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ORIGINAL ARTICLE

The role of ^{18}F-FDG PET/CT in the assessment of suspected recurrent gastric cancer after initial surgical resection: can the results of FDG PET/CT influence patients' treatment decision making?

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Abstract
Purpose ^{18}F-fluorodeoxyglucose (FDG) PET/CT has been widely used for staging, re-staging and for monitoring therapy-induced changes and response to therapy in patients with various types of cancer, but its utilization for gastric cancer has been limited. The purpose of this study was to evaluate the clinical role of FDG PET/CT in the detection of gastric cancer recurrence as compared with diagnostic CT and to assess the impact of FDG PET/CT results on patients' treatment planning.
Methods Thirty-four patients with suspected recurrent gastric cancer, who had previously undergone curative gastrectomy and lymph node dissection, were retrospectively analysed. The diagnostic CT and FDG PET/CT imaging were performed for all patients as clinically indicated. The results of FDG PET/CT were compared with the findings of the diagnostic CT. The changes in the clinical management of patients according to the results of FDG PET/CT were also evaluated.
Results FDG PET/CT was performed in 19 patients (55.9%) due to the suspicion of distant metastasis at diagnostic CT. The remaining 15 patients were suspected to have local recurrence at diagnostic CT (n=4) or gastroscopy (n=1) and due to an increase in tumour markers or clinical manifestations (n=10). The FDG PET/CT result was positive in 23 patients (67.6%) and negative in 11 patients (32.4%). In total, 24 (70.6%) of the 34 patients had documented recurrent disease by histopathology in 7 (29.1%) and by clinical follow-up in 17 (70.9%), while 11 patients had no evidence of recurrent disease. FDG PET/CT correctly confirmed recurrent disease in 23 of the patients with recurrence and it was classified as true-positive in these patients. However, FDG PET/CT was false-negative in one patient but recurrent disease was confirmed by histopathology. The overall sensitivity, specificity, accuracy, positive and negative predictive values of FDG PET/CT were significantly superior to those of diagnostic CT (95.8 vs 62.5%, 100 vs 10%, 97 vs 47%, 100 vs 62.5% and 90.9 vs 10%, respectively, p=0.012) in the detection of recurrent gastric cancer after initial surgery. The FDG PET/CT results changed the patients' management in 18 (52.9%) cases by leading to the use of previously unplanned treatment procedures in 9 (50%) patients and the avoidance of previously planned therapeutic procedures in 9 (50%) patients.
Conclusion FDG PET/CT is a superior post-therapy surveillance modality for the diagnosis of recurrent gastric cancer compared with diagnostic CT imaging after initial surgery. In addition, integrated FDG PET/CT was specifically helpful in optimizing the treatment plan and it might play an important role in treatment stratification in the future.

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Introduction

Gastric cancer is the fourth most common cancer worldwide. Although the incidence rate has decreased, it has still remained the second most common cause of cancer-related deaths [1, 2]. It is well documented that complete surgical removal of gastric tumours with lymph node dissection is the only currently available curative treatment. On the other hand, after radical surgery, disease recurrence occurs often, ranging from 22 to 48%, and its prognosis is very poor; the cumulative 5-year survival rate of all patients with gastric cancer has changed only slightly over the past four decades but still remains under 20% [3–6]. In their study Kodera et al. indicated that survival after the diagnosis of recurrent disease was better when recurrence was detected at an asymptomatic stage [7]. Some methods such as tumour markers, endoscopy or imaging studies have previously been used in order to detect gastric cancer recurrence. However, there are some limitations of tumour markers and endoscopy. Tumour markers cannot localize the recurrence site and endoscopy cannot detect extraluminal recurrence [8].

Computed tomography (CT) has been most frequently used in the detection of recurrence in patients with gastric cancer. It can detect both local recurrence and distant metastasis. There are only reports in respect to CT findings after radical gastrectomy published in the literature [9–11]. In these reports, the most important limitation of CT was defined as a lack of specificity in the diagnosis of locally recurrent gastric cancer because its diagnostic ability is dependent only on morphological changes of the involved organs and distorted anatomical structures. In addition, CT uses the size criteria. These factors result in difficulties in image interpretation [9]. Therefore, CT cannot precisely identify the presence and viability of tumours.

