The application of ^{18}F-FDG-PET/CT in gastric cancer staging and factors affecting its sensitivity

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Abstract

Objective: To evaluate the accuracy of fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography (^{18}F-FDG PET/CT), to correctly determine initial tumor stage in treatment-naive gastric cancer patients and to analyze the factors influencing the risk of false negative results. **Materials and Methods:** The baseline ^{18}F-FDG PET/CT scans of 111 previously untreated gastric cancer patients were retrospectively assessed. Sensitivity, specificity, positive (PPV) and negative prediction value (NPV) were evaluated. An array of clinical, pathological and metabolic variables was analyzed to identify factors contributing to the risk of a false positive (FP) and false negative (FN) PET/CT result in detecting primary and metastatic tumor sites. **Results:** The sensitivity, specificity, PPV and NPV of PET/CT to visualize distant metastases were 76.4%; 86.7%; 83% and 81.2%, respectively. In 13 (11.7%) patients the PET/CT exam was able to identify metastatic sites not recognized in radiographic staging, significantly altering the initially planned management. Of 64 PET/CT studies negative for distant metastases, 12 (18.75%) were clinically confirmed to be false negative. The risk of acquiring a FN result for primary tumor was 10.8% (12/111) and the overall risk of any FN readout for either primary and metastatic sites was 18.9% (21/111). The factors that contributed to increased probability of a FN result for primary tumor detection were early primary tumor stage T1-T2 (+16.2%; χ^2=5.0, P=0.025), female sex (+10.1%; χ^2=5.71, P=0.017) and neutrophil count below 4.2k/μL (9.7%; χ^2=6.1, P=0.014). Patients with non-intestinal Lauren histologic type (+18.7%; χ^2=8.9, P=0.003) or signet-ring/mucinous carcinoma (+9.6%; χ^2=7.7, P=0.005) had increased probability of PET/CT being unable to identify their distant metastases. Women and patients with low neutrophil count featured borderline insignificantly increased percentage of non-intestinal tumor histology (P=0.07 and P=0.057, respectively). **Conclusion:** Fluorine-18-FDG PET/CT is a valuable diagnostic method in gastric cancer patients which significantly contributes to determining the TNM stage and thus helps choose correct patient management. Histology and primary tumor stage as well as patient cohorts in which these factors may vary should be considered when evaluating results to decrease a chance of a false negative readout.

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Introduction

Gastric cancer (GC) is the fifth most frequent malignant tumor diagnosis worldwide and the third most frequent cause of cancer deaths. One million thirty-three thousand seven hundred and one (1.033.701) new cases and 782.685 deaths were recorded in 2018 [1]. In Europe the 5-year overall survival in GC is as low as 10%-30% which can be attributed to late diagnosis and lack of effective therapies in advanced stages [2, 3]. Up to 40% of recurrences in locally advanced T3-T4 stages involves distant lymphatic and peritoneal metastasis, typically occurring 2-3 years after primary definitive treatment [4-6]. Moreover, as much as one third of locally advanced GC patients features synchronic occult metastatic disease (OMD). This data suggests that introduction of routine diagnostic laparoscopy as well as fluorine-18-fluorodeoxyglucose positron emission tomography/computed tomography^{18}F-FDG PET/CT could improve early detection of OMD and alter management in these patients [7, 8]. According to both National Comprehensive Cancer Network (NCCN) and European Society for Medical Oncology (ESMO) guidelines the ^{18}F-FDG PET/CT should not be routinely performed as part of the initial workup, but is a valuable method to confirm pre-surgical staging [9] and detect disease dissemination [10]. In the recent years a number of publications highlighted the additional prognostic significance of PET/CT for GC as well as its added value in the planning of definitive GC radiotherapy [11, 12].

The PET/CT has been reported to feature greatest sensitivity in advanced local tumor stages (83%-98% for T2-T4), while for least advanced tumors it might be limited (26%-63%). The specificity is expected to be notably higher (62%-100%). The ^{18}F-FDG uptake

might be unrepresentative in diffuse, mucocellular/signet-ring carcinoma (SRC), peritoneal metastasis or primary tumors of limited size [5,13,14]. On the other hand, a number of random conditions may display ^{18}F-FDG uptake mimicking gastric malignancies, i.e. inflammation or increased ovarian uptake in pre-ovulation period (false positive for Krukenberg tumors) [15,16]. Previous studies also found tracer uptake in representative normal tissues to affect the tumor-to-background ratio, naming it another possible factor for risk of study inaccuracy [18-20].

