Importance of positron emission tomography-computed tomography (PET-CT) examination in rectal cancer staging - initial clinical experience

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ABSTRACT

Aim Accurate preoperative staging is essential in determining optimal therapeutic procedures and planning for individual patients. Advances in imaging technology have raised interest in the potential role of positron emission tomography-computed tomography (PET-CT) examination for staging of rectal cancer. The primary end point of the study was the correct classification of the tumor-node-metastases (TNM) tumor stage using whole-body PET-CT examination.

Methods This prospective study was performed from October 2011 to October 2012. Patients with histopathological diagnosis of rectal cancer after biopsy underwent PET-CT before surgical treatment and TNM staging. Twenty patients who fulfilled inclusion criteria were included in the study. All of the patients were operated and histopathology served as the standard of reference.

Results There was no statistical significance in T staging comparing PET-CT and histopathological staging, according to the Monte Carlo simulation (p=0.066). Also, there was no statistical significance between two methods in mesorectal fascia involvement analysis (p=1). There was statistical difference between PET-CT and histopathological staging. Sensitivity of the PET-CT for N staging was 86.7% and it was higher than for the histopathology. Two patients showed liver metastases.

Conclusion Positron emission tomography-computed tomography examination could play an important role in the initial staging for the rectal cancer. Good patient selection for preoperative chemoradiotherapy ensures survival benefit. Avoidance of unnecessary therapeutic procedures allows an acceptable quality of patient’s life.

Key words: imaging, stage, histopathology
INTRODUCTION

Visualization of the glucose metabolism was an important milestone in cancer diagnostic— for the staging, recurrence detection and treatment response measurement (chemotherapy or radiotherapy) (1-3). Positron emission tomography-computed tomography (PET-CT) is hybrid imaging which has played an important role in the oncological patients staging and recurrence detection during the past decade (3). The most widely used imaging tracer is 18F-fluorodeoxyglucose (18F-FDG) (3,4). 18F-fluorodeoxyglucose activity is high where there is intensive metabolic uptake, so physiologically high activity is visualized during bowel peristaltic movement, urinary excretion, and tissue reparation after injury (4). Pathological 18F-FDG accumulation is seen in inflammatory and malignant diseases. Anatomical imaging visualize a lesion when it reaches measurable size. Positron emission tomography provides lesion visualization based on metabolic uptake, which is size-independent (5-7).

Prospective randomized trials proved that preoperative chemoradiotherapy increases 5-year survival rate in patients suffering from rectal cancer (8-11). Therefore, initial tumor and nodal staging is essential in patient selection for preoperative chemoradiotherapy.

Tumor-node-metastases (TNM) classification is most often used in oncologic staging (2). Positron emission tomography-computed tomography can accurately define N and M rectal cancer stage (N presents nodal involvement, M presents distant metastases). Local tumor extension (T) is not clearly defined by PET-CT imaging and there are difficulties to differentiate T2 from T3 stage. Positron emission tomography-computed tomography could play an essential role in initial rectal cancer staging and could provide the best therapy decision— the most accurate surgical approach and chemoradiotherapy protocol (12-14).

The goal of this study was to answer the question whether PET-CT has an importance in rectal cancer staging.

PATIENTS AND METHODS

This prospective study was performed at Oncology institute of Vojvodina and Clinical Center of Vojvodina in the period from October 2011 to October 2012. Inclusion criteria were as follows: the rectal cancer diagnosis had been made for the first time after endoscopy, biopsy and histopathological examination, surgical treatment was indicated, Eastern Cooperative Oncology Group (ECOG) performance status (19) of the patient was 0.1 or 2, there was no surgical treatment of patient in the last 3 months, patients under 70 years of age and patients with no comorbidities, e.g. decompensated cardiovascular or respiratory diseases, unregulated diabetes, acute renal failure or acute infective diseases. Patients who had undergone surgery during the past 3 months in the period before PET-CT examination or chemotherapy and radiotherapy during the past 6 months were excluded from the study. Ethical Committee of the Oncology Institute of Vojvodina and Ethical Committee of the School of Medicine of Novi Sad approved this investigation by a written consent.