Whole-body positron emission tomography (PET) using ^{18}F-fluorodeoxyglucose (FDG), which exploits the increased utilization of glucose by malignant cells, is widely used for staging, re-staging and monitoring therapy-induced changes and response to therapy in patients with various cancers [12, 13]. However, in contrast to other malignancies, only limited reports are available on the clinical role of PET in patients with gastric cancer [14–20]. The majority of these studies were associated with staging of gastric cancer [14–18], and in two studies it was indicated that PET provided some additional information in the detection of recurrent gastric cancer [19, 20]. To date, the benefits of integrated FDG PET/CT in the diagnosis of recurrence for patients with gastric cancer have been investigated only in three studies [21–23] which found that FDG PET/CT was an effective and helpful diagnostic method in the diagnosis of recurrence. Furthermore, two of these trials analysed the impact of FDG PET/CT on treatment decisions [21, 23]. This study evaluated the clinical role of whole-body FDG PET/CT in the diagnosis and follow-up of recurrent gastric cancer patients according to the additional diagnostic information and subsequent clinical treatment. In addition, the results of FDG PET/CT were compared with diagnostic CT scans for the early detection of recurrence.

Materials and methods

Between February 2003 and September 2009 at Dr. Lutfi Kirdar Kartal Education and Research Hospital, 34 patients with suspected gastric cancer recurrence, who had undergone curative gastrectomy and FDG PET/CT imaging for diagnosis of recurrence, were retrospectively analysed. The FDG PET/CT scans had been carried out in all patients for a variety of indications: suspicion of distant metastasis at diagnostic CT, the suspicion of local recurrence at diagnostic CT or gastroscopy and the possibility of recurrence due to an increase in tumour markers or clinical manifestations. Moreover, diagnostic CT scans for all patients were performed previous to FDG PET/CT. The inclusion criteria were histopathologically confirmed diagnosis of gastric cancer with curative gastrectomy and suspected gastric cancer recurrence, whereas the exclusion criteria were contraindications to FDG PET/CT scanning, including a blood glucose level higher than 200 mg/dl and intolerance of FDG PET/CT owing to claustrophobia.

Clinical information such as age at diagnosis, tumour stage, grade, histopathological type and number of chemotherapy cycles administered, imaging study finding, serum carcinoembryonic antigen (CEA) and CA 19.9 levels at the time of FDG PET/CT performance were obtained from patients' charts after informed written consent was given by each subject included in the study.

Twenty-six (76.5%) patients were treated with the initial standard adjuvant therapy for gastric cancer, including a 5-fluorouracil and leucovorin calcium regimen after radical gastrectomy with lymph node dissection. The other eight patients (23.5%) did not receive adjuvant chemotherapy because of the early stage of disease in seven cases and one patient's refusal. In addition, 18 patients (52.9%) were treated with adjuvant radiotherapy. The majority of patients had an adenocarcinoma (n=26, 76.5%). The median age was 58.5 ranging from 32 to 79 years. Twenty-seven patients (79.4%) were men and seven (20.6%) were women. Patient characteristics are listed in Table 1.

Table 1 Characteristics of the patients with suspected recurrent gastric cancer

Characteristics	*n* (%)
Median age, years	58.5
Range	32–79
Gender	
Male	27 (79.4)
Female	7 (20.6)
Surgery type	
Proximal	8 (23.5)
Distal	12 (35.3)
Total	14 (41.2)
Tumour site	
Upper	9 (26.5)
Middle	13 (38.2)
Lower	11 (32.4)
Diffuse	1 (2.9)
Histopathology	
Adenocarcinoma	26 (76.5)
Signet ring cell type	8 (23.5)
Tumour differentiation	
Well differentiated	2 (5.9)
Moderately differentiated	20 (58.8)
Poorly differentiated	12 (35.3)
pT stage	
T1	1 (2.9)
T2	15 (44.1)
T3	17 (50.0)
T4	1 (2.9)
pN stage	
N0	11 (32.4)
N1	11 (32.4)
N2	10 (29.4)
N3	2 (5.9)
Clinical stage	
Stage I	6 (17.6)
Stage II	9 (26.5)
Stage III	17 (50.0)
Stage IV	2 (5.9)
Adjuvant chemotherapy	
Yes	26 (76.5)
No	8 (23.5)
Adjuvant radiotherapy	
Yes	18 (52.9)
No	16 (47.1)
Interval between diagnostic CT and FDG PET/CT	
Median, range	2 weeks (1–4 weeks)

Imaging technique

Chest and abdomen/pelvis diagnostic CT imaging were performed using the MS CT scanner (Siemens Somatom Sensation, 40-slice CT system). Images with 40×0.72 mm collimation were obtained. Axial, coronal and sagittal reformations with different thicknesses were acquired using maximum intensity projection (MIP)+multiplanar reformation (MPR) before and after administration of iomeprol contrast medium 1 ml/kg (60–100 ml) from the xiphoid process to the pubic symphysis with i.v. early arterial and portal phases for the abdomen and pelvis. For the thorax, axial images with 40×0.72 mm collimation and coronal and sagittal reformations using MIP+MPR before and after administration of 1 ml/kg (60–100 ml) iomeprol contrast medium were obtained from the thoracic inlet to inferior of the surrenal glands.

