, 17 (58.6%) patients were T2, 9 (31%) patients were T3 and 0 patient was T4. One post-neoadjuvant patient was excluded because MRI was not performed. MRI technique gave 9 (31%) accurate staging, 16 (55%) down staging and 4 (13%) over staging for the T parameter. Twelve (41%) patients had N0, 14 (48%) had N1 and 3 (10%) had N2. With MRI, 15 (51.7%) patients were staged correctly, 4 (13.7%) were down staged and 10 (34.4%) patients were over staged. On MRI imaging, 4 patients had lateral pelvic lymph nodes. Two patients underwent lateral pelvic lymph node excision. From both of these patients, 15 lymph nodes were removed and all were negative. In our study, abdominal MRI imaging detected that only one of 30 patients had metastasis in the liver. The biopsy from this metastatic mass was malignant. The accurate staging numbers obtained for all three imaging techniques are presented in Table 1.

Histopathological examination: 1 (0.3%) pT1, 11 (36%) pT2, 16 (53.3%) pT3 and 2 (0.6%) pT4. 18 (60%) pN0, 10 (33.3%) pN1, 1 (3.3%) pN2 and 1 (3.3%) pN3.

In statistical analysis, it was seen that all three imaging

Table 1. Accurate staging distribution of imaging modalities according to TNM parameters

	MRI	PET-CT	ERUS
T	9 (31%)	12 (40%)	12 (41%)
N	15 (51.7%)	17 (56.6%)	16 (55%)
M	1 (3.4%)	1 (3.3%)	-

PET-CT: Positron emission computed tomography, ERUS: Endorectal ultrasonography, MR: Magnetic resonance

techniques did not show any significant difference for T, N and M parameters (Table 2). For 21 patients who received neoadjuvant therapy, changes were observed in 13 patients in the T phase before and after neoadjuvant therapy with MRI and ERUS imaging techniques. The results obtained for both imaging techniques were statistically significant (p=0.001 for MRI and p=0.001 for ERUS).

When neoadjuvant therapy and MRI/ERUS imaging tests were compared in patients with differences in T stage, significant differences were observed in both imaging techniques and this suggests that both imaging techniques did not provide predictions for T stage change.

Discussion

Approximately 10% of patients have local recurrence of rectal cancer in modern surgery with adjuvant and neoadjuvant treatments (5). Nevertheless, today the most important findings that predict the possibility of recurrence of the tumor are the stage of the tumor, the penetration of the bowel wall and lymph node involvement during diagnosis (6). It is controversial that local recurrence has no effect on survival, but it decreases the quality of life significantly. Preoperative staging of the rectal tumor and planning of the treatment are therefore essential. Although there are different approaches, the accepted methods for staging are ERUS, pelvic MRI and CT.

In many studies, the success of T staging with ERUS has been reported as 81-94%, with an over staging rate of 10% and a down staging rate of 5% (7-9). The most important clinical condition that negatively affects the accuracy of ERUS in rectal lesions is stenotic tumors (10,11). With ERUS imaging, it may be difficult to differentiate very early stage cancer, such as adenoma, which only affects the mucosa. Staging of adenoma and T1 tumors that have previously undergone ERUS may also lead to mistakes. The most common cause of upper staging is the formation of inflammatory cell accumulations around the tumor, desmoplastic changes and hypervascularity

Table 2. p-values and statistical analysis of the accuracy of diagnostic tests (p<0.05 was considered statistically significant. Chi-square test for T and N stages, Fisher Exact test for stage M)

	T	N	M
MRI vs PET	0.47	0.70	1.00
MRI vs ERUS	0.41	0.79	-
ERUS vs PET-CT	0.91	0.91	-

PET-CT: Positron emission computed tomography, ERUS: Endorectal ultrasonography, MRI: Magnetic resonance imaging

by inducing a tumor, causing the appearance of tumor invasion in ERUS. In particular, pT2 tumors are staged as uT3 (12). In our study, pT2 was detected in 2 (10%) of 10 patients who were determined as uT3 after neoadjuvant treatment. In this study, 12 of 30 patients (41%) received accurate staging in T invasion, 6 patients (20%) resulted in over staging and down staging in 11 patients (38%) was observed. Accuracy rates in our study were lower than in the literature series.