Despite many reports showing the added value of ^{18}F-FDG PET/CT in GC, doubts arise whether it is best suitable for its staging due to concerns about the false negative results in aforementioned conditions. In the present study we therefore aim to assess the diagnostic reliability of ^{18}F-FDG PET/CT as a staging tool for treatment-naive GC in an unselected patient cohort and analyze an array of clinical and metabolic features to identify ones increasing the risk of incorrect results.

Materials and Methods

Patient cohort

The study was approved by the local ethics committee (approval No. KB/493-59/09) in accordance with the Helsinki Declaration of 1975, revised in 2000. The recruitment process included GC patients who underwent ^{18}F-FDG PET/CT imaging between 2008 and 2019 in Maria Skłodowska-Curie National Research Institute of Oncology, Gliwice Branch, Poland. One hundred and eleven unselected patients with no tumor treatment prior to the PET/CT examination were enrolled in the study. Initially, all patients underwent diagnostic abdominal contrast-enhanced CT, chest CT/X-rays or upper gastrointestinal gastroscopy with lesion biopsy followed by a histopathological examination. Lab tests included hematology, blood chemistry, neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR); carcinoembryonic antigen (CEA) and carbohydrate antigen 19-9 (CA19.9) markers as well as serum albumin (ALB). The PET/CT exam was performed to determine or confirm the disease stage. For clinical tumor staging (TNM), American Joint Committee on Cancer (AJCC) v.7 was utilized. Histology was grouped according to both Japanese classification for gastric cancer (JCGC) [22] and Lauren type [23]. Patients with a history of other malignancies, acute inflammatory disease, non-neoplastic bone marrow or liver disease, surgical interventions in the abdominal cavity less than 4 weeks prior to the study or decompensated diabetes were excluded from the study.

PET/CT protocol

Fluorine-18-FDG PET/CT was performed using one of the two hybrid PET/CT scanners available in the Department of PET Diagnostics: Biograph™ mCT, (Siemens, Erlangen, Germany) or Gemini XL (Philips, Eindhoven, the Netherlands) according to an internal protocol. Specifically, after 6 hours of fasting, patients were intravenously given the radiotracer (^{18}F-FDG), with activities ranging 185-555MBq (3.7MBq/Kg). Buscopan 20mg was also given. Prior to ^{18}F-FDG administration, each patient had a blood glucose concentration level of <200mg/dL. Acquisition was performed 60±10 minutes after tracer injection and drinking of 500mL of water. Computed tomography scans were performed without contrast agent within an average of 9.6 seconds on exhaust breath phase. The PET layer acquisition took 17-20 minutes, approximately 2 minutes for each bed position, ranging from skull base to the upper 1/3 of the femur. Both PET and CT scans involved the same region of the body with the same field of view (FOV) and slice thickness of 3mm. The PET/CT scanners installed in the Department of PET Diagnostics are periodically cross-calibrated with the same dose probe according to the manufacturer's recommendations.

PET/CT interpretation and assessment of metabolic parameters

The PET/CT images were evaluated on Syngo.via PET/CT to find all sites of tracer uptake suspected for tumor lesions; first independently, and subsequently referred to the findings in other prior imaging studies as well as the prior or later acquired pathology reports. For patients with positive ^{18}F-FDG uptake around gastric lesions, a spheroid-shaped volume of interest (VOI) was drawn over each lesion, and maximum standardized uptake value (SUVmax) of the tumor was recorded. Accordingly, VOI were determined based on contrast-enhanced CT images and gastroduodenoscopy reports. Standardized uptake value was calculated using the following formula: *decay-corrected activity (kBq)/tissue volume (mL)]/[injected FDG activity (kBq)/body mass (g)]*.

Positron emission tomography-negative were considered the lesions withSUVmax<2.5 or diffuse, only minimally increased uptake in normal stomach wall that was difficult to demarcate and without a macroscopic substrate in CT. Sensitivity, specificity, positive (PPV) and negative predictive value (NPV) were calculated with regard to ability of PET/CT to identify distant metastases. For primary tumor detection no true negative (as well as false positive) results were obviously possible, therefore only sensitivity could be calculated.