The median interval between diagnostic CT and FDG PET/CT was 2 weeks (range 1–4 weeks). The patients fasted for at least 6 h prior to imaging and their blood glucose levels were obtained prior to tracer injection. The blood glucose levels of all patients were below 200 mg/dl at the time of FDG injection. Each patient received 10–15 mCi (370–550 Mbq) of FDG as a tracer intravenously. Following this, the patients rested on a comfortable chair for 1 h to allow FDG biodistribution. For the optimal delineation of bowel structures, 400–600 ml of contrast material diluted to 2.4% (v/v) with water was ingested 1 h before CT imaging. No urinary bladder catheterization was performed, and no diuretics were administered at this time. Whole-body imaging was performed 1 h after radiotracer injection using a Siemens Biograph Duo PET/CT scanner with lutetium orthosilicate (LSO) detectors. First, low-dose CT was performed with 140 kV, 50 mA, a table speed of 22.5 mm/s and without any specific breath-holding instructions. Scanning from the top of the skull down to the upper thighs was performed in a single step with the patients in the supine position. CT data were used for attenuation correction (5 mm contiguous axial cuts). Immediately afterwards, a PET emission scan was obtained without changing the patient's position. Six to eight bed positions were used with an acquisition time of 5 min for each bed position. The PET scan was acquired in a three-dimensional mode over the same anatomical regions, starting at the level of the mid-thighs. The PET image data sets were reconstructed iteratively using the CT data for attenuation correction and coregistered images were displayed on a workstation.

Image analysis

The diagnostic CT images were interpreted by an experienced radiologist who had no knowledge of the FDG PET/

CT findings. Recurrent viable tumours on diagnostic CT images were identified by the presence of a highly contrast-enhanced, predominantly solid lesion in the gastric region. Relapses of disease were also identified as areas of abnormal contrast enhancement in the pelvis, the abdomen and in the thorax. The diagnosis of lymph node involvement by neoplastic disease on the diagnostic CT images was based on morphological criteria. The presence of distant metastases was also evaluated.

All FDG PET/CT images were analysed by an expert nuclear medicine physician who had knowledge of the diagnostic CT findings. Attenuation-corrected PET images, CT scans and coregistered PET/CT images were interpreted using a dedicated image fusion workstation and a final consensus was reached for all patients. Any foci of increased FDG uptake, except for areas of physiologically increased FDG uptake, that corresponded to a CT abnormality (tissue or lymph node) were considered to be positive for recurrent lesions. Suspicious findings on CT were evaluated as negative if they did not correspond to an area of increased FDG uptake. Standardized uptake values (SUV) greater than 3.0 were considered to be indicative of malignant lesions in the light of previous reports [24, 25].

Follow-up

The final diagnosis of recurrence was obtained from the results of histopathological examination after surgery, laparotomy or biopsy, or clinical follow-up of at least 6 months. Clinical recurrence was defined as the detection of recurrent disease by contrast-enhanced diagnostic CT within 6 months of the FDG PET/CT scan. Recurrent disease detected more than 6 months after the FDG PET/CT scan was interpreted as a new recurrence. For the assessment of treatment response following chemotherapy, a complete response (CR) was defined as the disappearance of all measurable disease, a partial response (PR) represented a decrease of at least 30% of the tumour volume and progressive disease (PD) was defined as more than a 20% increase in tumour volume or any new sites of disease, according to Response Evaluation Criteria In Solid Tumors (RECIST) guidelines [26].

Statistical analysis

The sensitivity, specificity, accuracy, positive predictive value (PPV) and negative predictive value (NPV) for tumour detection of FDG PET/CT scans were calculated using the McNemar test of correlated proportions with Yates' continuity correction. For the purpose of statistical analysis, a true-positive lesion was a lesion seen on FDG PET/CT images and found to be positive for tumour tissue at histological examination or clinical follow-up. A false-positive lesion was a lesion seen on FDG PET/CT images but found to be negative for tumour tissue at histological analysis or clinical follow-up. Moreover, a true-negative lesion was defined where no lesion was seen on FDG PET/CT images and the results of histopathological examination for tumours or clinical follow-up were negative. A false-negative lesion was a lesion that was missed at image analysis but was found to be positive for malignancy at histopathological analysis or clinical follow-up. The analyses were carried out using SPSS 17.0 (SPSS Inc., Chicago, IL, USA) software. The significance of the differences among the results of FDG PET/CT and diagnostic CT were determined by the chi-square test. The receiver-operating characteristic (ROC) analysis was performed for detection of a cutoff value of SUV_{max} which showed the presence of recurrent lesions. All p values were two-sided in tests and p values less than 0.05 were considered to be statistically significant.

