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Evaluation of relationship between maximum SUV measured on 18F-FDG PET/CT with tumor pathological types, size, lymph node metastasis and distant metastasis in non-small cell lung cancer

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Abstract

Background: Lung cancer is the most commonly diagnosed cancer, of which the non-small cell lung cancer (NSCLC) accounts for approximately 80% of the newly diagnosed lung cancer. The prognosis of lung tumors depends on early and accurate staging as well as the histopathological type of the tumor. It is suggested that NSCLC with different histopathological types and primary tumor sizes can elicit variable max.SUV values on 18F-fluorodeoxyglucose-positron emission tomography/computed tomography (18F-FDG) PET/CT with different lymph nodes and distant metastatic potential. In this study, we aim to evaluate the relationship between the maximum SUV measured on (18F-FDG) PET/CT with tumor pathological type, primary tumor size, lymph node metastasis, and distant metastasis in NSCLC.

Results: This is a cross-sectional analysis of the (FDG-PET/CT) findings of 40 patients with NSCLC. Statistical analysis is used to determine correlation between max.SUV and tumor size, with each pathological type, nodal (*N*) staging and distant metastasis (*M*) staging. The primary lung tumors histopathological types were 25 (62.5%) adenocarcinomas, 12 (30%) squamous cell carcinomas and 3 (7.5%) large cell carcinomas. The max.SUV and tumor size of the squamous cell carcinoma group were significantly higher than max.SUV of adenocarcinoma and large cell cancer groups ($P = 0.000009$). A significant positive correlation was found between the primary tumor max.SUV and tumoral size. Neither lymph node nor distant metastases involvement was correlated with tumor max.SUV.

Conclusions: The tumor size and histologic subtype both strongly influence FDG uptake in lung cancer. Nonetheless, max.SUV cannot be regarded as a predictive of metastases or lymph node involvement.

Keywords: Lung cancer, 18F-FDG, PET/CT, Adenocarcinoma, Squamous cell carcinoma

Background

Lung cancer is the most commonly diagnosed cancer worldwide with about 1.61 million cases, representing nearly 12.7% of total cancers. The non-small cell lung cancer (NSCLC) accounts for approximately 80% of newly diagnosed lung cancer. The prognosis of lung tumors depends on early and accurate staging as well as the histopathological type of the primary tumor, with the squamous cell carcinoma type regarded to be of a worse prognosis than that of adenocarcinoma [1].

Although CT scanning has long been the go-to imaging modality to stage lung cancer, it is yet hindered by

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many limitations and pitfalls. It may be incapable of distinguishing a tumor from atelectasis, does not reflect tumoral metabolic activity and suggests no idea about the pathology of the tumor [2]. Therefore, that can have negative outcome on patient's treatment plans and prognosis [3].

Imaging using fluorodeoxyglucose-positron emission tomography/computed tomography (18F-FDG PET/CT) is primarily depended on visual assessment of glucose metabolism of tumor cells and has been used primarily as a staging and restaging tool. In addition, 18F-FDG PET/CT is of essential value for the assessment of the indeterminate lung or metastatic nodules as well as assessment of therapeutic response to chemo-radiation. The quantification of FDG uptake by the abnormal tumor cells reflected by variabilities of max.SUV index can be widely used as a quantitative parameter for the analysis of 18F-FDG PET images. In addition, there is a close correlation among the clinical, radiologic, and molecular characteristics and histopathologic pattern of NSCLC [1].

Recently, some authors have shown that different pathological types and sizes of NSCLC can produce different max.SUV values on PET/CT with variable metastatic potential, meaning that the higher primary tumor max.SUV can predict a higher extensional or metastatic potential [4]. Additionally, it has been demonstrated that possibility of malignancy can increase with increasing max.SUV and the increasing max.SUV is associated with a higher grade of tumor, nodal, and metastatic staging [5].

Therefore, an insightful understanding of biological mechanisms as well as the genetic differential expression involved in lung tumor cells can be helpful and lead to a better selection of treatment modalities for patients and better prognosis [6].

In this study, we aim to evaluate the relationship between the maximum SUV measured on (18F-FDG) PET/CT with tumor pathological type, primary tumor size, lymph node metastasis, distant metastasis in non-small cell lung cancer.

