Role of $^{18}$F-FDG PET/CT in Gastric Carcinomas: Comparison with Contrastenhancement Computed Tomography

Gonca Kara Gedik$^{1,*}$, Farise Yilmaz$^{2}$, Mustafa Koplay$^{2}$ and Oktay Sari$^{1}$

$^{1}$Department of Nuclear Medicine, Selcuk University, Turkey
$^{2}$Department of Radiology, Selcuk University Faculty, Turkey

Abstract

Purpose: The purpose of this study was to investigate the usefulness of $^{18}$fluorodeoxyglucose Positron Emission Tomography /Computed Tomography ($^{18}$F-FDG PET/CT) in patients with gastric carcinoma and to compare it with contrast enhancement CT.

Materials and Methods: The files of 20 patients (5 female, 15 male, mean age: 68 years) who underwent both $^{18}$F-FDG PET/CT and contrast enhancement CT for staging or restaging of gastric carcinoma were retrospectively evaluated. For each modality, the sensitivity, specificity, positive (PPV) and Negative Predictive Values (NPV) and accuracy was calculated in terms of gastric lesion detection, lymph node metastases or distant metastases. The diagnostic performances of two techniques were compared.

Results: For detecting gastric lesion, the sensitivity, specificity, PPV, NPV and accuracies of $^{18}$F-FDG PET/CT and contrast enhancement CT were 86%, 100%, 100%, 91%, 94% and 100%, 80%, 78%, 100% and 88%, respectively. In terms of lymph node metastases, the results were 75%, 71%, 60%, 83%, 93% and 88%, 92%, 88%, 92%, 90%, respectively. About distant metastases, the results were, 64%, 89%, 90%, 62%, 74% and 64%, 44%, 64%, 44%, 57%, respectively. The differences of the sensitivity and specificity of gastric lesion and metastatic lymph node detection were not statistically significant between two imaging techniques (p >0.05, McNemar test). $^{18}$F-FDG PET/CT appeared as a more specific modality than contrast enhancement CT for evaluating distant metastases in patients with gastric carcinoma but difference could not be found as statistically significant (p >0.05, McNemar test).

Conclusion: $^{18}$F-FDG PET/CT is a useful diagnostic modality for the evaluation of gastric lesion and lymph node metastases and it has a comparable diagnostic performance with the standard imaging procedure of contrast enhancement CT in patients with gastric carcinoma. For distant metastases, complimentary usage of these techniques may be more beneficial in evaluation of patients with gastric carcinoma.

Keywords: Gastric carcinoma; Positron emission tomography/computed tomography; Contrast enhancement computed tomography

Introduction

Gastric cancer is the 4th most common cancer worldwide and its mortality rate is second to lung carcinoma [1]. Surgery has a curative potential and is the treatment of choice for early gastric cancer. The primary aim of surgery is to eliminate the malignant tumor by resection of the stomach and proper lymphadenectomy [2]. Although markedly reduced in recent years, surgical morbidity from gastrectomy is still significant so preoperative determination of local extent of disease and distant metastases is essential for planning the patient management. In order to avoid unnecessary surgical procedures patients with advanced disease, who will not benefit from surgery but must be referred combined chemotherapy and radiotherapy, must be carefully selected. This question, whether the disease is localized or metastatic, can be answered by preoperative imaging studies including endoscopic ultrasonography, contrast enhancement computed tomography and occasionally laparoscopy.

With the recent technical advances in Computed Tomography (CT) and with the development
of helical and multislice scanning, CT stands up as the primary staging modality in gastric carcinoma. However, CT is an anatomy-based diagnostic technique which causes false negative results in normal sized invaded lymph nodes and false positive in enlarged inflammatory lymph nodes [3]. Like CT, especially for lymph node staging, other morphology-based imaging tool such as endoscopic ultrasonography and magnetic resonance imaging are also reported as insufficient to guide therapeutic plans [4].

Positron Emission Tomography (PET) uses the radiolabeled glucose analogue 18fluorodeoxyglucose (18F- FDG), which shows altered glucose metabolism in malignant tissue. PET imaging can be combined with anatomic imaging such as CT which enables the system to provide information about the anatomic localization of abnormal foci of FDG uptake. After the introduction of combined PET/CT modality into clinical practice in oncology environment, this imaging system has been rapidly adopted in a wide spectrum of indications. In gastric carcinoma, preliminary results suggest that it is of greater value in recurrent disease rather than for pretherapy staging, but the benefits of PET/CT still remain uncertain [5].