Results

A total of 34 patients who underwent FDG PET/CT and diagnostic CT imaging for the determination of suspected recurrent gastric cancer were retrospectively analysed. Overall, 24 of the 34 patients (70.6%) developed recurrent disease during the follow-up period (median 24.4 months, range 6–112.5 months). Of the 24 patients with recurrent disease, 7 (29.1%) were documented to have recurrence by pathological examination after surgery or surgical biopsy, while recurrence was confirmed in 17 (70.9%) by clinical follow-up as previously defined. The SUV_{max} ranged from 4.3 to 20.3 (mean 11.1±4.8).

The decision to perform the FDG PET/CT scans was based on one of the following clinical indications. The indications and results of FDG PET/CT, mean SUV_{max} values, mean sizes of lesions and the sites of recurrence are listed in Table 2. In 19 of 34 patients (55.9%), FDG PET/CT scans were performed because of suspicion of distant metastasis at diagnostic CT and to accurately localize the extent of disease for treatment planning. The median time to FDG PET/CT after the completion of initial treatment was 5.3 months (range 2–26.7 months). The mean SUV_{max} value and mean size of lesions at the time of FDG PET/CT imaging were 12.5±5.61 (range,3.3–20.3) and 4.1±2.15 cm (range 1.5–9), respectively. Of these 19 FDG PET/CT scans, 12 (63.1%) correctly revealed recurrent disease. Recurrence was confirmed histopathologically in three patients and by clinical follow-up for a median of 27.1 months (range 7.6–107 months) after FDG PET/CT in nine cases. The FDG PET/CT results were true-positive in these 12 patients. However, the FDG PET/CT results

Table 2 Number of positive FDG PET/CT imagings and confirmed recurrences, mean SUV_{max}, the size of lesions and the sites of recurrence in patients with gastric cancer according to the indications of FDG PET/CT scan

Indications of FDG PET/CT	No. of patients (%)	FDG PET/CT positive (true or false), *n* (%)	Confirmed recurrence, *n* (%)	SUV_{max}, mean±SD	The size of lesions, cm, mean±SD (range)	The sites of recurrence
Suspicion of distant metastasis at diagnostic CT	19 (55.9)	12 (63.1)	12 (63.1)	12.5±5.61	4.1±2.15 (1.5–9)	Gastric operation site, liver, mediastinal, left axillary, para-aortic, left common iliac, celiac, retroperitoneal LNM, bone and surrenal glands
Suspicion of local recurrence at diagnostic CT	4 (11.8)	2 (50)	2 (50)	7.5±0.7	4.5±2.12 (3–6)	Gastric operation site
Suspicion of local recurrence at gastroscopy	1 (2.9)	False-negative	NA	NA	NA	NA
Possibility of recurrence due to increase in tumour markers or clinical manifestations	10 (29.4)	9 (90)	9 (90)	9.9±3.56	3.27±0.66 (2.5–4.5)	Liver, lung, gastric operation site, mediastinal, para-aortic, peripancreatic, supraclavicular, right iliac and left internal iliac LNM, peritoneum

NA not applicable, *SD* standard deviation, *SUV_{max}* maximum standardized uptake value, *LNM* lymph node metastasis

were classified as true-negative in the remaining seven patients. Following FDG PET/CT scans, two patients underwent surgical resection followed by chemotherapy. The other ten patients were treated with chemotherapy alone. The overall sensitivity, specificity, accuracy, PPV and NPV of FDG PET/CT in the determination of recurrent gastric cancer in this setting were 100, 100, 100, 100 and 100%, respectively.

FDG PET/CT was carried out in four patients (11.8%) due to the suspicion of local recurrence at diagnostic CT. The median interval between initial treatment and FDG PET/CT was 6.9 months (range 2.5–13.1 months). The mean SUV_{max} value and mean size of lesions were 7.5±0.7 (range, –8) and 4.5±2.12 cm (range,3–6), respectively. In two of four patients (50%), FDG PET/CT scans correctly identified recurrent disease. Recurrence was documented by pathology in one case and by clinical follow-up after a median of 36.5 months (range 6–112.5 months) in one patient. The FDG PET/CT results were classified as true-positive in these cases. After the FDG PET/CT scan, surgical resection was successfully performed in one of these patients. The other patient was treated with recurrent chemotherapy alone. In the remaining two patients, FDG PET/CT scans were true-negative and no recurrent disease was detected by clinical follow-up during the 6-month period after FDG PET/CT.