The following metabolic parameters were evaluated: maximum and mean SUV of normal liver parenchyma ($SUVliv_{max}$ and $SUVliv_{mean}$, respectively) and spleen SUV ($SUVspl_{max}$ and $SUVspl_{mean}$), as well as bone marrow ^{18}F-FDG uptake (BMU) were evaluated. The mean SUV of normal liver ±2SD, measured in two 1.5cm-sized spheroid-shaped VOI in the right lobe, was classified as normal liver uptake. The average value of the two counted as $SUVliv_{mean}$. The SUVmax of these VOI was recorded and the higher value was determined as $SUVliv_{max}$. Correspondingly, $SUVspl_{max}$ and $SUVspl_{mean}$ were calculated.

Subsequently, the bone marrow ^{18}F-FDG uptake was measured for each patient by drawing the spheroid-shaped VOI over the vertebral bodies of at least six vertebrae of both thoracic and lumbar spine, typically including Th10-Th12 and L3-5 and excluding ones in which compression fracture, severe degenerative arthritis or post-surgical spinal abnormalities was observed. The mean SUV of each vertebral body was measured using an automatic isocontour set at 75% of the maximum SUV within each VOI. The mean value of mean SUV of vertebral bodies was defined as BMU. Practical

examples of VOI in these locations are depicted on Figure 1. The following composite parameters were recorded: maximum SLR ($SUVspl_{max}/SUVliv_{max}$), mean SLR ($SUVspl_{mean}/SUVliv_{mean}$) and BLR ($BMU/SUVliv_{mean}$).

Statistical analysis

Statistical calculations were performed using the Statisticav.13.1 (Statsoft Inc. Tulsa, U.S.) and Stata 15 (Stata, College Station, U.S.). All results with ($P<0.05$) were considered statistically significant.

The impact of clinical and metabolic variables of the risk of false results was calculated using logistic regression. For continuous variables identified significant in this analysis, cut-off thresholds were calculated by ROC (receiver operator characteristics). The comparisons between groups defined by the continuous variable threshold or nominal variables were done by Chi-square test. Possible dependencies between glucose levels and metabolic variables were evaluated by Pearson or Spearman's R coefficient, depending upon the distribution observed.

Results

The median patient age was 64 years (range: 37-85) and more than two third of the patients were men (71.2%). Metastatic disease at initial presentation was confirmed in almost half (46.9%) of the patients. After initial diagnosis, 52 patients (47%) received one or multiple treatment modalities with definitive intention, in 38 (34%) the upfront applied oncological treatment was palliative and in 21 (19%) only best supportive care was possible. The detailed clinical and pathologic characteristics of the cohort are displayed in Table 1.

The PET/CT sensitivity, specificity, PPV and NPV to detect distant metastases was 76.5%, 86.5%, 82.98% and 81.25%. The sensitivity regarding the primary tumor visualization was 89.2%.The study accuracy regarding the regional lymph nodes could not be assessed as they were not routinely pathologically staged in all patients, in particular those disqualified from surgical treatment. Worth highlighting is the fact that in 12% of all patients the PET/CT managed to identify metastatic sites of disease that were not suspected in previously performed imaging which eventually spared the patients the morbidity of aggressive primary treatment and helped modify the treatment to the most beneficial one while preserving quality of life.

In total, for 21patients out of 111 (18,9%) false negative PET/CT results were reported. Three patients were false negative in PET/CT for both primary tumor and distant metastases, in all these cases the clinically identified metastatic sites were extraperitoneal lymph nodes. For 9 patients ^{18}F-FDG PET/CT, while being able to find the primary tumor, could not identify the