Having received the written consent, all patients underwent PET-CT examination prior to surgery. All patients were imaged as whole body imaging (from the skull base to the proximal femur bone) 120 min after intravenous administration of the 18F-fluorodeoxyglucose. Oral contrast agent (7.5ml) was given 2 hours before the administration. Imaging protocol was as follows: CT topography, low-dose CT (70mA) and 18FDG PET. SUV max value was used for FDG activity measurement. The CT data were used for attenuation correction of PET emission images. Analyzing PET-CT images, staging was performed for each patient according to the TNM classification. Tumor extension out of the rectal wall was investigated, mesorectal fascia involvement including FDG avid lymph nodes, their number and localization. After PET-CT examination, patients underwent surgery. Total mesorectal excision, amputation of the rectum, anterior rectal resection and rectosigmoid resection were performed. Lymphadenectomy was performed for each patient following the recommended 12-nodes standard. Liver metastases were resected. Histopathological examination was routinely performed and pathologists defined the stages T (T1,T2,T3,T4), N (N1,N2) and M (M0,M1,MX). Stages defined by PET-CT were correlated with histopathological rectal cancer stages. Descriptive techniques were used for frequency analyses and for calculating sensitivity. For significance calculation of
the contingency tables $X^2$ test was used. Monte Carlo simulation and Fisher’s exact test were also used for the table fields where number of cases was smaller than demanded.

**RESULTS**

Twenty patients (10 males and 10 females) were identified. Mean age was 62.89 years. Four (22.2%) patients had T2 stage, twelve (66.7%) T3 and two (11.15%) T4 stage (Table 1). The average tumor diameter measured as the FDG activity diameter was 5.57 cm (2.5-13 cm range). The average SUV max value of the primary tumor was 26.06 gm/ml. Of the 20 patients, six (33.3%) had N0 stage, seven (38.9%) N1 stage and five (27.8%) N2 stage (Table 1). $^{18}$F-fluorodeoxyglucose avid lymph nodes were localized in presacral, perirectal and inguinal regions. The average diameter of the lymph node measured as the FDG activity diameter was 2.092 cm. The average SUV max value of the lymph nodes was 5.73 gm/ml. Two patients (10%) had liver metastases detected on the PET-CT examination. Diameters were 1.2 and 2.7 cm and SUV max values 3.99 and 5.55 gm/ml, respectively. After surgery and histopathological TNM staging, the results showed that there was no statistical significance in T staging comparing PET-CT and histopathological staging, according to the Monte Carlo simulation (p=.066). Also, there was no statistical significance between two methods in mesorectal fascia involvement analysis, according to the Fisher’s exact test (p=1). There was statistical difference between PET-CT and histopathological staging. Sensitivity of the PET-CT for N staging was 86.7% and it was higher than for the histopathology. By analyzing lymph node size our results showed negative correlation of high significance. Lymph node diameters measured on the PET-CT images were much bigger than by the histopathology (T-test). Positron emission tomography-computed tomography changes in therapy management were noted in 58.8% of the patients.

**DISCUSSION**

Initial staging for rectal cancer is of incremental value. Our results show that PET-CT is as accurate as the histopathological examination for T staging and mesorectal fascia involvement. There is no statistical significance between these two methods. Transrectal ultrasound was in use for rectal cancer evaluation during the past decade. It is highly accurate for the T1 and T2 stages but for the T3 and T4 stages MR imaging is a superior technique (10). Gearhart et al compared preoperative staging performed with TRUS, CT and PET-CT and histopathology was the reference standard (5). In this study, after PET-CT examination the change in therapeutic management occurred in 27% of the patients. Most studies emphasize that PET-CT is limited for the T staging (6). MERCURY study has shown that MR imaging is accurate in the evaluation of the extramural tumor extension in 95.6% of the patients (11). However, some studies indicated that PET-CT could not be replaced with MR imaging in the rectal cancer evaluation (17). It is well known that in defining IA rectal cancer stage, all the parameters must be included - T stage, mesorectal fascia penetration and N stage. MR imaging is in that point of view accurate in only 40% of the patients (17). Other studies claim that MR is a superior diagnostic tool for this purpose, because PET has low spatial resolution (18). Further randomized controlled trials are needed to estimate cost-effectiveness of those two imaging procedures.