The FDG PET/CT scans were also performed due to an increase in tumour markers or clinical manifestations indicating the possibility of recurrence in ten patients. In this setting, the median time to FDG PET/CT after the completion of initial treatment was 4 months (range 3–8.4 months). Furthermore, the median serum CEA and CA 19.9 levels were 24.06 ng/ml (range 1.12–173.7) and 15.3 U/ml (range 0.60–1,000). The mean SUV_{max} value and mean size of lesions were 9.9±3.56 (range 5.6–15.4) and 3.27±0.66 cm (range 2.5–4.5). Of these ten FDG PET/CT scans, nine (90%) correctly indicated recurrent disease. Recurrence was confirmed histopathologically in two patients and by clinical follow-up after a median time of 18.7 months (range 7.7–64.9) in seven cases. The FDG PET/CT scans were true-positive in these nine patients. Following FDG PET/CT scans, all nine patients with recurrent disease received chemotherapy. The FDG PET/CT scans were classified as true-negative in the other case and recurrent disease was not observed by clinical follow-up during the 6-month period after FDG PET/CT. The overall sensitivity, specificity, accuracy, PPV and NPV for FDG PET/CT in the detection of recurrent disease in this setting were 100, 100, 100,100 and 100%, respectively.

In the remaining patient (1 of 34 patients), FDG PET/CT was performed for the suspicion of local recurrence at gastroscopy. This patient was a 54-year-old man and despite the finding of stage IIIA disease being found, adjuvant therapy could not be administered because of his refusal after the initial surgery. The FDG PET/CT result was classified as false-negative. Thereafter, recurrence was correctly confirmed by laparotomy and peritoneal biopsy. He was treated by recurrent chemotherapy alone.

The diagnostic CT scan was performed for all patients before the FDG PET/CT scan. In total, 34 diagnostic CT scans were compared with FDG PET/CT scans. Fifteen CT scans (44.1%) correctly revealed recurrent disease and the diagnostic CT was true-positive in these patients. However, the diagnostic CT scan was classified as false-negative in

nine patients and false-positive in nine patients. In the remaining patient the diagnostic CT scan was true-negative. The overall sensitivity, specificity, PPV, NPV and accuracy of diagnostic CT in determining recurrent gastric cancer in this setting were 62.5, 10, 62.5, 10 and 47%, respectively. The results of the diagnostic CT scans were confirmed with FDG PET/CT after a median of 2 weeks (range 1–4 weeks).

A total of 34 FDG PET scans were carried out in all of the patients described above. The overall patient-based sensitivity, specificity, accuracy, PPV and NPV of FDG PET/CT in determining recurrent gastric cancer were 95.8, 100, 97, 100 and 90.9%, respectively. The scanning study analysis in the 34 patients showed a higher sensitivity, specificity, accuracy, PPV and NPV by FDG PET/CT than by the diagnostic CT scans (p=0.012). Table 3 summarizes the results of the FDG PET/CT and diagnostic CT scans for all patients.

The ROC analysis indicated that the sensitivity and the specificity of the presence of recurrence with a cutoff value of 2.3 SUV_{max} during FDG PET/CT were accurately indicative of recurrent lesions in 95.8% [95% confidence interval (CI) 78.9–99.9%] and 100% (95% CI 69.2–100%), respectively (AUC=0.977, p=0.0001) (Fig. 1). In 23 of 34 patients (67.6%), the cutoff value of SUV_{max} was greater than 2.3. In this subgroup, the FDG PET/CT scan revealed recurrent disease. The remaining 11 cases had a cutoff value of SUV_{max} which was less than or equal to 2.3, and FDG PET/CT was classified as true-negative in 10 patients while 1 case was categorized as false-negative.

In the present study we detected that FDG PET/CT had a high impact on patients' management or care. Further diagnostic or treatment plans were changed in 18 patients (52.9%). In 9 (50%) of 18 patients, suspected recurrent lesions were accurately confirmed by FDG PET/CT; thereafter, they were treated with previously unplanned surgery or recurrent chemotherapy. However, the remaining nine (50%) cases with abnormal diagnostic CT scans were revealed to have lesions with physiological or inflammatory uptake of FDG leading to cancellation of previously planned diagnostic procedures and chemotherapy. The results of the changes in patients' management are listed in Table 4.

Metastatic perigastric and mesenteric lymph nodes (SUV_{max} 7.8 and 4.9, respectively) in the FDG PET/CT scan of a 72-year-old man with gastric cancer are shown in Fig. 2.