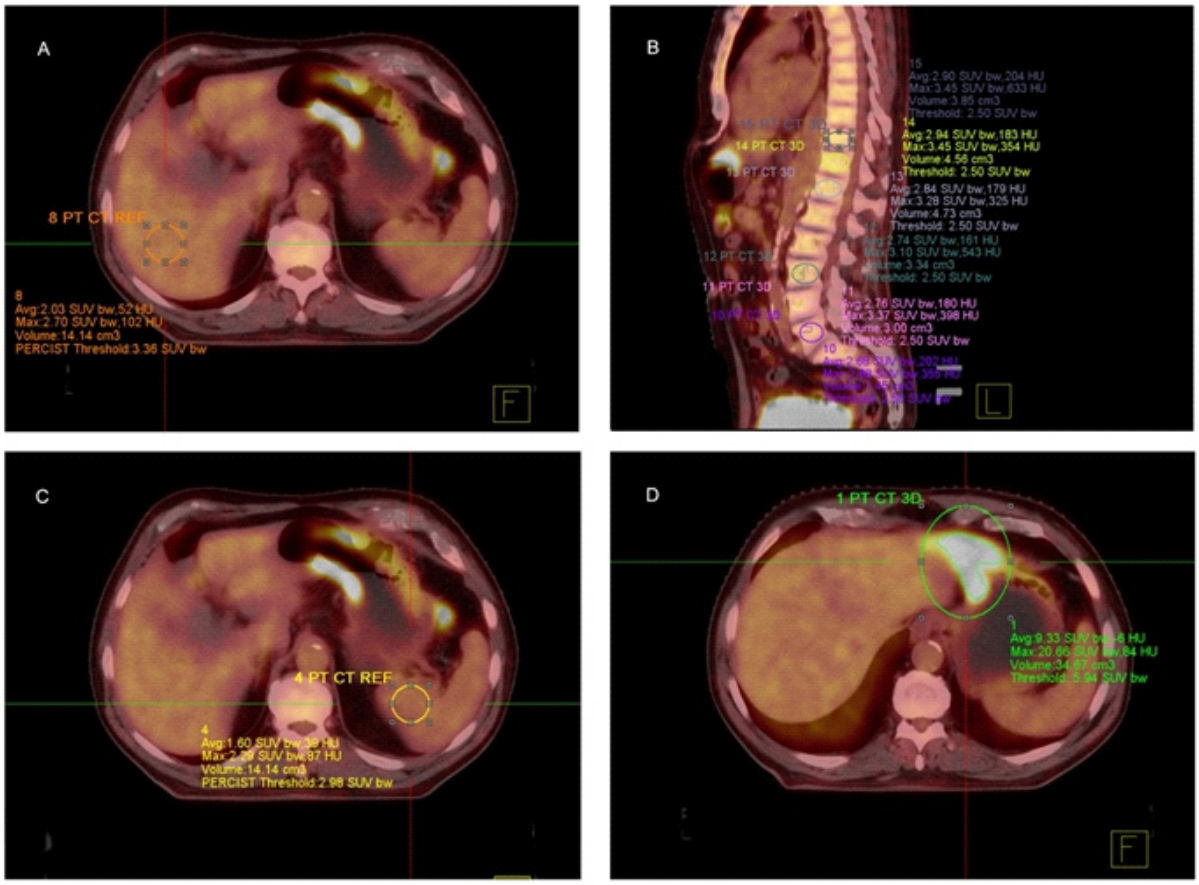

Figure 1. Axial scans of fused PET/CT with exemplary ROI for measuring ^{18}F-FDG uptake: A. Normal liver parenchyma; B. Thoracic/lumbar vertebrae; C. Normal spleen parenchyma; D. Primary tumor

clinically confirmed distant metastases which in all cases involved peritoneal tumor spread. Contrast-enhanced abdomen/pelvis CT did not detect these lesions in any of the mentioned cases either.

The risk of acquiring a false negative result of ^{18}F-FDG PET/CT for the primary tumor was therefore 10.8% (12/111), for 64 studies identified negative for metastases, the offset of FN results was 18.8% (12/64). Clinical factor analysis identified early tumor stage (T1-T2), female sex and low neutrophil count as predictive for increased probability for not recognizing the primary tumor. For neutrophil count, ROC analysis identified a threshold of 4.2k/μL as the most relevant

Table 1. *Clinical characteristics of patients (n=111).*

Variable		Patient no. (%)	Median	Range
Age (years)			64	(37-85)
Sex	Male	79 (71)		
	Female	32 (29)		
Performance status	0	45 (41)		
	1	50 (45)		
	2	16 (14)		
Weight loss	<5%	30 (27)		
	5-10%	24 (22)		
	>10%	57 (51)		
Tumor location in stomach	Upper	27 (24)		
	Middle	7 (6)		
	Lower	28 (25)		
	Multiple	49 (45)		
cTstage (AJCC v.7)	T1-2	29 (26)		
	T3-4	82 (74)		
Lymph node status	N0	32 (29)		
	N1	79 (71)		
Distant metastasis	M0	60 (54)		
	M1	51 (46)		
Location	Extraperitoneal lymph nodes	26 (23)		
	Liver	18 (16)		
	Peritoneum	16 (14)		
	Lungs& Mediastinum	11 (10)		
	Bones	4 (4)		
Histopathology (JCGC)	PAC/TAC	42 (28)		
	PDAC	33 (30)		
	SRC/MAC	36 (32)		
Lauren classification	Intestinal type	70 (63)		
	Diffuse type	41 (37)		
Tumor differentiation	G1	6 (6)		
	G2	20 (18)		
	G3	67 (60)		
	Gx (Not specified)	18 (16)		
Therapy	Surgery	49 (44)		
	Radical/Palliative or diagnostic	21(19) / 28(25)		
	Systemic therapy	53 (48)		
	Part of definitive treatment/Palliative	25 (23) / 28 (25)		
	Radiation therapy	53 (48)		
	Radical/Palliative	31 (28) / 22 (20)		

