We enrolled 110 patients who underwent positron emission tomography/computed tomography (PET/CT) scans to detect benign clinical conditions in addition to malignancy, and this leads to additional investigation and expenditure. The purpose of our study was to assess the endoscopic and histopathologic results of incidental 18F-FDG uptake in the GI tract.

**Patients and Methods:** We enrolled 110 patients who underwent gastroscopy/colonoscopy for incidental GI tract involvement in PET/CT. Histopathologic and endoscopic results were compared with FDG uptake level, pattern of uptake (diffuse/focal), and site of involvement.

**Results:** In our study, 52.7% of the patients were male and the mean age was 57±11 years. Among the participants, 47.3% and 52.7% of patients had upper GI tract and colorectal involvement in PET/CT, respectively. Gastritis and colonic polyps were the most common endoscopic diagnoses that caused FDG uptake in the upper and lower GI tract, respectively. Endoscopic evaluation was normal in 23.6% of patients with pathologic FDG involvement. The rates of adenomatous polyps, malignancy, and hyperplastic polyps were 18.5%, 13.6%, and 6.8%, respectively. The mean SUVmax were higher in malignant lesions than in non-malignant lesions (14.3±8.9 vs. 9.3±5.3; p=0.02). Diffuse or focal FDG involvement patterns on PET/CT did not help to discriminate malignancy in the GI tract.

**Conclusion:** Malignancy was detected in only 13.6% of patients with FDG involvement in the GI tract, and the involvement pattern (diffuse/focal) and SUVmax did not differentiate malignancy. (Acta gastroenterol. belg., 2018, 81, 471-475).

**Key words:** incidental; malignancy; gastrointestinal tract; PET/CT.

**Introduction**

18F-fluorodeoxyglucose (18F-FDG) is frequently used in positron emission tomography/computed tomography (PET/CT). 18F-FDG is a glucose analogue marked with fluorine-18, a positron-emitting isotope. When it enters the cell it becomes phosphorylated and cannot leave (1). 18F-FDG accumulates in malignant tissues more than in normal tissues due to increased glucose metabolism. Despite the proven benefits of 18F-FDG PET, it also has significant deficiencies, 18F-FDG accumulation in tissues with benign clinical conditions is the most important of these deficiencies. The major benign conditions with high 18F-FDG accumulation are inflammatory and infectious diseases (2). In recent years, PET/CT has been used routinely in oncology and the frequency of use is rapidly increasing. Incidental 18F-FDG involvement in the gastrointestinal (GI) tract is common (3). In the literature, the rate of incidental 18F-FDG involvement in the colorectal region is up to 2.4% (4). Although the involvement pattern in this situation is useful to show malignancy in the GI tract, endoscopic evaluation is inevitable (5). However, some of these patients are normal and additional investigations are meaningless; therefore, these additional procedures may cause financial loss. Beyond the financial implications, incidental FDG involvement causes serious anxiety in patients and physicians. Endoscopists are worried about missing possible lesions in these cases and this prolongs procedures unnecessarily. In this study, we investigated the endoscopic and histopathologic significance of incidental 18F-FDG uptake in the GI tract in patients with extraintestinal malignancies.

**Material & Methods**

**Patients**

In our study, we included a total of 110 patients who underwent gastroscopy/colonoscopy between November 2008 and November 2015 due to incidental upper/lower GI tract involvement in PET/CT. PET/CT indications in this study were staging for non-GI malignancy and evaluation of malignancy suspicion. Endoscopic evaluations of the patients were performed within one month of the PET/CT. Patients with FDG uptake in the GI tract were questioned for GI symptoms before the endoscopy procedure. Patients with chronic GI symptoms (abdominal pain, alteration in defecation habits, diarrhea, constipation, etc) were excluded from the study because PET/CT involvement in such cases might not be incidental. We also excluded patients with previous chemotherapy and/or radiotherapy, known inflammatory bowel disease, previous GI surgery, GI malignancy, and antidiabetic/anti-inflammatory drug use (Figure 1). Endoscopic evaluations were performed in a single endoscopy center and all pathologists were
PET/CT images were reviewed for abnormally increased tracer uptake foci by an experienced nuclear medicine physician. Each increased uptake in gastrointestinal structures identified in PET images was correlated with corresponding CT sections, and a PET/CT scan was considered to be positive if early or delayed images of abnormal FDG uptake were noted with a corresponding abnormality in CT.