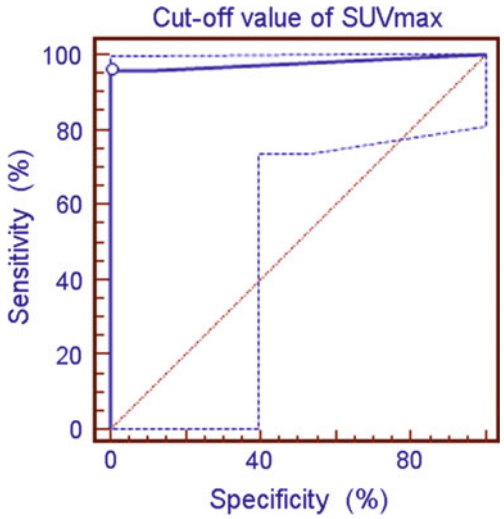

Fig. 1 ROC curve shows the SUV_{max} cutoff value during FDG PET/CT that was indicative of recurrence

Table 3 Comparison of the results of FDG PET/CT with the results of diagnostic CT scan

Performance	FDG PET/CT	Diagnostic CT
True-positive (*n*)	23	15
True-negative (*n*)	10	1
False-positive (*n*)	-	9
False-negative (*n*)	1	9
Sensitivity (%)	95.8	62.5
Specificity (%)	100	10
PPV (%)	100	62.5
NPV (%)	90.9	10
Accuracy (%)	97	47

PPV positive predictive value, *NPV* negative predictive value

Discussion

In the present study we found that the overall sensitivity, specificity, accuracy, PPV and NPV of FDG PET/CT were significantly superior to those of diagnostic CT in the diagnosis of recurrent gastric cancer after initial surgery. In addition, integrated FDG PET/CT was specifically helpful in optimizing treatment decisions.

Relapse patterns after radical surgery indicate that subsequent recurrence of gastric cancer is common in the

Table 4 Changes of patients' management based on FDG PET/CT results

Initial plan	FDG PET/CT findings	FDG PET/CT contribution	No. of patients (%)
Observation	Precise localization of recurrent lesion	Additional treatment instituted	9 (50)
Additional diagnostic or treatment procedure	Physiological or inflammatory uptake of FDG	Cancellation of unnecessary diagnostic or treatment rocedures	9 (50)