The aim of this study is to evaluate the potential role of 18F-FDG PET/CT in gastric cancer and to compare the diagnostic accuracy of 18F-FDG PET/CT with contrast enhanced CT for detection of gastric lesion, lymph node and distant metastases.

Materials and Methods

Patients

18F- FDG PET/CT scans of patients with gastric carcinoma performed for staging or restaging in Selcuk University Faculty of Medicine Department of Nuclear Medicine, between October 2012 and September 2015 were retrospectively reviewed. The ethics committee of our institution approved this study (meeting date: 16.02.2016, no: 2016/3) and written informed consent was obtained from all patients.

For inclusion the study, the required patient characteristics were as followed: male or female patients with histopathologically confirmed gastric carcinoma who underwent 18F- FDG PET/CT scan and contrast enhancement CT within 30 days. Patients with non epithelial gastric tumors, patients who either did not have or who underwent contrast enhancement CT more than 30 days within 18F-FDG PET/CT and patients lost to follow-up, were excluded from the study. Ultimately, the study included 20 patients (5 female, 15 male, age range: 36-81 years, mean: 68 years).

18F-FDG PET/CT technique

Images from the skull base to the mid thigh were acquired in 8 or 9 bed positions with an acquisition time of 2 minutes per bed position with integrated 18F- FDG PET/CT scanner (Biograph CT, Siemens, Germany). Patients were advised to fast for at least 6 hours and 370 Mega Becquerel (MBq) of 18F-FDG was injected to the patients whose blood glucose level was <200 mg/dl. PET/CT studies were performed 1 hour after the administration of the radiopharmaceutical. After radiopharmaceutical injection, 1000 ml water without contrast material was also applied orally. The CT part of the integrated scan was carried out without contrast enhancement by using 16 slice CT with the acquisition parameters of 190 mA, 5 mm slice thickness and 140 kV. Right after the CT imaging, PET scan was performed without changing the position. The CT data were used for the attenuation correction of PET scanning.

Contrast enhancement CT technique

Contrast enhancement CT examinations were performed with a dual-source 128 x 2-slice DSCT scanner (Somatom Definition Flash, Siemens Healthcare Forschern, Germany) which has two X-ray tubes located at 95º angle and 128-channel two-detector row. The acquisition parameters were as follows: slice thickness 3 mm, spiral pitch factor 0.6, gantry rotation time 280 ms, kVp 120, 180-420 mAs. All scans included oral and intravenous contrast enhanced administration. Water was also orally applied prior to CT examination in order to provide gastric distention. IV contrast medium (iomeol, iodine content 350 mg/mL; Omnipaque, GE Health care) was administered from brachial vein at a flow rate of 2-3 mL/s. In order to reduce the artifact of contrast medium, a saline solution (40 ml) was injected.

F-FDG PET/CT and contrast enhancement CT interpretations

18F-FDG PET/CT and contrast enhanced CT examinations were reviewed by 2 nuclear medicine physicians and by 1 radiologist, respectively. All of the reviewers were experienced and unaware of the patient medical history. The images of 18F- FDG PET/CT and contrast enhancement CT were reviewed for evidence of primary tumor / locally recurrent disease, lymph node and distant metastases.

Acquired images of 18F-FDG PET/CT were analysed on Siemens Syngo.via PET-CT workstation. 18F-FDG PET/CT was considered as positive for primary tumor if any increased FDG uptake greater than the adjacent normal gastric wall. Focal or diffuse increased FDG uptake in postsurgical area was accepted as recurrent disease. FDG uptake of lymph node was considered as malignant if fatty hilum was not observed. For mediastinum, lymph nodes showing FDG uptake higher than mediastinal vascular structures, interpreted as metastatic. Any lesion in sites different from the stomach or lymph nodes showing FDG accumulation regarded as distant metastases. Volume of interest was drawn on the high FDG uptake area and maximum Standardized Uptake Value (SUVmax), which is a semiquantitative parameter for the FDG uptake normalized to the injected dose and patient weight, was calculated for each gastric lesion of showing FDG uptake.

For contrast enhancement CT, a gastric lesion was considered to be cancerous when a polipoid mass or gastric wall thickening of >3 mm was observed. Lymph nodes were described as metastatic if they were larger than 10 mm in the short-axis diameter. If there was at least one lesion in regions different from the stomach and lymph nodes, it was regarded as distant metastases.