cut-off point as shown on Figure 2.The increased risk of false negative results concerning distant metastases was significantly higher for undifferentiated and mucinous/signet ring carcinoma or diffuse Lauren histologic subtypes as well as for location in peritoneum and extraperitoneal lymph nodes. No metabolic risk factors for FN results were identified for neither primary nor metastatic lesions. Details about FN distribution in subgroups defined by statistically significant ones are presented in Table 3.

Table 2. *Metabolic characteristics of patients (n=111).*

Variable		Patient no. (%)	Median	Range
^{18}F-FDG uptake in primary tumor	FN TP	12 (11) 99 (89)		
^{18}F-FDG uptake in metastatic sites	TP FP TN FN	39 (35) 8 (7) 52 (47) 12(11)		
Tumor SUVmax			8.99	(1.24-47.74)
Liver SUVmax			2.68	(1.74-4.24)
Liver SUVmean			2.03	(1.11-3.05)
Spleen SUVmax			2.36	(1.39-3.82)
Spleen SUVmean			1.76	(1.12-2.98)
Bone marrow SUVmean			2.12	(1.07-4.85)

FN-false negative, TP-true positive, FP-false positive, TN-true negative

Due to lack of a convincing explanation for the sex and neutrophil count influence, we evaluated their distribution in subgroups defined by other variables to assess whether they were cofounded by another better explainable factor. Although not statistically significant, we found a notable trend for women to feature higher percentage of diffuse-type histology (50% vs 31% for men, P=0.07) which we identified to feature a higher risk of FN result for metastasis detection. The same variable we suspect to be a possible explanation of the observation regarding neutrophil count influence (47% of non-intestinal type tumors in NEU ≤4.2 group vs 29.5% in the patient with NEU >4.2; P=0.057).

There were no statistically significant correlations between blood glucose levels and any of the analyzed tumor and normal tissue uptake parameters. The 8 false positive observations were mostly associated with random (inflammatory, degenerative) events, therefore no analysis on risk factors for false positive results would be conclusive. The cases of false positive PET/CT results are characterized in Table 4.

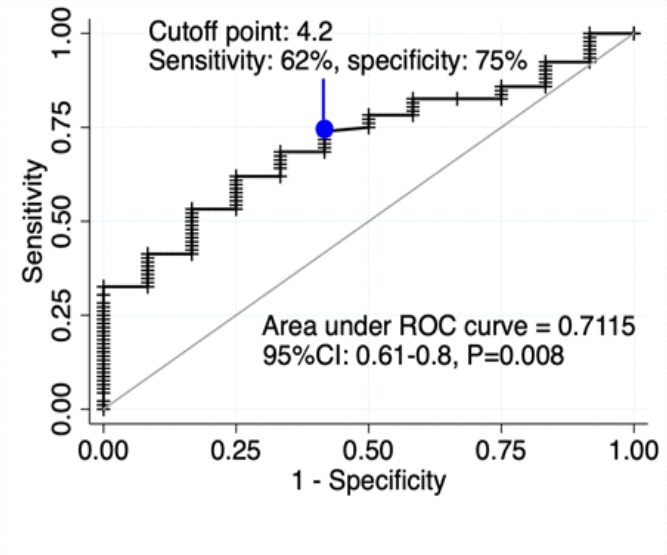

Figure 2. ROC curve demonstrating the most optimal neutrophil count cut-off point for predicting the risk of false positive ^{18}F-FDG PET/CT result in primary tumor detection.