In this study, lymph node diameters were much bigger at the PET-CT examination compared with histopathological analysis. This fact could be connected with histopathological preparation. Particularly, during the process of sample preparation, perilymphatic tissue was extracted, but it contained malignant cells that showed FDG activity at the PET-CT examination. This is very important because it implicates that whole lymph node along with perilymphatic tissue should be included in the radiotherapy field for the treatment.

Magnetic resonance nowadays presents the golden standard for rectal cancer staging (11) but PET-CT

<table>
<thead>
<tr>
<th>Stage</th>
<th>No (%) of patients</th>
<th>Cumulative percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>T2</td>
<td>4 (22.2)</td>
<td>22.2</td>
</tr>
<tr>
<td>T3</td>
<td>12 (66.7)</td>
<td>88.9</td>
</tr>
<tr>
<td>T4</td>
<td>2 (11.1)</td>
<td>100</td>
</tr>
<tr>
<td>N0</td>
<td>6 (33.3)</td>
<td>33.3</td>
</tr>
<tr>
<td>N1</td>
<td>7 (38.9)</td>
<td>72.2</td>
</tr>
<tr>
<td>N2</td>
<td>5 (27.8)</td>
<td>100</td>
</tr>
</tbody>
</table>

*T2, the cancer has grown through submucosa and extends into the muscularis propria; T3, the cancer has grown through the muscularis propria and into the outermost layers with extension to the immediately adjacent structures; T4, the cancer has grown through the wall of the colon or rectum and is attached to or invades into nearby tissues or organs; N0, no metastasis in nearby lymph nodes; N1, cancer cells are found in or near 1 to 3 nearby lymph nodes; N2, cancer cells are found in 4 or more nearby lymph nodes

Table 1. Frequencies of the T and N stages in the patient’s sample*
is whole body imaging so it can detect liver and lung metastases which affects the therapy selection. Another advantage of the PET-CT over MR is pointed out at the lymph node evaluation. Our study has shown PET-CT sensitivity of 86.7% for the lymph node detection which is similar to the results from the literature (16), and also that therapy modality would have been changed in 58.8% of the patients if every patient had undergone PET-CT examination before surgery. In the literature, the difference in staging occurs in 31-53.8% of the patients after PET-CT examination, compared with CT and MR imaging (12,20). In 17-29% of the patients therapeutic modality has been changed (5). This study implicates that PET-CT should be incorporated in the standard diagnostic protocol for the rectal cancer assessment.

Rectal cancer management requires the best approach to each patient and the best diagnostic and therapeutic option from case-to- case. PET-CT examination could play an important role in the initial staging for the rectal cancer and it provides accurate TNM classification.

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**TRANSPARENCY DECLARATIONS**

Competing interests: none to declare.
Značaj pozitronske emisione tomografije-kompjuterizovane tomografije (PET-CT) u određivanju stadija karcinoma rektuma – prvi klinički rezultati

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SAŽETAK

Cilj Napretkom tehnologije u radiologiji nametnulo se pitanje kakva je vrednost pozitronske emisione tomografije-kompjuterizovane tomografije (PET-CT) u određivanju stadija karcinoma rektuma po tumor-node-metastases (TNM) klasifikaciji.


Rezultati Nakon operacije i patohistološkog određivanja stadija po TNM klasifikaciji, rezultati su pokazali da, na osnovu Monte Karlo simulacije, nije postojala statistički značajna razlika između stadija određenih PET-CT pregledom i patohistološki (p=.066). Takođe, nije ustanovljena statistički značajna razlika između dve navedene metode u proceni penetracije mezorektalne fascije (p=1). U analizi N stadija, koji se odnosi na limfne čvorove, ustanovljena je statistički značajna razlika između PET-CT pregleda i patohistološke analize. Senzitivnost PET-CT pregleda u određivanju N stadija je 86,7%, te je ona bila veća u odnosu na patohistološki pregled. Kod dva pacijenta su dijagnostikovane metastaze na jetri.

Zaključak PET-CT pregled bi mogao da zauzme značajnu ulogu u inicijalnom određivanju stadija karcinoma rektuma. Bolja selekcija pacijenata za preoperativnu hemioradioterapiju omogućuje korist u preživljavanju pacijenata. Izbegavanje nepotrebnih terapijskih procedura obezbeđuje prihvatljiviji kvalitet života za bolesnike.

Ključne riječi: pregled, stadij, patohistološki