In the next step, disease involved areas for thoracic and abdominal parts were introduced for metastatic lymph node and distant metastatic areas. Each patient took a score according to the number of disease involved areas for each imaging modality. In thoracic region, mediastinum, parasternal, both axillas, and right and left lung were determined as lymph node and distant metastatic areas, respectively. If a patient had metastatic noduler lesions in right and left lungs, he took a score of 2 for distant metastasis for thoracic region. If mediastinal lymph nodes were involved with metastatic disease, the patient took score 1 for lymph node metastases for thoracic region regardless the number of involved stations. In abdominal region, perigastric, paraaortic-paracaval, right and left inguinal and mesenteric lymph node areas were determined as disease involved areas for lymph node metastases. Periton, liver, right and left adrenal glands and spleen were determined as distant metastatic areas for abdomen. For each area, the patient took score of 1. If a patient had bone involvement,
he took a score of 1 for distant metastases, regardless of the number of involved bones.

Gold standard for comparison the results of contrast enhancement CT and 18F-FDG PET/CT was accepted as surgical intervention/biopsy (n: 8 patients) or clinical-instrumental follow-up of at least 6 months (contrast enhancement CT, 18F-FDG PET/CT or magnetic resonance imaging, n: 12 patients). When only one regional CT was present (thorax or abdomen), only that region was taken into consideration during comparison of 18F-FDG PET/CT and contrast enhancement CT. For both imaging modalities; any reported disease involved area, proved as gastric pathology, lymph node metastases or distant metastases by follow-up studies or by surgery, has been classified as true positive. If an area was reported as disease involved but turned out to be reactive by biopsy or no more observed in follow-up studies without taking chemo/ radiotherapy, it was classified as false positive. An area which was not reported as disease involved by one of the modality but as involved by other and proved as gastric lesion, lymph node or distant metastases, by pathology or in follow-up studies, false negativity was assigned for the former technique. If an area was reported as free of disease by one of the modality but as metastatic by the other one, and biopsy or follow-up clarified the absence of disease, true negativity was concerned for the former modality.

### Statistical analysis

Sensitivity, specificity, negative and positive predictive values and accuracy of 18F-FDG PET/CT and contrast enhancement CT were calculated for gastric lesion, lymph node and distant metastases. For lymph node and distant metastases, area based analysis was performed. The diagnostic performance of two modalities was compared by McNemar test. Statistical significance was assumed when a p value was less than 0.05.

### Results

In 14 patients 18F-FDG PET/CT was performed for restaging and in 6 for staging. Ten patients underwent both thorax and abdomen contrast enhancement CT and 18F-FDG PET/CT and in remaining 10, only one regional contrast enhancement CT was present. The mean time interval between 18F-FDG PET/CT and contrast enhancement CT was 12 days (range: 2-30 days). Clinical and pathological characteristics of patients and the results of both imaging modalities are shown in Table 1.

### Gastric lesions

Totally, 7 gastric lesions were clarified as primary diagnosis/tumor recurrence with gold standard in 20 patients. 18F-FDG PET/CT resulted positive for gastric lesions in all of 6 of 7 lesions (86%, Figure 1). Mean SUVmax was calculated as 17.40 (range: 3.67-35.30).
In 1 patient who was submitted for restaging, 18F-FDG PET/CT failed to show increased activity in gastric lesion. Contrast enhancement CT detected all gastric lesions (100%). There were no false negative results and 2 lesions were falsely reported as positive for gastric lesion with contrast enhancement CT. Results concerning sensitivity, specificity, PPV, NPV and accuracy are depicted in Table 2 and the differences of sensitivity and specificity were not statistically significant between two imaging modalities (p = 1.00 and p = 0.5, respectively, McNemar test).

**Lymph node metastases**

Eight metastatic lymph node areas were clarified in 20 patients. 18F-FDG PET/CT resulted positive for metastases in 10 lymph node areas. Among these, 6 of them were true and 4 were false positive areas. Two metastatic lymph node areas were missed in 2 patients with 18F-FDG PET/CT (patients no:11 and 20, Table 1 and Figure 2). Contrast enhancement CT resulted positive for lymph node involvement in 8 lymph node areas. One false positive (patient no: 4, Table 1) and 7 true positive areas were noted with contrast enhancement CT. One false negative area in 1 patient (patient no:9, Table 1 and Figure 3) was also recognized. Contrast enhancement CT was found more sensitive and specific than 18F-FDG PET/CT (88% vs. 75% and 92% vs. 71%, respectively; Table 2) but the differences were not statistically significant (p = 1.00 and p = 0.375, respectively, McNemar test).