The Statistical Package for Social Sciences (SPSS) version 22.0 for Windows (IBM SPSS Statistics Data Editor) was used for statistical analysis of the data. Descriptive data are given as number of participants and frequency. Categorical variables are expressed as the number of cases and the percentage value. Comparisons of categorical variables were performed using Chi-square and Fisher’s exact tests. Continuous variables are given as mean and standard deviation or median and minimum-maximum. The Shapiro-Wilk test was used to determine whether the continuous variables were normally distributed. For continuous variables, Student’s t-test and the Mann-Whitney U test were used according to the normality of variable distribution. In order to determine the cut-off value of SUVmax, Receiver Operating Characteristics (ROC) curve analysis was used. A p value of <0.05 was considered statistically significant.

**Results**

**Endoscopic evaluation results**

One hundred ten patients were included in the study. Of these, 52.7% (n=58) were male and their mean age was 57±11 years (range, 20-78 years). Esophagogastroduodenoscopy (EGD) was performed in 47.3% of cases (n=52) because of upper GI involvement in PET/CT. The remainder (52.7%) was evaluated using total colonoscopy due to involvement in the colorectal area. The stomach was the most frequent site of involvement in the upper GI tract (27.3%), followed by the esophagus (14.5%). Gastritis was the most common endoscopic diagnosis (32.7%) that caused FDG uptake in the upper GI tract (detailed in Table 1).

In the lower GI tract, the most common site of FDG uptake was the rectosigmoid colon segment (81%). The most common endoscopic diagnosis that caused FDG uptake in the lower GI tract was colonic polyps (46.6%). Endoscopy was normal in 29.3% of patients with colonic FDG uptake. In other words, PET/CT had a serious rate of false positivity in the lower GI tract. However, only three cases (5.2%) with incidental FDG uptake in the lower GI tract had mass lesions with a malignant appearance at colonoscopy.

The overall rate of patients with mass lesions that were suspicious of malignancy in endoscopy (upper and lower) was 13.6%. However, 23.6% of patients with pathologic FDG involvement in the overall GI tract had normal endoscopy (see Table 1 for details) (Figure 2).
Positron emission tomography/computed tomography in gastrointestinal tract

Histopathological evaluation results

For both upper and lower GI involvement, the most frequent histopathological diagnoses were inflammatory conditions (38.8%) (see Table 1 for details). The adenomatous polyp ratio was 18.5% and malignancy rate was 13.6%. However, 6.8% of lesions that caused pathologic FDG involvement in the GI tract were hyperplastic polyps. Twenty-three patients had normal histopathology despite pathologic FDG involvement in PET/CT (Table 1) (Figure 3).

When we analyzed histopathologies of upper and lower GI tract separately, gastritis (46.8%) was the most common cause of FDG uptake in the upper GI tract. The malignancy rate in the upper GI tract was 19.1% (Table 1). In the lower GI tract, the most common histopathology that caused FDG uptake was adenomatous polyps (34%) (12 tubulovillous adenoma [n=12], tubular adenoma [n=7]). The malignancy rate in the lower GI tract was 8.9%. Thus, the majority of FDG uptake in the lower GI tract was due to non-neoplastic causes (57.1%).

SUVmax analysis results

SUVmax analysis was performed on the data of 72 patients with both histopathology and PET results. The

<table>
<thead>
<tr>
<th>Sex, n (%)</th>
<th>Male</th>
<th>58 (52.7%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean±SD</td>
<td>57±11</td>
<td></td>
</tr>
<tr>
<td>Site of FDG uptake, n (%)</td>
<td>Colorectal 56 (50.9%), Stomach 30 (27.3%), Esophagus 16 (14.5%), Duodenum 6 (5.5%), Terminal ileum 2 (1.8%)</td>
<td></td>
</tr>
<tr>
<td>Endoscopic diagnosis, n (%)</td>
<td>Inflammation 39 (35.5%), Gastroduodenitis 19 (17.3%), Esophagitis 9 (8.2%), Colitis 8 (7.3%), Diverticulitis 2 (1.8%), Terminal ileitis 1 (0.9%), Polyp 30 (27.3%), Normal endoscopy 26 (23.6%), Mass lesion 15 (13.6%)</td>
<td></td>
</tr>
<tr>
<td>Histopathologic diagnosis, n (%)</td>
<td>Inflammation 40 (38.8%), Gastritis 19 (18.4%), Colitis 13 (12.6%), Esophagitis 6 (5.8%), Duodenitis 1 (1%), Ileitis 1 (1%), Normal 23 (22.3%), Adenomatous polyps 19 (18.5%), Malignancy* 14 (13.6%), Hyperplastic polyps 7 (6.8%)</td>
<td></td>
</tr>
</tbody>
</table>