Methods

This cross-sectional study included forty patients with a pathologically proven lung cancer who were referred to the radiology department for baseline assessment between September 2019 and September 2020 well before initiating their therapeutic regimen. The inclusion criteria were the adult patients aged 18 or above of both sexes with a pathologically proven lung cancer. The exclusion criteria were patients with primary lung lesion less than 1 cm, patients of age less than 18 years old, pregnant female patients, patients with a known allergy to the iodinated contrast media, patients with renal impairment expressed by high serum creatinine or patients who had received chemotherapy, radiotherapy or underwent surgical intervention for treatment of the lung neoplasm prior to the PET/CT examination. Patients with multiple primary neoplasms, if found, were also excluded.

Patient preparation

Relevant clinical history and informed consent was taken from all patients who were asked to fast 4–6 h prior to the examination. Patients' weight, renal function tests and blood glucose level were assessed prior to (18F-FDG) administration. Blood glucose level should be less than140mg/dL. A wide bore (18–20 g) IV cannula was inserted for administration of the (18F-FDG) dose and contrast material.

FGD-PET-CT imaging

The eligible patients were injected with 18F-FDG according to each patient's weight, with an average FDG dose of 7.5 MBq/kg (megabecquerel/ kg), and then, the patients were asked to stay in secluded waiting rooms resting in silence without activity for about 40 min with oral hydration. PET/CT images was acquired using a GE Discovery IQ machine (GE Medical, Milwaukee, USA). Imaging from the skull vertex to mid-thigh initiated 40 min after tracer injection. Initially a low dose non-contrast CT for attenuation correction and anatomic localization was performed, followed by a post-contrast CT examination after administration of contrast. Immediately after CT, the PET scan was performed for about 25 min. The PET dataset was re-constructed using the manufacture-provided standard iterative algorithm software with attenuation correction based on the CT scan data. Computerized tomography integrated positron emission tomography fusion images in axial, sagittal, and coronal planes were generated.

Imaging analysis

Experienced radiologist and nuclear medicine consultants have interpreted the images. The primary lung tumor size was defined as the greatest dimension of the tumor in the lung window on axial cuts. The max.SUV of the tumor which is defined as the peak SUV of 1 pixel with the highest count within the tumor in chest was measured by placing regions of interest encompassing the tumor on axial views. It is then calculated automatically by the manufacturer-provided software. The software used was the advantage workstation (GE, ADW 4.5 PET/CT work station). SUV.max is calculated according to the following formula:

$$\mathrm{SUV}_{\max} = \frac{C(\mu Ci/\mathrm{ml})}{\frac{\mathrm{ID}(\mu Ci)}{w(\mathrm{kg})}}$$

Maintenance and calibration of PET/CT camera as well as the workstation remained optimal according to manufacturer guideline to assure consistent and reproducible results. *T*-staging was assessed, and the patients' age and sex were obtained from records. The presence of nodal metastasis and distant metastasis were assessed. *N* and *M* stages were determined according to the 8th edition of the TNM classification of lung tumors.

Statistical analysis

Statistical analysis was performed using MedCalc statistical software for Windows (MedCalc Software, Mariakerke, Belgium). Data for continuous variables were expressed as either median, interquartile range and range or mean ± standard deviation and as both number and percentage for categorical data. Mann–Whitney U-test was used for comparison of two independent groups. Comparison of max.SUV between multiple groups was performed using the Kruskal–Wallis test, and Conover post hoc test was used for pairwise comparisons of the different groups. Chi-squared test was used for comparison of categorical data between the two groups. Spearman's rank correlation was used to describe the correlations. For all tests all *P* values were two-tailed and a *P*-value less than 0.05 was considered significant.

Results

Forty patients (9 females and 31 males) were included in this study. Their ages ranged from 35 to 88 years with a median of 63.5 years, an IQR of 57–70 years and a mean (± standard deviation) of 62.95 years (± 10.01 years). The number of males was significantly higher than the number of females in this study ($x^2 = 12.1$, $P = 0.0005$). Figures 1, 2, 3 and 4 show cases of NSCLC with different histopathological types.

Histopathological analysis of the primary lung tumors revealed the presence of 25 (62.5%) adenocarcinomas, 12 (30%) squamous cell carcinomas (SCC) and 3 (7.5%) large cell carcinomas. Tumor size ranged from 1.9 to 16.5 cm with a median size of 4.85 cm, an IQR of 3.2–6.45 cm and a mean (± SD) size of 5.21 cm (± 2.64 cm).