Discussion

The increasingly effective yet aggressive treatment standards of newly-diagnosed gastric cancer require a conclusive and reliable workup in order to apply such management only to patients who have a high likelihood of having benefit of it. The results of our study confirm a good clinical use of ^{18}F-FDG PET/CT in the staging of gastric cancer, in particular in distant metastases detection. The real-life sensitivity and specificity observed in our study cohort was 76.47% and 86.67%, respectively. These results are in line with previous publications which reported overall (non-organ-specific) sensitivity between 50% and 100%. Comparably to our outcomes, specificity was typically higher at 82%-100% [8, 21-23]. Due to histologic verification not being a common procedure, no organ-specific analysis of sensitivity and specificity could be performed in our cohort yet similar to the existing reports we observed peritoneum as the main site of metastases omitted by PET/CT studies [24-26]. In groups in which we could perform an accuracy analysis focused on peritoneum metastasis, a sensitivity of 28%-67% was found, notably inferior to that of standard contrast-enhanced abdominal CT (76%-80%) [5, 24, 26-28]. The underlying reasons could be the small size of single nodular lesions which are typically below the useful spatial resolution of the scanners (6-8mm) [29,30] or their postulated very poor blood

Table 3. *Analysis of variables significantly influencing the risk of false negative PET/CT.*

Variable	Value	Risk of FN PET in all patients	Risk of FN PET in patients with given value	Difference versus standard risk (+/-)	χ^2	P
Primary tumor detection						
Primary tumor stage	T1-T2	10.8%	24.1%	+13.3%	7.23	0.007
	T3-T4		6.1%	-4.7%		
Neutrophil count	NEU≤4.2		20.5%	+9.7%	6.1	0.014
	NEU > 4.2		4.9%	-5.9%		
Sex	Female		21.9%	+10.1%	5.71	0.017
	Male		6.3%	-4.5%		
Metastasis detection						
JCGC histologic type	MAC/SRC	18.8%	28.6%	+9.8%	7.74	0.005
	PAC+TAC + PDAC		0%	-18.8 %		
Lauren histologic type	Diffuse type		37.5%	+18.7%	8.86	0.003
	Intestinal type		7.5%	- 11.3%		
Metastasis location	Peritoneum		56.3%	+ 37.5%	20.73	< 0.001
	Extraperitoneal lymph nodes		11.6%	- 7.2%		
	Other		0%	- 18.8%		

MAC/SRC - Mucinous adenocarcinoma/ Signet-ring cell carcinoma; PAC - Papillary adenocarcinoma; TAC - Tubular adenocarcinoma; PDAC - Poorly differentiated adenocarcinoma;

Table 4. *Characteristics of PET/CT observations false positive for distant metastases.*

No.	Suspected site in PET/CT	SUVmax of suspected site	Comment
1	Subdiaphragmatic lesion	9.1	Clinical course corresponded to an abscess
2	Pretracheal lymph node	3.1	9mm lesion, stable for next 22 months of follow-up, therefore most likely inflammatory
3	Mesenterium/Large bowel	18.3	Morphologically located within the bowel, stable for next 20 months, clinically corresponding to diverticulitis
4	Extraperitoneal lymph nodes	3.2	Stable and unsuspected in control CT 3 months post PET/CT, most likely reactive
5	Diffuse, increased uptake in lungs	4.7	Regressive in subsequent control CT, concluded to be pneumonia
6	Mediastinal lymph nodes	3.8	Stable and unsuspicious in control CT, considered reactive
7	Mediastinal lymph nodes	5.8	Multiple nodes which due to history of coal mine work and observed emphysema were considered symptomatic for anthracosis
8	Th5 vertebral body	8.4	No morphologic correlation with CT and normal uptake in control PET/CT after 7 months, considered artefact/functional marrow

supply which directly translates into low radiotracer penetration [26]. Despite these limitations it seems that the addition of PET/CT to staging workup, at least for cases featuring increased risk of synchronous dissemination (due to stage or aggressive histology) does improve the optimal treatment selection [12].On the group where both laparoscopy and ^{18}F-FDG PET/CT were added to routine diagnostic procedure, otherwise overlooked metastatic dissemination was found in 27% (10% was attributable to PET/CT alone) of their whole analyzed cohort. Aside from obvious gain of sparing patients the consequences of unnecessary invasive procedures, this helped reduce the costs by estimated 12'000 USD per patient [8]. In our group the percentage of OMD detected by PET/CT alone was 11%. By complementing this with the fact that a significant percentage of false negative results observed in our group were metastases located in the peritoneum (75%) and therefore potentially detectable by diagnostic laparoscopy, we estimate the OMD detection rate in our cohort using the two procedures combined at 20%.This result would confirm the previously published data [8].