SD : standard deviation ; FDG : Fluorodeoxyglucose ; *Seven patients were missing in the histopathologic results analysis ; **Adenomatous polyps: 12 tubulovillous adenoma, 7 tubular adenoma ; * Malignancy types : Upper GI tract : 5 adenocarcinoma, 3 lymphoma, 1 neuroendocrine tumor ; Lower GI tract : 4 adenocarcinoma, 1 angiosarcoma.

**Table 1. — Characteristics of the patients**

**Table 2. — SUVmax levels of different histopathologies**

<table>
<thead>
<tr>
<th>Histopathology</th>
<th>Median SUVmax</th>
<th>Minimum-Maximum SUVmax</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n=15)</td>
<td>7.8</td>
<td>4.5 - 16</td>
</tr>
<tr>
<td>Lymphoma (n=2)</td>
<td>14.4</td>
<td>9.9 - 19</td>
</tr>
<tr>
<td>Adenocarcinoma (n=5)</td>
<td>13.5</td>
<td>5.6 - 31.3</td>
</tr>
<tr>
<td>Diverticulitis (n=2)</td>
<td>10.7</td>
<td>10.3 - 11.1</td>
</tr>
<tr>
<td>Tubulovillous adenoma (n=10)</td>
<td>10.4</td>
<td>3.1 - 29.8</td>
</tr>
<tr>
<td>Nonspecific Colitis (n=8)</td>
<td>9</td>
<td>7.2 - 20.4</td>
</tr>
<tr>
<td>Neuroendocrine tumor (n=1)</td>
<td>8.5</td>
<td>8.5</td>
</tr>
<tr>
<td>Tubular adenoma (n=6)</td>
<td>6.4</td>
<td>4.2 - 9.8</td>
</tr>
<tr>
<td>Hyperplastic polyp (n=4)</td>
<td>8</td>
<td>3.8 - 17.8</td>
</tr>
<tr>
<td>Esophagitis (n=5)</td>
<td>7.4</td>
<td>5 - 11.4</td>
</tr>
<tr>
<td>Duodenitis (n=1)</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Gastritis (n=13)</td>
<td>6.5</td>
<td>4.2 - 27.7</td>
</tr>
</tbody>
</table>

*SUVmax values were given for the patients with both histopathology and PET results.
highest SUVmax values were found in lymphoma, adenocarcinoma, diverticulitis, and tubulovillous adenoma in the GI tract, respectively. Detailed SUVmax values according to histopathologic diagnoses are given in Table 2. The mean SUVmax was significantly higher in malignant lesions than in non-malignant lesions (14.3±8.9 vs. 9.3±5.3) (p=0.02). However, it was found that diffuse or focal involvement pattern on PET/CT did not help to discriminate malignancy in the GI tract (p>0.99). Also in our study, we evaluated the value of late SUVmax measurement. It was found that increased late SUVmax did not lead to malignant/nonmalignant discrimination (p>0.99). When ROC analysis was performed and we chose a SUVmax cut-off of 8.05 in the upper GI tract for the differentiation of malignancy, it had a sensitivity and specificity of 86% and 64%, respectively (area under the curve (AUC): 0.732). Also, in the lower GI tract, a SUVmax cut-off of 9.1 for malignancy had a sensitivity and specificity of 65% and 65%, respectively (AUC: 0.576).