Primary tumor max.SUV values ranged from 4.5 to 25 with a median of 15.6, an IQR of 9.9–17.6 and a mean (± SD) of 14.1 (± 5.45). As regards the (T) staging of the lung tumors, 9 (22.5%), 11 (27.5%), 14 (35%) and 6 (15%) masses were T1, T2, T3 and T4, respectively. Regarding the lymph node staging of the patients, 9 (22.5%), 5 (12.5%), 14 (35%) and 12 (30%) patients were *N*0, *N*1, *N*2 and *N*3, respectively. Regarding the metastatic staging of the patients, 10 (25%), 7 (17.5%), 8 (20%), and 15 (37.5%) patients were *M*0, *M*1a, *M*1b and *M*1c, respectively. Table 1 shows the descriptive data of the whole study population.

Comparison of tumor max.SUV between males and females revealed no significant difference in SUV values of both groups ($P = 0.66$). Patients were divided into two groups according to age using the median value of 63.5 years. No significant difference was found between the max.SUV values of both groups ($P = 0.64$). Comparison of tumor max.SUV between the different tumor histological types revealed that the max.SUV of the squamous cell carcinoma group was significantly higher than that of adenocarcinoma and large cell cancer groups ($P = 0.000009$), whereas no significant difference existed between the SUV values of the adenocarcinoma and large cell cancer groups (Table 2).

Patients were divided into two groups according to size of the primary tumor using the median value of 4.85 cm. Max.SUV was significantly higher in the group whose tumor size was larger than 4.85 cm ($P = 0.01$).

When patients were classified into two groups determined by the presence and absence of lymph node metastasis, no significant difference was found between the max.SUV of both groups ($P = 0.63$) (Table 3). Furthermore, no significant difference was seen in max.SUV of all groups when patients were categorized according to their specific lymph node stage (*N*0, *N*1, *N*2, *N*3) ($P = 0.91$).

When patients were classified into two groups determined by the presence and absence of distant metastasis, no significant difference was found between the max. SUV of both groups ($P = 0.46$) (Table 4). Furthermore, no significant difference was seen in max.SUV of all groups when patients were categorized according to their specific distant metastasis stage (*M*0, *M*1a, *M*1b, *M*1c) ($P = 0.12$).

A significant positive correlation was found between the primary tumor max.SUV and tumoral size ($r_s = 0.54$, $P = 0.0003$), as shown in scatter diagram of (Fig. 5).

A negative statistically insignificant correlation was found between tumoral max.SUV and the age of patients ($r_s = -0.09$, $P = 0.598$), as shown in scatter diagram of (Fig. 6).

Discussion

Lung cancer is regarded as one of the chief causes of cancer-related deaths around the world with a dismal 5-year survival rate of 15%. As a result, the ability to detect and effectively treat lung cancer continues to represent a substantial public health challenge. PET-CT scan which detects the accumulation of a radiolabeled glucose analog within tissues has gained precedence over other imaging modalities in the