**Distant metastases**

Totally 14 distant metastatic areas were identified in 20 patients. Among these 14 distant metastatic areas, 18F-FDG PET/CT correctly detected 9 of them and 5 areas were missed with this modality. One

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**Table 2:** Results concerning the sensitivity, specificity, accuracy, PPV and NPV of both imaging modalities.

| Abbreviations: GL: Gastric Lesion; LNM: Lymph Node Metastases; DM: Distant Metastases; PPV: Positive Predictive Value; NPV: Negative Predictive Value; CECT: Contrast Enhancement CT |

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false positive are was noted with $^{18}$F-FDG PET/CT (patient no: 7, Table 1). Similarly, contrast enhancement CT, resulted in 9 true positive and 5 false negative areas. There were 5 areas which were reported as false positive with contrast enhancement CT and in 1 patient, metastatic bone lesions were only detected with $^{18}$F-FDG PET/CT but were missed with contrast enhancement CT (patient no: 13, Table 1 and Figure 4). In 1 patient bilaterally located metastatic surnearal lesions were falsely reported as adenoma with both imaging modalities (patient no: 20, Table 1). Peritoneal seeding was missed in 2 patients with $^{18}$F-FDG PET/CT but detected with contrast enhancement CT (patients no: 2 and 15, Table 1). Omental metastases in 1 patient was correctly detected with $^{18}$F-FDG PET/CT but was missed with contrast enhancement CT (patient no: 17, Table 1). The sensitivity of both imaging modalities were calculated as 64%, the specificity of $^{18}$F-FDG PET/CT was higher than contrast enhancement CT but the difference was not statistically significant ($p = 0.125$, McNemar test, Table 2).

**Discussion**

$^{18}$F-FDG PET/CT has emerged to provide increased accuracy compared with the conventional tools for the diagnosis of primary and recurrent gastrointestinal tumors including esophageal and colorectal cancer [6]. In gastric carcinoma, correlation of primary tumor of FDG uptake with histopathological features of gastric cancer has been investigated and $^{18}$F-FDG PET/CT is reported to have limited role in primary diagnosis because of relatively high number of primary tumors that are not avid for $^{18}$F-FDG such as signet ring cell carcinoma and cancer with high mucinous content [7,8]. For the detection of recurrent gastric cancer; in some studies it is reported that FDG-PET has a low diagnostic accuracy [9]. On the other hand by Bilici et al. [10] $^{18}$F-FDG PET/CT has been reported as a superior post-therapy surveillance modality for the diagnosis of recurrent gastric cancer compared with diagnostic CT. In our study, 6 of 7 (86%) gastric lesions were correctly detected with $^{18}$F-FDG PET/CT. For detecting gastric tumors, sensitivity of 21% to 100% has been reported in the literature [11]. In recurrent gastric carcinoma, sensitivity values such as 78% and 75 % have been reported for $^{18}$F-FDG PET/CT [12,13]. High sensitivity results of 86% for detecting gastric lesion was reached in our study. Moreover, high SUVmax of 9.29 was calculated in one of the patients with signet cell carcinoma which is discordant with the reported low sensitivity in this type of cancer due to extracellular or intracellular mucin component. Our high sensitivity results can be attributed to preparation of patients before $^{18}$F-FDG PET/CT examination. It has been shown that distension of stomach using water improves the diagnostic performance of $^{18}$F-FDG PET/CT in detecting both primary and recurrent gastric tumors [14,15]. In our department we use water prior to PET/CT acquisition to achieve this distension which may have an effect on value of our sensitivities. The localization of tumor has also been discussed that may affect the detection of gastric carcinomas and gastro esophageal junction carcinomas was reported to have a higher sensitivity than other stomach parts [16]. In our study, 3 of 7 lesions were located in corpus, 3 including the one which $^{18}$F-FDG PET/CT was missed in antrum and 1 was in cardia which supported the independency of gastric carcinoma detectability by site like other studies [17]. The data about sizes of the tumors was not available in our study so the effect of size of the tumor on lesion detectability could not be drawn. Except 2, all the patients showing FDG uptake, had a diagnosis of gastric adenocarcinoma, so the differences of SUVmax values between different histologic subtypes could not be assessed. The patient missed with $^{18}$F-FDG PET/CT but correctly diagnosed with contrast enhancement CT was a patient with gastric adenocarcinoma and we thought that physiologic gastric FDG uptake in gastric smooth muscle adjacent to the primary tumor obscured the lesion. Coexisting inflammatory changes may also play role in accumulating $^{18}$F-FDG in gastric mucosa. On the other hand, contrast enhancement CT correctly detected all the primary and recurrent tumors. Since contrast enhancement CT is based on size dependent interpretation criteria, areas showing wall thickening but free of disease, 2 patients were falsely reported to have tumor recurrence by contrast enhancement CT which reduced the specificity of this technique. We thought that morphologic changes evolved after surgery and deteriorated anatomy, caused these false positive results. Although the differences were not statistically significant, in terms of detecting gastric lesions, $^{18}$F-FDG PET/CT was found to be more specific (100% vs. 80%) but less sensitive (86% vs. 100%) than contrast enhancement CT in our study which was concordant with the results of Altni et al [11].