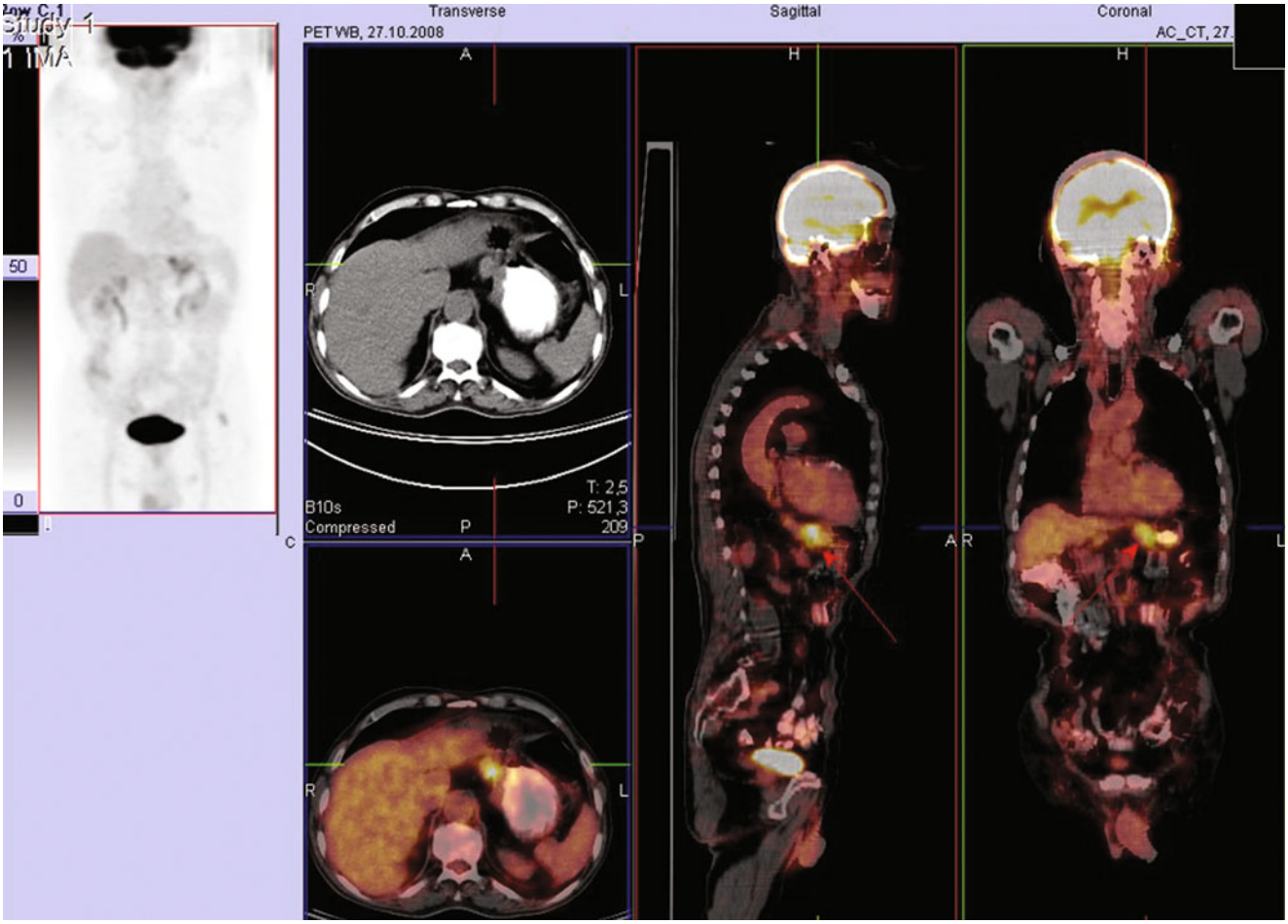

Fig. 2 FDG PET/CT images in a 72-year-old man with gastric cancer. The scan was carried out because of the suspicion of distant metastasis at diagnostic CT and an increase in tumour markers. The images show metastases in the perigastric and mesenteric lymph nodes. He was treated with recurrent chemotherapy and then CR was achieved

tumour bed and nodal regions as well as all over the body [27, 28]. The optimal modality for the diagnosis of early recurrence in gastric cancer patients is unknown. Available conventional imaging and endoscopy are the standard methods for staging and re-staging of gastric cancer, but they offer little diagnostic advantage over clinical surveillance alone and do not excel in the diagnosis of suspected recurrence [29–31]. These techniques are entirely structure based and their interpretation suffers from low tumour specificity, particularly in postoperative surveillance where the disruption of normal anatomical planes and postoperative fibrotic and inflammatory changes preclude accurate diagnosis [19].

FDG PET has been documented to provide increased accuracy compared with the conventional methods for the diagnosis of primary and recurrent gastrointestinal cancers, such as colorectal and oesophageal cancers [32, 33]. There are only limited reports in respect to the clinical role of FDG PET in patients with gastric cancer [14–20]. Jadvar et al. found that PET provided some additional information in the detection of recurrent gastric cancer and that it might be useful in the post-therapy evaluation of recurrent disease [20]. On the other hand, De Potter et al. indicated that FDG PET was not suitable for screening purposes in the follow-up of treated gastric cancer [19]. There are only three reports in the English medical literature about the benefits of integrated FDG PET/CT in the diagnosis of recurrence for patients with gastric cancer [21–23], and in these studies the effectiveness and helpfulness of FDG PET/CT as a diagnostic modality in the detection of recurrent gastric cancer was documented.

Our study demonstrated the feasibility of using FDG PET/CT for the diagnosis of tumour recurrence in patients with previously treated gastric cancer and equivocal imaging findings. Park et al. evaluated the role of FDG PET/CT in detecting recurrence in gastric cancer patients [22]. They analysed 105 patients with suspected recurrent gastric cancer and found that FDG PET/CT confirmed true recurrence in 75 patients, with 108 sites of recurrence. In addition, the authors indicated that in patients with gastric

cancer, the sensitivity, specificity, PPV, NPV and accuracy of FDG PET/CT for the diagnosis of true recurrence on a per-person basis were 75, 77, 89, 55 and 75%, respectively. Thereafter, they concluded that FDG PET/CT was relatively accurate in detecting recurrence in postoperative patients with gastric cancer. However, in their study the effect of FDG PET/CT on patients' management was not evaluated.

In another study performed by Sun et al., they evaluated the value of FDG PET/CT in postoperative follow-up of gastric cancer patients [21]. The authors found that FDG PET/CT was true-positive in 12 of 23 patients and false-positive in only 2 patients. According to the final diagnosis of recurrence, they detected that overall the accuracy, PPV and NPV of FDG PET/CT were 82.6, 77.7 and 85.7%, respectively. Recently, Sim et al. [23] retrospectively analysed the utility of FDG PET/CT as compared with contrast CT in 52 patients with suspected gastric cancer recurrence. They found that gastric cancer recurrence was correctly confirmed in 38 patients and the sensitivity and specificity of FDG PET/CT were similar to those of contrast CT in all sites except the peritoneum (68.4 vs 89.4% and 71.4 vs 64.2%, respectively). However, the authors indicated that contrast CT was more sensitive than FDG PET in the detection of peritoneal seeding (p=0.039).

We also compared enhanced FDG PET/CT with enhanced diagnostic CT in the detection of suspected recurrent gastric cancer. The overall sensitivity, specificity, accuracy, PPV and NPV for FDG PET/CT were significantly superior to those of diagnostic CT (95.8 vs 62.5%, 100 vs 10%, 97 vs 47%, 100 vs 62.5% and 90.9 vs 10%, respectively, p=0.012). The superiority of FDG PET/CT over contrast CT was not indicated in only one study of the aforementioned trials [23]. Our results were better than those of the aforementioned reports [21–23]. However, the present study had a small sample size and this might have influenced the results.

