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PROGNOSTIC PARAMETERS IN RECURRENT COLORECTAL CANCER: ROLE OF CONTROL OR RESTAGING FDG-PET/CT

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Running head: FDG-PET/CT in recurrent colorectal cancer

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Abstract

**Background/Aim:** Colorectal cancer (CRC) ranks the third most frequent cancer in the world. Approximately 40% of the disease recur after surgical resection. Determination of predictive parameters for recurrence may aid in stratification of patients and contribute to patient management. There are still very few studies which sought factors to predict the recurrence of CRC. The aim of the study was to examine the predefined risk factors in metastatic development and evaluate clinical significance of 18F-fluorodeoxyglucose uptake.

**Methods:** The study was conducted with 56 patients for whom FDG-PET/CT was requested for the suspicious recurrence or metastasis by routine conventional screening tests. 33 patients in whom recurrence/metastases were established with final histopathologic diagnosis formed malignant group, 23 patients benign group. Risk factors of age, serum CEA and Ca 19.9 levels, SUVmax, tumor size (TS), CT/MRI findings, sex, primary tumor localization (PTL), lymphovascular invasion (LVI), perineural invasion (PNI), initial neoadjuvant therapy (INAT), initial metastatic lymph node excision (ILNM), stage, tumor differentiation (DIF) were compared between these groups.

**Results:** CEA, Ca 19.9, SUVmax, TS, PNI, ILNM, FDGP, CTP and DIF were found statistically significant by univariate analysis. After multivariate analysis, SUVmax and ILNM remained as the main risk parameters impacting metastasis/recurrence. Mean SUVmax was 7.25 in benign group, while it was 11.7 in malignant group (p=0.019). ILNM was present in 66.5% of malignant group, 30.5% in benign group (p=0.015). For an estimated cutoff value of 6.3 and 12.5 on ROC curve, the calculated specificities were 61% and 87%, respectively.
**Conclusion:** ILNM and SUVmax are the main risk factors in recurrent colorectal cancer and these patients must be followed up carefully. FDG-PET/CT is very sensitive for the detection of recurrence/metastasis and SUVmax appears to improve its specificity.

**Keywords:** FDG-PET/CT, recurrent colorectal cancer, risk factors, metabolic tumor parameters.
Introduction

Colorectal cancer (CRC) ranks the third most frequent cancer and it was the fourth most frequent cause of cancer-related death in the world. Approximately 40% of the disease recur after surgical resection of the primary tumor in two years (1). There are some well-known predefined clinicopathologic risk factors for recurrent/metastatic CRC. These are age, serum CEA and Ca 19.9 levels, tumor depth (invasion), maximum standardized uptake value (SUVmax) on FDG-PET/CT, tumor size (TS), CT/MRI findings, sex, primary tumor localization (PTL), lymphovascular invasion (LVI), perineural invasion (PNI), initial neoadjuvant therapy (INAT), initial metastatic lymph node excision at primary surgery (ILNM), stage, type of surgery, localization of metastasis (organ), cytogenetic factors, tumor differentiation (DIF). Detecting the recurrence is mandatory for convenient therapy. Different laboratory and imaging tests are handled to identify recurrent and/or metastatic CRC. Most guidelines recommend thoracoabdominal CT, routine serial carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (Ca 19-9) assays to monitor the disease (2).

CEA is expressed by a lot of epithelial tumors and its serum levels may rise in non-malignant disorders (3). Nearly 70% of patients with CRC display an elevated CEA level at the time of diagnosis. This fact made it a routine monitoring marker for the disease recurrence (4). Unfortunately, latest meta-analysis studies have declared conflicts about its utility in the detection of recurrent disease. They are stating roundly sensitivities of 65% and specificities of 90% that can be considered poor for a biomarker (5). Ca 19.9 assays have also a poor performance. It has been reported that Ca 19-9 was expressed only in 20-40% of metastatic CRC (6).
Imaging acts the key role in postoperative assessment of metastatic disease. Molecular imaging with 18F-fluorodeoxyglucose positron emission tomography (FDG-PET) combined with computed tomography (CT) is the most recent modality for this purpose (7). The main limitation of CT and other morphological imaging techniques evaluating the recurrence of all types of cancer like CRC is size of the lesion and/or distortion of normal anatomic structures. FDG-PET/CT accomplish this deficit by the capability to show recurrent CRC as in many other cancers, through pathologically increased tumor metabolism before the appearance of morphological changes (8). As a glucose analogue, FDG reflects increased glucose consumption of cancer cells and a great majority of CRC are FDG-avid. FDG-PET/CT has been used for primary staging, evaluation of treatment response and restaging in CRC just like in many other cancers. It is more sensitive than conventional tests in patients with suspected recurrence and/or metastasis. But it has some intrinsic limitations. Inflammatory pathologies, fibrosis or edema following irradiation and/or surgery may cause increased 18F-FDG uptake (9,10).