Discussion

PET/CT is one of the major imaging technical innovations that has been routinely used in oncology. However, it often causes problems. One of these is incidental FDG involvement of the GI tract, and this is not a rare situation. Studies on this topic usually focused on incidental FDG involvement in the colorectal region. The rate of incidental FDG uptake in the colorectal area varies in the literature; the rate was 1.35% in the study of Peng et al., whereas it was 0.6% in the study by Shimidi et al (6,7). The different rates in the literature are due to the fact that different and nonhomogeneous patient populations were studied. However, these rates still provide information on the frequency of incidental FDG uptake in the colorectal area and reveal the magnitude of the problem. The aim of our study was not to determine the incidence of incidental FDG uptake in GI tract, but to determine the endoscopic and histopathologic results of incidental involvement in a homogeneous patient group. Many patients with conditions such as inflammatory bowel disease, previous GI surgical history, and those using antiinflammatory and antidiabetic medication were excluded from our study in order to create a homogeneous group. Patients were questioned before the endoscopic evaluation regarding chronic GI symptoms and those using antiinflammatory and antidiabetic medication were excluded from our study in order to create a homogeneous group. Patients were questioned before the endoscopic evaluation regarding chronic GI symptoms and those who responded positively were excluded because FDG involvement patients with GI symptoms such as abdominal pain, defecation changes, chronic diarrhea, and dysphagia cannot be assessed as incidental involvement and needs referral for further evaluation. Most studies evaluating incidental FDG uptake in the GI tract are retrospective and there is no assessment for GI disease. For instance, in the study of Fuertes et al., as in other studies, the authors did not evaluate current GI symptoms and included/excluded patients according to their past medical records only (8).

Another important point in our study was that we evaluated patients with colorectal involvement and those with upper GI tract involvement in PET/CT. In daily practice, FDG uptake in the upper GI tract is not rare, as was also shown in our study results. Almost half of our patients had incidental upper GI involvement in PET/CT. In a similar study, Goldin et al. found the incidental upper GI involvement rate as 60% in their study population (9). In our study, the most common cause of incidental FDG uptake in the upper GI tract was inflammation.

However, 19.1% of patients with FDG uptake in the upper GI tract had malignancies. The malignancy rate was slightly higher in the upper GI (25.6%) in the study of Goldin et al (9). In our study, 8.9% of patients with colorectal FDG involvement had cancer. This rate was lower than in the literature. In another study, patients with colonic FDG involvement were evaluated and 28.2% were diagnosed as having malignancies (10). The difference between these ratios might be attributed to the different patient characteristics included in the studies and their different involvement patterns in PET/CT. In our study, we included patients with focal involvement and those with diffuse FDG involvement in the GI tract. Also, our study patients were a homogeneous group comprising patients who were asymptomatic for GI diseases.

Patients with diffuse involvement in the GI tract were not included in most studies in the literature. In our study, there was no difference between focal vs. diffuse FDG involvement in the GI tract in terms of the presence of malignancy. Our study revealed a malignancy rate of 12.1% in GI tract areas with diffuse involvement. Chung et al.’s study, as with many other studies, evaluated patients with focal involvement only (11). Therefore, the studies on nonfocal incidental FDG involvement in the GI tract are limited in the literature. As shown in our study, the rate of malignancy in patients with diffuse GI involvement on PET/CT is too high to ignore. Patients with diffuse uptake and focal involvement must be evaluated endoscopically.

Malignant lesions, as expected, were found to have higher SUVmax levels compared with the remainder in our study. Other studies have attempted to determine a SUVmax cut-off for colorectal malignancies. Luboldt et al. found that a SUVmax cut-off of ≥5 improved the accuracy of colorectal mass detection (12). This result is compatible with our study in which all malignant lesions had an SUVmax ≥5. Another important point to note is that this cut-off in our study did not detect adenomatous polyps, which are premalignant lesions. Also, our study showed that many benign conditions might have very high SUVmax values. Therefore, all patients with FDG involvement in the GI tract should be assessed endoscopically irrespective of their SUVmax level so as not to miss any neoplasia.

In conclusion, we might say that it is not possible to differentiate GI tract lesions according to the pattern of involvement (diffuse or focal) or SUVmax level in PET/
CT. Our study showed that the malignancy rate was high in patients with FDG uptake in the upper gastrointestinal tract. Endoscopic evaluation is necessary for all patients with involvement of GI system in PET/CT, independent of the pattern of uptake and SUVmax level.

Acknowledgement and Conflicts of Interest Declaration

All co-authors of the study declare not having any conflict of interest and we don’t have any grand support for this study. Our thanks to Mr. David F. Chapman for language editing.

References