FDG PET/CT had the greatest utility in patients with a suspicion of distant metastasis at diagnostic CT and the possibility of recurrence indicated by an increase in tumour markers or clinical manifestations. In these settings, a total of 29 patients underwent FDG PET/CT and recurrent disease was correctly identified in 21 patients. In the other eight patients, the results of FDG PET/CT were true-negative. The sensitivity, specificity, accuracy, PPV and NPV of FDG PET/CT in these categories were 100, 100, 100, 100 and 100%, respectively.

The ability to identify the extent and correct location of disease in some recurrent cancers is important for the subsequent selection of therapeutic modalities. In a study carried out by Sun et al. [21], a change in clinical management was observed in 30.4% of cases when FDG PET/CT information was introduced into conventional follow-up findings. Sim et al. [23] also investigated the role of FDG PET/CT in the assessment of suspected recurrent gastric cancer and demonstrated that the treatment decision in seven patients was made according to the FDG PET/CT findings and the diagnostic accuracy of PET/CT was 42.8%.

After comparing the FDG PET/CT scan with diagnostic CT in the detection of gastric cancer recurrences in the present study, the patients' clinical management was changed in 52.9% of cases. Nine (50%) patients with negative diagnostic CT scans and no clinical symptoms of recurrent disease were found to have suspected recurrent lesions on FDG PET/CT; thereafter, they were treated with previously unplanned recurrent treatment modalities. All of the patients in this setting had true-positive FDG PET/CT scans. However, the remaining nine (50%) cases with abnormal diagnostic CT scans were revealed to have lesions with physiological or inflammatory uptake of FDG on FDG PET/CT. In these cases, previously planned diagnostic procedures or chemotherapy were cancelled. Our results were thus compatible with those in the literature for modification of treatment planning.

Some malignant tumours are known to be non-FDG avid, such as neuroendocrine tumours, renal cell carcinomas, prostatic carcinomas, bronchoalveolar carcinomas and mucinous and low-grade tumours, so these tumours can result in false-negative PET findings [34]. However, some histopathological types of gastric cancer have no FDG uptake and thus they can pose false-negative findings. In the mucinous and signet ring cell carcinoma, as well as poorly differentiated adenocarcinoma, a low rate of FDG uptake has been previously indicated by some reports [15, 17, 18]. Park et al. detected that 13 of 17 false-negative patients had poorly differentiated adenocarcinoma, mucinous carcinoma, signet ring cell carcinoma [22], bronchoalveolar carcinomas and mucinous and low-grade tumours. In our study, only one false-negative patient was found by the FDG PET/CT scan and he had signet ring cell carcinoma histology, as compatible with the literature.

The ROC analysis showed that an FDG PET/CT SUV_{max} cutoff value of 2.3 accurately indicated recurrent lesions. Because the patients with true-negative PET/CT scans were included into ROC analyses, 10 of 11 patients whose SUV_{max} values were less than 2.3 had true-negative PET/CT scan and in only 1 patient was SUV_{max} 2.3. This may be associated with the small sample size in the subgroup including cases who had SUV_{max} cutoff values less than or equal to 2.3, despite high specificity and sensitivity of SUV_{max} cutoff values in the ROC analysis. In this subgroup, FDG PET/CT scans were true-negative, except for one case with negative diagnostic CT. However, the mean SUV_{max} values of 23 patients with true-positive PET/CT and 1 patient with false-negative PET/CT were 11.1±4.8 (range 4.3–20.3).

The major limitations of this study were the small sample size and the retrospective nature of the study. In addition, an at least 6-month follow-up period may not be sufficient to confirm the absence or presence of recurrence. However, although our results need to be confirmed by prospective studies including larger sample sizes, we believe that our results contribute to the literature because of the impact of FDG PET/CT findings on patients' management and the superiority of FDG PET/CT over diagnostic CT in patients with suspected gastric cancer recurrence.

In conclusion, our results confirm that FDG PET/CT is a highly effective modality for post-therapy surveillance for the detection of recurrent gastric cancer compared with diagnostic CT imaging, especially in patients with an indication of distant metastasis at diagnostic CT and an increase in tumour markers or clinical manifestations. Moreover, our results, together with those in the literature, demonstrate that integrated FDG PET/CT allows optimization of the treatment plan and might play an important role in treatment decision making. Future studies will need to address the effect of FDG PET/CT on the survival of patients and their clinical management, and the relationship between clinicopathological variables and the findings of FDG PET/CT.

Conflicts of interest None.

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