There are still very few studies which sought factors to predict the recurrence of CRC. The goal of this study is to examine the predefined risk factors in metastatic development and evaluate clinical significance of 18F-fluorodeoxyglucose uptake on FDG-PET/CT during the follow-up after primary curative surgery and/or chemoradiotherapy for recurrence in patients with CRC.

**Methods**

This retrospective cohort study was conducted with 56 patients in nuclear medicine and general surgery departments of a tertiary health care hospital between 2009 and 2016. Inclusion criteria were as follows: histopathologically established diagnosis of CRC by
surgical specimen after primary surgery, pathologic FDG uptake on control (evaluation of treatment response) or restaging FDG-PET/CT requested for the suspicious recurrence or metastases by routine conventional screening tests in the follow-up, confirmation of all these abnormal uptakes by colonoscopy or histopathology. All cases were treated by surgery and/or chemoradiotherapy. The neoadjuvant chemotherapy was administered to patients 6 weeks before the primary surgery and consisted of 5-fluorouracil. The files of the patients were retrieved from the archive and looked over retrospectively.

We evaluated the lesions on FDG-PET/CT in 56 patients. Indications for FDG-PET/CT were suspicion of recurrence/metastasis (32 patients) and treatment response monitoring (24 patients). Elevated CEA and/or Ca 19-9 levels raised the suspicion of recurrence in 11 cases, conventional imaging in 21. All FDG uptakes were confirmed by colonoscopic findings or histopathologically. The reference range of Ca 19.9 was 0-35 U/ml; normal range of CEA was <2.5 ng/ml for nonsmokers, <5 ng/ml for smokers. Tumors were staged by the seventh edition of American Joint Committee on cancer classification. Predefined risk factors for recurrence were age, serum CEA and Ca 19.9 levels, SUVmax, TS. CT/MRI findings, sex, PTL, LVI, PNI, INAT, ILNM, stage, FDG uptake pattern (FDGP), pattern of lesions on CT (CTP), DIF. PTL was classified as distal rectum (4 cm), middle rectum (5-9 cm), rectosigmoid region, sigmoid (descending) colon and cecum-transverse/right colon. DIF was defined as low grade, moderate differentiation, high grade and mucinous component. FDGP was heterogeneous, diffuse or focal. CTP was soft tissue mass, wall thickening or hypodense lesion. 33 patients in whom recurrence/metastasis was established with final histopathologic diagnosis formed malignant group, 23 patients benign group. The above-mentioned parameters were compared between these groups.
**FDG-PET/CT Imaging Protocol**

Patients were hungry at least for 6 hours and their blood glucose levels were obliged to be below 150 mg/dl before the injection of an activity of 370-555 MBq of $^{18}$F-FDG calculated according to patient’s body weight. Images were acquired one hour later with an integrated PET/CT scanner (Discovery 690-GE Healthcare). Unenhanced low dose CT and PET emission data were obtained from mid-thigh to the vertex of the skull in supine position with the arms raised over head. CT data were collected by an automated dose modulation of 120 kVp (maximal 100 mA) with the collimation of 64×0.625 mm, field of view (FOV) of 50 cm, noise index of 20%, reconstruction to images of 0.625 mm transverse pixel size and 3.75 mm slice thickness. PET data acquisition were performed in 3D mode with the scanning period of 2 min per bed position and an axial FOV of 153 mm. The emission data were corrected in a standardized way consisting of random, scatter and attenuation. Iterative reconstruction was done in a matrix size of 256×256 by Fourier rebinning and VUE Point FX [3D] with 3 iterations, 18 subsets).

Two nuclear medicine specialists unaware of patient history interpreted FDG-PET/CT images visually. Focally or heterogeneously increased FDG uptake, diffuse or heterogeneously increased FDG uptake and/or soft tissue mass on CT component, hipodense or nodular lesion on CT with or without FDG uptake, diffuse uptake accompanied by wall thickening, consolidation or ambiguous lesions on CT with or without uptake were supposed as pathologic. SUVmax corrected for body weight were computed by a standard protocol on a dedicated Workstation from the activity at the most intense voxel in three-dimensional tumor region from the transaxial whole-body images on attenuation-corrected PET/CT images. The corresponding CT scan of lesions was framed
as a guideline if their boundaries were difficult to demarcate for the determination of SUVmax.