The biggest problem with ERUS is the presence of false positive metastatic lymph nodes. The appearance of a large reactive lymph node can easily be considered malignant and may be omitted in imaging for a small metastatic lymph node (13-15). In our study, with ERUS, pathological lymph node was detected in 13 patients (44%). ERUS yielded accurate lymph node staging for 16 (55%) patients. These results show that there are deficiencies in the visualization of lymph nodes and the correlation of the displayed lymph nodes with pathology is needed.

The accuracy rates reported in MRI and T staging varied between 67% and 88% (16,17). The superiority of MRI to ERUS is the capability of viewing wider localizations. The advantage of MRI is that it can display mesorectum, mesorectal fascia and lymph nodes in perirectal fatty tissue (18-20). In our study, T staging was accurate in 31% of cases. This suggests that results of some of the patients are associated with neoadjuvant therapy. The efficacy of MRI in the evaluation of mesorectal fascia is high and the accuracy of MRI in mesorectal fascia involvement is between 91% and 100% in various studies (21,22). False positivity is the biggest problem in MRI lymph node evaluation. The reason is that large, malignant lymph nodes may cause reactive hyperplasia, or microscopic tumor invasion is detected in a small, benign lymph node. In the literature, accuracy rates in lymph node involvement with MRI vary between 43% and 85% (21-23). MRI technique performed 15 (51.7%) accurate staging, 4 (13.7%) down staging and 10 (34.4%) over staging for the N parameter.

Colorectal cancers are the leading tumors in which distant metastasis staging is important. The imaging of metastasis and the primary tumor both can be made with PET, but navigation of the tumor can be achieved by simultaneous tomography (23-25). PET-CT could not provide information about the degree of infiltration of the rectal wall because of the limited statical resolution. For this reason, PET-CT is not recommended for T staging. We could not find an appropriate study for the evaluation

of T and N staging. PET-CT showed distant metastasis in three patients. Two of the suspected metastatic lesions in PET-CT were detected in the lungs. Biopsies were performed from the lesions and found to be benign nodules. Metastatic lesion was detected in the liver and metastasectomy was performed in one patient. PET-CT gave false positivity in 2 out of 3 patients (66.6%) for distant organ metastasis. The only isolated liver metastasis in one patient did not change our treatment strategy. In the literature, PET-CT analysis changed the staging of 17% of patients and differentiated the treatment management (26-28).

Another 37 patients in the lower rectum tumor study group changed the treatment scheme in 27% of patients (29). In our study, although the treatment scheme was not changed, biopsy was performed for 2 patients and it was a waste of time for the patient's treatment.

Conclusion

In this study, the efficacy of ERUS, MRI and PET-CT imaging techniques in the evaluation of locoregional dissemination was investigated in determining the surgical strategy of rectum cancer. PET-CT has a high rate of false positivity in detecting the presence of distant metastases. MRI and ERUS were found to be reliable in the evaluation of T stage in patients undergoing neoadjuvant therapy. In respect to this, our study has a limited patient number and should be supported by further clinical studies.

Ethics

Ethics Committee Approval: A prospective randomized clinical trial was planned and Local Ethics Committee approval was obtained (no: B.30.2.BAV.0.05.05/231, date: 01.02.2012).

Informed Consent: All patients included in the study were informed succinctly and informed consent forms were signed.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Development of Study Idea: M.M., Y.D.F., G.Ç., Design of the Study: M.M., Y.D.F., C.Ç., Data Acquisition and Process: M.M., Y.D.F., G.Ç., Data Analysis and Interpretation: G.Ç., C.Ç., H.K.B., Literature Review: C.Ç., H.K.B., S.A., Manuscript Writing: H.K.B., S.A., Manuscript Review and revision: S.A., Y.D.F.

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