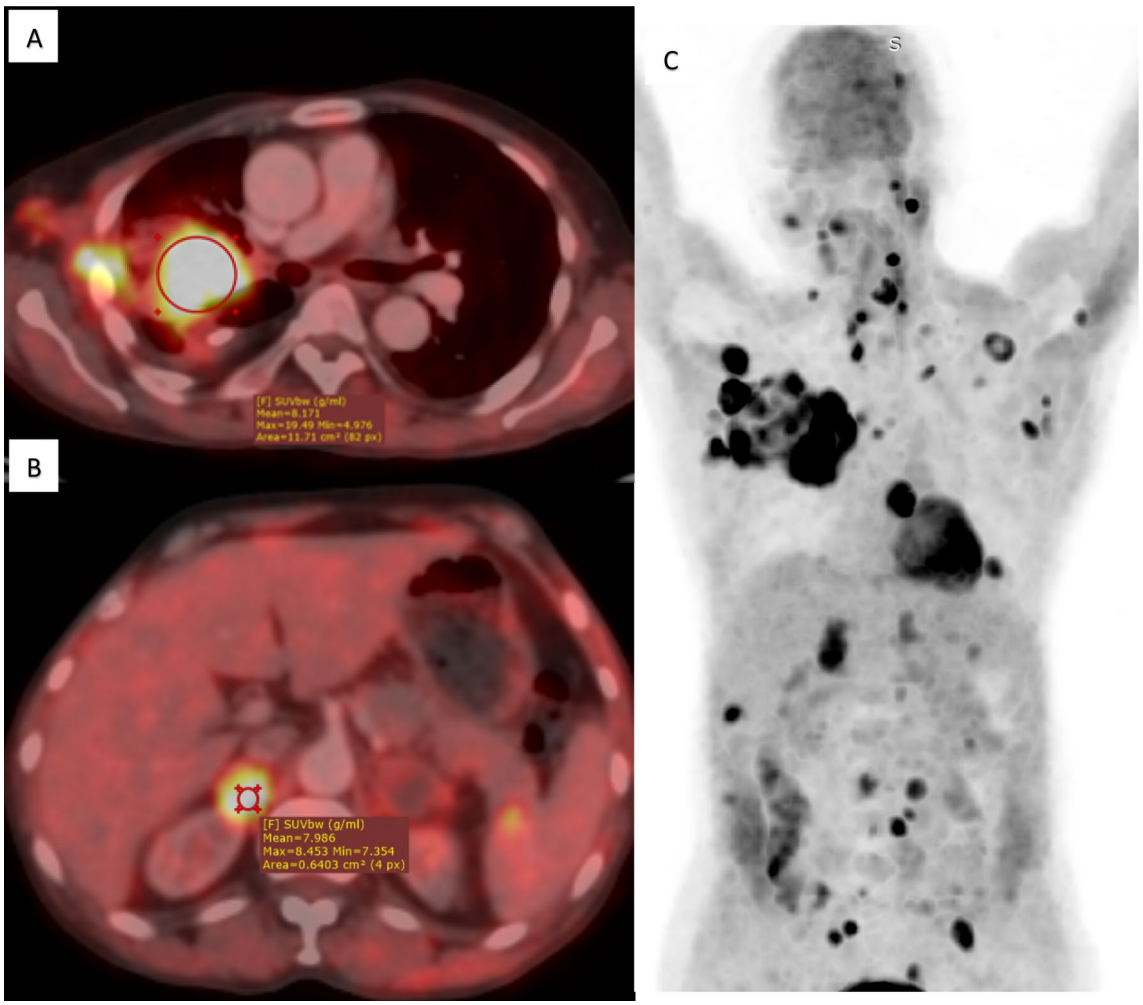

Fig. 1 A 55-year-old male patient whose CT chest revealed multiple pulmonary masses, underwent (FDG) PET/CT scan. (Fig. 1). **A**–**C** (FDG) PET/CT, **A** Axial view: A large infiltrative metabolically active right lung upper lobe soft tissue mass lesion measures 7.4 × 12 × 8.5 with max.SUV ~ 19.15. **B** Right adrenal lesion measuring 2.5 cm, with max.SUV ~ 8.4. **C** Full-body coronal MIP PET showing the primary lung mass and metastasis to lymph nodes, cerebral, pleural, adrenal, osseous deposits. The tissue sampling was obtained via endoscopic biopsy proved to be squamous cell carcinoma (SCC)

(See figure on next page.)

Fig. 2 A 57-year-old male patient whose prior chest CT revealed a large pulmonary mass. (Fig. 2). **A–D** (FDG) PET/CT. **A** axial view: A large metabolically active right lower lobe posterior segment mass lesion is noted measuring about 6.73 × 5.45 cm eliciting metabolic activity of max. SUV ~ 19.1. Irregular surrounding atelectasis and associated overlying pleural thickening/infiltration. **B** Metabolically active aortocaval, portohepatic lymphadenopathy with max.SUV ~ 11.69. **C** Left adrenal metabolically active lesion with max.SUV ~ 7.9. **D** Full-body coronal MIP PET showing the primary lung mass and lymph nodes with adrenal metastasis. The tissue sampling was obtained via endoscopic biopsy proved to be squamous cell carcinoma (SCC)

diagnostic work-up of lung cancer. Not only can PET-CT accurately demonstrate the extent of loco-regional involvement and metastatic disease, thus guiding treatment, but it has also been successful in following up the therapeutic response. Furthermore, it has been suggested that the standard uptake value (SUV), the quantitative parameter measured on PET scans, can predict patient survival as patients with higher lung tumor SUV are at a greater risk of relapse or death [7]. Therefore, the current study aimed at investigating the clinical, demographic and pathological factors that might be linked to tumor SUV.