**Statistical Analysis**

The whole data were analyzed by IBM Corporation Released 2013; IBM SPSS Statistics for Windows, Version 22.0, Armonk, NY:IBM Corporation. Number and percentage values were used for the description of categorical data; mean, median, standart deviation (SD), minimum (min) and maximum (max) values for continuous data. Student’s t test (age) and Mann-Whitney U test (serum CEA and Ca19.9 levels, SUVmax, TS) were performed for categorical variables; Fisher’s exact test (CT/MRI findings) and Chi-square test (sex, PTL,LVI, PNI, INAT, ILNM, stage, FDGP, CTP, DIF) for continuous variables in the univariate analysis. The parameters which were found statistically significant in univariate analysis were processed with multivariate analysis. The variables having a value of p<0.05 were accepted as statistically significant. ROC curve was drawn to evaluate the diagnostic value of SUVmax on recurrent disease. Informed consent was deemed as a retrospective study using records, documents and data of patients referred to our clinic for the test. The study was approved by Our Institutional Review Board Committee.

**Results**

Mean age of the patient population was 58.2±11.1 years (30-89); 27 of them was male (48.2%), 29 female (51.8%). Primary tumor localization was distal rectum (11%), middle rectum (18%), rectosigmoid region (27%), sigmoid colon (16%) and cecum-transverse/right colon (28%). Mean serum Ca19.9 and CEA levels, SUVmax, TS were 229.5 U/ml (MV:8.5, 0.1-5548), 6.56 ng/ml (MV:2.19, 0.3-71), 9.9±6.3 and 34.7±19.7 mm, respectively. The incidence of LVI, PNI, ILNM were 62.5%, 37.5%, 52%, respectively. 55.5% of the patients were treated by INAT. 11% of the cases were at stage I,
27% at stage II, 37% at stage III, 25% at stage IV. 28.5% of the patients had heterogeneous FDG uptake, 25% diffuse uptake, 37.5% focal uptake and 10% no uptake. Soft tissue mass was seen in 50% of the cases, wall thickening in 34%, hypodense lesion in 16% on CT as CTP. 25% of the tumors were low grade, 57% moderately differentiated, 11% high grade and 7% with mucinous component.

CEA, Ca 19.9, SUVmax, TS, PNI, ILNM, FDGP, CTP and DIF were found statistically significant after the procession of all potential risk factors by univariate analysis. Univariate analysis of predefined potential risk factors (except PTL, FDGP, CTP, DIF) impacting on metastasis/recurrence, their mean values and percentages between benign conditions and malignant group were illustrated in Table 1. These factors (LVI was included instead of FDGP) entered multivariate analysis, SUVmax and ILNM remained as the main risk parameters impacting metastasis/recurrence (Table 2). Mean SUVmax was 7.25 in benign group, while it was 11.7 in malignant group. There was a statistical difference according to SUVmax values between benign and malignant groups (p=0.019). A box-plot graph shows the distribution of SUVmax in benign conditions versus recurrent/metastatic disease (Figure 1). ILNM was present in 66.5% of malignant group, 30.5% in benign group and there was a statistical significance between them (p=0.015). A bar graph depicts the presence of ILNM in benign and malignant groups (Figure 2).

There was not a statistically significant difference between malignant and benign groups according to PTL (p=0.944). FDGP, CTP and DIF were statistically meaningful in univariate analysis between malignant and benign groups (p=0.014, p=0.006 and p=0.037, respectively). Focal FDG uptake was present in 81% of recurrence whereas diffuse uptake was seen in 64% of benign group. Soft tissue mass on CT is the main pattern (78.5%) in malignant group, while wall thickening was present in 68.5% of benign conditions. High
grade and mucinous component were a clear risk factor for recurrence/metastasis. ROC curve for SUVmax was drawn (Figure 3). AUC (area under curve) was 0.717 (CI: 0.581-0.854) (p=0.006). Sensitivities and specificities for chosen cutoff values were represented in Table 3.