The presence of lymph node metastases is an important prognostic factor in gastric carcinoma. $^{18}$F-PET/CT assesses metabolic and functional aspects better than the anatomic features of the tumor so occult metastases can be better detected than the conventional anatomy based imaging techniques. However, $^{18}$F-FDG is not specific for neoplastic cells and inflammatory tissue may also show intense $^{18}$F-FDG uptake. In our study, 1 patient in whom FDG uptake of right paratracheal lymph node was observed, but clarified as reactive in follow-up, was falsely classified as metastatic. Conversely, another patient with metastatic lymph nodes located in lung hilum were missed by $^{18}$F-FDG PET/CT because of physiological FDG uptake in lung hilum which is a frequent finding in $^{18}$F-FDG PET/CT but correctly diagnosed by CT. Another patient was a 55 year-old male with metastatic lymph node in perigastric area who was presented with recurrent disease. In this patient recurrent disease could be correctly detected with $^{18}$F-FDG PET/CT but metastatic perigastric lymph node was missed. A known limitation of $^{18}$F-FDG PET/CT systems is about their spatial resolution which prevents discriminating perigastric lymph nodes from primary tumors. However, in our patient the reason of false negativity was the low FDG uptake of metastatic lymph node. One parasternal metastatic lymph node area showing FDG uptake was missed with contrast enhancement CT but was caught by $^{18}$F-FDG PET/CT because enlargement of lymph nodes was not observed in disease involved lymph node on contrast enhancement CT.

In our study, the sensitivity of $^{18}$F-FDG PET/CT was found higher than the results of Altni et al. [11] Ha et al. [18] and Kwee et al. [19]. The diagnostic performance of $^{18}$F-FDG PET for detecting lymph node involvement depends on many factors including the avidity of primary tumor for $^{18}$F-FDG. In our study group, 18 of 20 (90%) patients had a diagnosis of nonmucinous type adenocarcinoma which has been reported to be as $^{18}$F-FDG avid.

The trend of higher sensitivity of contrast enhancement CT than $^{18}$F-FDG PET/CT for lymph node metastases in gastric carcinoma reported in the literature was also obvious in our study. Specificity, PPV and NPV were also higher for contrast enhancement CT than $^{18}$F-FDG PET/CT. Taken together, contrast enhancement CT was more accurate than $^{18}$F-FDG PET/CT for evaluating lymph node metastases.

In evaluating distant metastases, same results appeared for both...
modalities in terms of sensitivity (64%). Sensitivity values in gastric carcinoma for distant metastases reported with 18F-FDG PET/CT changes in the literature. For detecting solid organ metastases sensitivity of 95.2% was reported by Chung et al. [20] for 18F-FDG PET/CT. However, reported a value of 60% for distant metastases evaluation. 18F-FDG PET/CT displays functional aspects of tumor and metabolic abnormalities preclude the morphologic changes shown by anatomic imaging like CT. This drawback of anatomic imaging recognized also in our study and metastatic bone deposits that were hidden in well preserved anatomic structures, could only be detected with 18F-FDG PET/CT, which was discordant with the results of Yoshioka et al. [21]. Like reported in the literature for evaluating peritoneal dissemination, low sensitivity compared to contrast enhancement CT was noted also in our study and 2 patients with peritoneal implants could only be detected with contrast enhancement CT [3,21]. The specificity of 18F-FDG PET/CT for detecting distant metastases was higher than contrast enhancement CT but was not statistically significant which can be attributed to the low number of patients in each group. The higher specificity 18F-FDG PET/CT than contrast enhancement CT for detecting distant metastases was concordant with the literature [11] and the low specificity of contrast enhancement CT can be attributed to size dependent interpretative criteria of this imaging modality.

The limitation of our study was its retrospective origin. That’s why small number of patients could be included to the study. Lack of data about the size of primary tumor and histological confirmation of lymph node or distant metastatic areas can also be counted as limitations of our study.

In conclusion, our data showed that 18F-FDG PET/CT is a useful diagnostic modality for the evaluation of gastric carcinoma in detecting primary tumor, recurrent disease, lymph node and distant metastases. It has a comparable diagnostic performance with the standard imaging procedure of contrast enhancement CT in gastric carcinoma. Its higher specificity may reduce futile laparotomies. Because of the additive information provided by each modality, complimentary usage of these techniques may be more beneficial in evaluation of patients with gastric carcinoma.

References