The primary gastric tumors were detected by PET/CT with a relatively high sensitivity of 89%, falling again well within the range previously described by the literature (83%-98%). The same also concerns the first of the factors we identified as contributing to an increased probability for a false negative result, namely the early primary tumor stage. The studies which could estimate the sensitivity for this subgroup found it significantly decreased compared to the general population at 26%-63% [5,13,14,21]. Early T1-T2 tumors which by definition feature small depth of invasion and typically smaller size may be less ^{18}F-FDG-avid due to the same mechanism explained about peritoneal metastases: low tracer diffusion and thickness of the lesion likely below the spatial resolution of PET.

Tumor histology (in both JCGC and Lauren classifications) was found to our study to significantly contribute to an increased risk of omitting metastases in PET/CT review, consistent with previously published reports [31,32]. By analysis of this risk with accordance to JCGC classification we found all false negative cases to be attributable to undifferentiated or signet ring-cell/mucinous adenocarcinoma histology, no false negative results were seen for papillary and tubular histologies. It has been proven that lower ^{18}F-FDG uptake in these tumor types is caused by diffuse infiltration type, lower tumor cell density and high contribution of mucinous structures which all reduce the tracer concentration in the tumor tissue. Another reason might be significantly lower activity of GLUT-1 transporter protein; one of the studies mentioned its average over expression rate of 24% in SRC as compared to 94% in papillary and tubular subtypes [33, 34]. Patient age has also to be considered as the Lauren diffuse type which is poorly a prognostic and more prone for ^{18}F-FDG PET/CT inaccuracy, tends to be more frequent in younger patients [35].

Regarding the, the unexpectedly observed, increased risk of a false negative result for primary tumor detection in women and patients with low neutrophil count, possibly we attribute it to a higher percentage of diffuse-type histology

tumors in these subgroups. This association has already been described for female sex [36, 37]. Neutrophil count is a known measure of inflammatory state and one of its derivatives, namely NLR has been identified as a notable prognostic factor in gastric cancer [38]. However, data on correlation of neutrophil count with tumor uptake or its histology is scarce: a single study on lung cancer demonstrated a straight correlation between tumor SUVmax and neutrophil count [39]. Overall this data cannot be unanimously interpreted as there are too many potentially confounding factors.

A number of limitations of our study needs to be mentioned. While the unstratified and previously untreated patient cohort can possibly reflect the "real-life" clinical conditions, due to its retrospective character it did not routinely include certain diagnostics that would render the sensitivity and specificity data more reliable. This mostly concerns the regional lymph nodes; they were not separately included into the PET/CT reliability assessment because their pathologic analysis was only done in a minority of patients. Within our cohort we assessed that in 38% of patients who had lymph nodes described as suspicious (due to enlargement and/or contrast uptake) these did not accumulate ^{18}F-FDG. The opposite situation did not occur in any of the cases. In published metanalysis, sensitivity of PET/CT to detect metastatic lymph nodes in gastric cancer (median: 34.3%; range: 33.3%-64.6%) was demonstrated to be significantly inferior to specificity (median: 93.2%; range: 85.7%-97%) [40]. The sensitivity of the contrast-enhanced CT was comparable to that of PET/CT 64.5% and 56.6%, respectively [41, 42]. After reviewing existing literature, we concluded that neither other studies featured sufficient sensitivity and specificity, so that can be used as standalone reference method for staging local lymph nodes, in contrary to the pathologic assessment [43]. We are convinced however, that an analysis of a patient subgroup with pathologically staged lymph nodes, will be a highly valuable addition if patient numbers are adequate for analysis. Another limitation that might have influenced our results is that a staging laparoscopy was not performed in all of our patients, possibly lowering the amount of occult peritoneal tumor involvement that has already been mentioned to be frequently undetectable by PET/CT.

In conclusion, our study confirmed that ^{18}F-FDG PET/CT is a valuable addition to the staging procedure of gastric cancer. It frequently delivers additional information that can alter the previously established disease stage, thus leading to improved tailoring of the therapy to individual patients. It also confirmed previously described data of decreased PET/CT sensitivity in early tumor stages, non-intestinal histology and metastasis located in peritoneum. It also highlighted neutrophil count and sex as variables potentially associated with less ^{18}F-FDG-avid tumor histology, which might be of relevance when performing PET/CT to identify the primary tumor site for metastases of unknown origin. The data should be backed up by further biochemical parameters and verified prospectively.

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