Recurrence and/or metastasis developed in 59% of the patients (Figure 4). Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of FDG-PET/CT for the detection of recurrence and/or metastasis were 91%, 56.5%, 75% and 81%, respectively. FDG-PET/CT results and final histopathologic diagnosis were represented in Table 4. FDG-PET/CT was true positive in 45% of patients with normal Ca 19-9 and/or CEA levels and true negative in 12% of cases with elevated Ca 19.9 and/or CEA levels according to histopathological confirmation or colonoscopy findings. In the follow-up, CT or MRI detected suspicious malignancy in 50% of the patients (28/56) and further examination with FDG-PET/CT was true negative in 32% of these cases (9/28) according to histopathology.

Discussion

Recurrent disease is seen in 30–50% of patients with CRC after curative resection (11). The recurrence rate was 59% in our study and it is higher than literature. The most frequently encountered location of recurrence occurs in the area of surgery (12) and our findings were in agreement with this. Primary aim of follow-up surveillance is to identify recurrences at the earliest moment for an immediate cure. Most of the relapsed cases are not operable at the time of diagnosis and 1/3 of the patients with isolated locoregional or distant metastases survive 5 years (13). Determination of predictive parameters for recurrence may aid in stratification of patients and contribute to patient management with
intense follow-up. FDG-PET/CT may be a prognosticator and changes treatment planning in recurrent colorectal carcinoma (14).

Mean age of CRC patients fluctuates around 60 years and younger ages are accepted as a risk factor for recurrence in literature (11). Average age of our patient population was 58 years and this is in accordance with previous studies. But we observed that age is not a risk factor in our study. Many articles explained stage and LVI as having association with recurrent CRC. Kobayashi et al. evaluated stage of the disease in 5230 consecutive patients and found advanced stage a risk factor (15). Ryuk et al. found high postoperative Ca 19-9 level, LVI, ILNM and advanced stage as risk factors for recurrence (1). Interestingly, we didn’t identify stage and LVI significant statistically in univariate analysis (p=0.253 and p=0.058, respectively). This is possibly due to undersampling or inconvenient data for statistics and not important clinically. PTL is a risk factor in many papers and recurrence in right colon is more incident (16). However PTL was not a meaningful prognosticator in our study and this is contrary to previous reports.

High serum CEA and Ca 19-9 levels assayed at follow-up after curative resection are prognostic factors for CRC (17). They were also risk factors in our study (p=0.009 and p=0.047, respectively). But FDG-PET/CT yielded true positive results at a rate of 45% in patients whose Ca 19-9 and/or CEA levels were normal while it was true negative just in 12% of the cases with elevated Ca 19.9 and/or CEA levels according to histopathological confirmation. The relationship of recurrence with the use of neoadjuvant therapy is still unclear (18). It was not a significant parameter in our study. Tsai et al. determined PNI as the most important factor in their study of 778 patients (19). Tsai et al. showed that DIF, ILNM, LVI, PNI were risk factors in their study of 259 patients (20). Our findings are in agreement with them except LVI.
It has been reported that FDG-PET/CT is more accurate than CT or MRI for recurrence in several studies. Odalovic et al found FDG-PET/CT more sensitive and specific than MRI (21). Scott et al showed that FDG-PET/CT detected 45 additional lesions in a multicenter prospective trial of 93 patients (22). Detection of a lesion on CT/MRI was not a risk factor (p=0.200) and FDG-PET/CT was more sensitive than CT/MRI findings at the follow-up in our study. It was true negative in 32% (9/28) of the cases on whose CT or MRI were seen lesions which were suspicious of malignancy according to histopathology. TS and DIF (undifferentiated high grade tumors and mucinous component) are clear risk factors for recurrence/metastasis (23). It is well-known that malignant lesions usually appear as focal FDG uptake with a soft tissue mass on FDG-PET/CT whereas diffuse uptake accompanied by wall thickening on CT component is mostly the main pattern in benign conditions (24). Recurrences tend to occur in large and high grade tumors with usually focal FDG uptake accompanied by a soft tissue mass on CT component. FDGP, CTP and DIF were statistically meaningful in univariate analysis between malignant and benign groups in the study (p=0.014, p=0.006 and p=0.037, respectively). ILNM is a strong predictor for recurrence in almost every study and it was the cutest factor together with SUVmax in univariate analysis (p=0.008 and p=0.006, respectively). At the same time, they came out from multivariate analysis as the only predictors impacting recurrence/metastasis amongst all risk factors (p=0.015 and p=0.019, respectively). All our results are in line with these.

The use of FDG-PET/CT in the follow-up of CRC is controversial. Recent data recommend no indication except inconclusive CT with suspicion of distant metastasis or in the presence of negative CT and serial CEA increases (12). Many studies declared that FDG-PET/CT is very sensitive, but not so specific for the detection of recurrence in CRC.
It has some limitations. FDG is accumulated in cancer cells at a relatively higher rate during glucose metabolism. However, cancer cells are not the only metabolically hyperactive ones. Inflammatory, infectious and some nonneoplastic diseases can have increased FDG accumulation causing a low specificity for CRC (25) as it was also in our study. The benign pathologies in our study consisted of granulation tissue, fibrin and inflammation, fibrosis, pyelonephritis, ulceration of colonic mucosa, fibrosis and inflammation, polip, secondary changes to radiotherapy or operation. Lots of benign conditions like ours and physiologic FDG uptakes exhibiting focal or diffuse FDG accumulations in gastrointestinal tract can be seen in patients with CRC during the follow-up and confused with true pathologic lesions. It is essential to distinguish them by colonoscopic biopsy. Previously some quantitative parameters based on volume-of-interest FDG uptake were introduced to augment its diagnostic accuracy in several cancers. SUVmax is the first one. Determination of a cutoff level of SUVmax which differentiates between benign conditions and recurrence would certainly be helpful in CRC.

We investigated the value of SUVmax for the discrimination between benign and malignant conditions. Gade found a lower mean SUVmax of 8.6 (7), Marcus 7.3 (26) in recurrent CRC when compared to ours of 12.7. Shamim et al found a significant increase according to mean SUVmax in recurrence (11.8 for recurrence versus 3.7 for benign conditions) in a study of 32 patients with CRC (27). They were 11.7 for recurrence against 7.2 for benign group in our study and there was a significant difference. Our results revealed that SUVmax was very helpful in the differentiation of recurrent disease from benign conditions and it improved the diagnostic accuracy of FDG-PET/CT. For an estimated cutoff value of 6.3 and 12.5 on ROC curve, the calculated specificities were 61%
and 87%, relatively. According to our findings, SUVmax was very beneficial for increasing the specificity when compared with the one of FDG-PET/CT alone (56.5%).

Several studies reported that neighboring organ invasion and depth of tumor infiltration were significant prognostic factors for postoperative recurrence and survival rate in patients with CRC undergoing curative resection (23). Although the depth of wall invasion by the primary tumor is an important prognostic factor, we couldn’t research it due to lack of sufficient data about it and this is a limitation in our study. Small patient number and study design are also inevitable limitations. Ideally, prospective studies with large numbers are needed. There was a slight selection bias for our patient population. Lack of some other risk factors (type of surgery, localization of metastasis, especially cytogenetic factors) effecting recurrence/metastasis are the other limitations.

**Conclusion**

Initial lymph node metastasis and high SUVmax values on control or restaging FDG-PET/CT are the main risk factor in recurrent colorectal cancer and these patients must be followed up carefully. FDG-PET/CT is very sensitive for the detection of recurrence/metastasis and SUVmax appears to improve its specificity.

**Conflict of Interest**

No conflict of interest was declared by the authors.

**Disclosure**

The authors declare that they have no conflict of interest.


TABLE 1: Univariate analysis of some predefined potential risk factors impacting on metastasis/recurrence, their mean values and percentages between benign conditions and malignant group.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Malignant Group</th>
<th>Benign Conditions</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>59±11</td>
<td>57.8±11.3</td>
<td>0.711</td>
</tr>
<tr>
<td>Sex (%)</td>
<td>Male (45.5)</td>
<td>Male (52.2)</td>
<td>0.621</td>
</tr>
<tr>
<td></td>
<td>Female (54.5)</td>
<td>Female (47.8)</td>
<td></td>
</tr>
<tr>
<td>Serum Ca 19.9 (U/ml)</td>
<td>382 (MV:11)</td>
<td>9.7 (MV:7)</td>
<td>0.047</td>
</tr>
<tr>
<td>Serum CEA (ng/ml)</td>
<td>9.42 (MV:3.5)</td>
<td>2.45 (MV:1.7)</td>
<td>0.009</td>
</tr>
<tr>
<td>SUVmax</td>
<td>11.7±6.2</td>
<td>7.25±5.57</td>
<td>0.006</td>
</tr>
<tr>
<td>Mean tumor size (mm)</td>
<td>39±21.7</td>
<td>28.5±14.7</td>
<td>0.038</td>
</tr>
<tr>
<td>CT/MRI findings (%)</td>
<td>Positive (84.8)</td>
<td>Positive (69.6)</td>
<td>0.200</td>
</tr>
<tr>
<td></td>
<td>Negative (15.2)</td>
<td>Negative (30.4)</td>
<td></td>
</tr>
<tr>
<td>LVI (%)</td>
<td>Present (72.7)</td>
<td>Present (52.2)</td>
<td>0.058</td>
</tr>
<tr>
<td></td>
<td>Absent (27.3)</td>
<td>Absent (47.8)</td>
<td></td>
</tr>
<tr>
<td>PNI (%)</td>
<td>Present (48.5)</td>
<td>Present (21.7)</td>
<td>0.042</td>
</tr>
<tr>
<td></td>
<td>Absent (51.5)</td>
<td>Absent (78.3)</td>
<td></td>
</tr>
<tr>
<td>INAT (%)</td>
<td>Yes (54.5)</td>
<td>Yes (56.5)</td>
<td>0.884</td>
</tr>
<tr>
<td></td>
<td>No (45.5)</td>
<td>No (43.5)</td>
<td></td>
</tr>
<tr>
<td>ILNM (%)</td>
<td>Present (66.7)</td>
<td>Present (30.4)</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>Absent (33.3)</td>
<td>Absent (69.6)</td>
<td></td>
</tr>
<tr>
<td>Stage (%)</td>
<td>I (6.1)</td>
<td>I (17.4)</td>
<td>0.253</td>
</tr>
<tr>
<td></td>
<td>II (21.2)</td>
<td>II (34.8)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>III (45.5)</td>
<td>III (26.1)</td>
<td></td>
</tr>
<tr>
<td>Variable</td>
<td>B</td>
<td>Odds Ratio</td>
<td>CI</td>
</tr>
<tr>
<td>----------</td>
<td>-----</td>
<td>------------</td>
<td>-------------</td>
</tr>
<tr>
<td>SUVmax</td>
<td>0.136</td>
<td>1.146</td>
<td>1.022-1.284</td>
</tr>
<tr>
<td>ILNM</td>
<td>1.532</td>
<td>4.626</td>
<td>1.351-15.834</td>
</tr>
</tbody>
</table>

TABLE 3: Cut-off values, related sensitivities and specificities of SUVmax for recurrence.

<table>
<thead>
<tr>
<th>Cutoff values</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Area Under Curve (%95 Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.5</td>
<td>51</td>
<td>87</td>
<td>0.717 (0.581-0.854)</td>
</tr>
<tr>
<td>6.3</td>
<td>76</td>
<td>61</td>
<td></td>
</tr>
</tbody>
</table>

TABLE 4: Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of FDG-PET/CT according to final histopathologic diagnosis.

<table>
<thead>
<tr>
<th>Histopathologic Diagnosis</th>
<th>FDG-PET/CT Results</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Positive</td>
<td>Negative</td>
<td>Sensitivity</td>
<td>Specificity</td>
<td>PPV</td>
<td>NPV</td>
<td></td>
</tr>
<tr>
<td>Malign</td>
<td>TP=30</td>
<td>FN=3</td>
<td>91%</td>
<td>56.5%</td>
<td>75%</td>
<td>81%</td>
<td>33</td>
</tr>
<tr>
<td>Benign</td>
<td>FP=10</td>
<td>TN=13</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>23</td>
</tr>
<tr>
<td>Total (n)</td>
<td>40</td>
<td>16</td>
<td>91%</td>
<td>56.5%</td>
<td>75%</td>
<td>81%</td>
<td>56</td>
</tr>
</tbody>
</table>
FIGURE LEGENDS

FIGURE 1: Box-plot graph of the distribution of SUVmax in benign conditions versus recurrent/metastatic disease.
FIGURE 2: Bar graph of initial lymph node metastasis (ILNM) in benign and malignant groups.
FIGURE 3: ROC curve for SUVmax
FIGURE 4: A female patient aged 67 years with rectal cancer was operated and treated by chemoradiotherapy. Her axial PET (A), CT (B), fusion (C) and maximum intensity projection (MIP) (D) images on FDG-PET/CT exhibited circular FDG uptake in rectum (long arrow) with a SUVmax of 10.1 and TLG of 154 accompanied by wall thickening on CT component. Besides, there is focal FDG uptake in presacral area (short arrow) which was considered as metastatic lymph node (SUVmax:9.6). These uptakes raised the suspicion of a probable recurrence and histopathology confirmed both of them as malignant. In whole body MIP images there is a metastatic foci in liver which shows FDG uptake (thick arrow) (SUVmax:8.8).