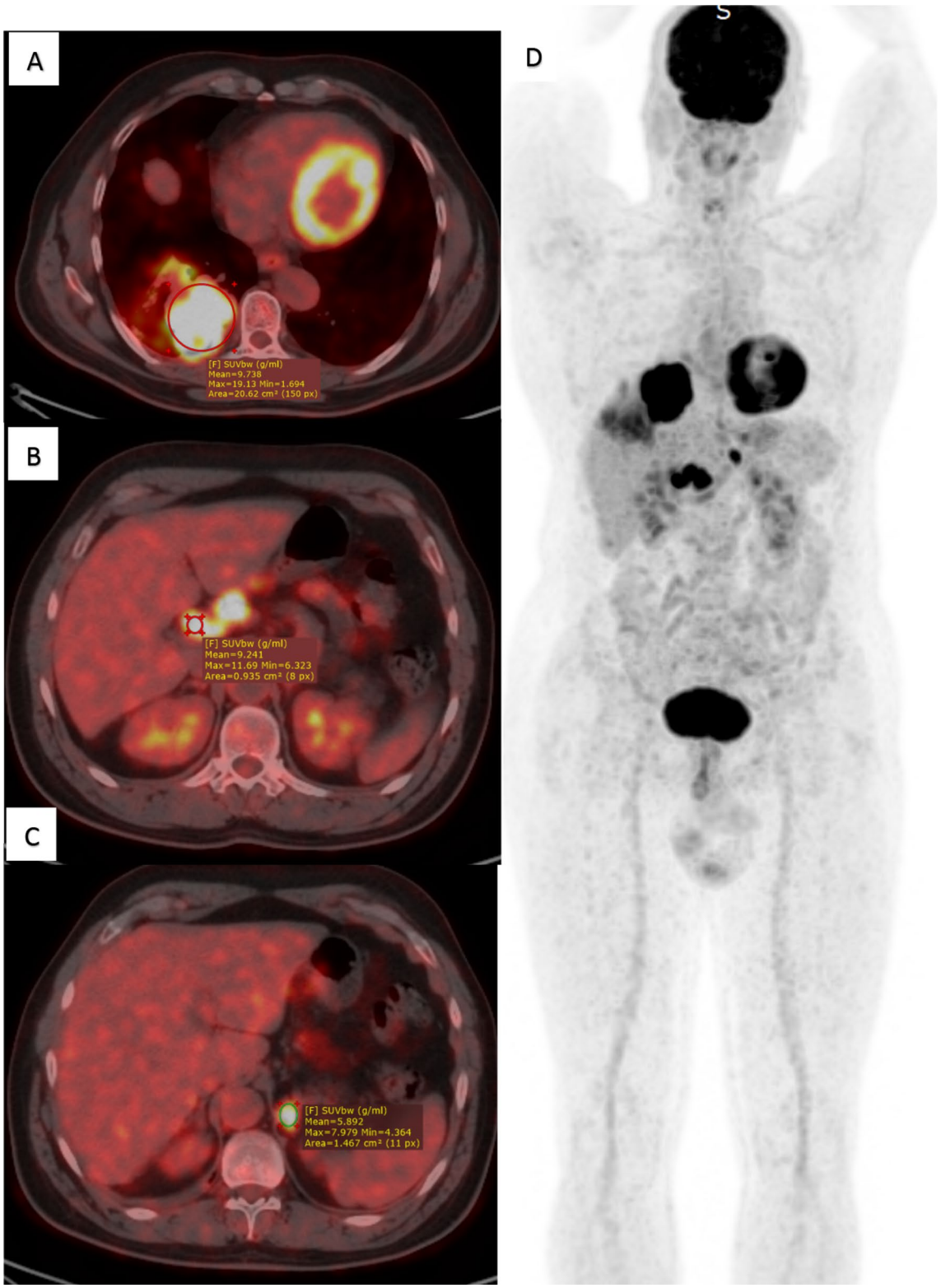

Fig. 2 (See legend on previous page.)

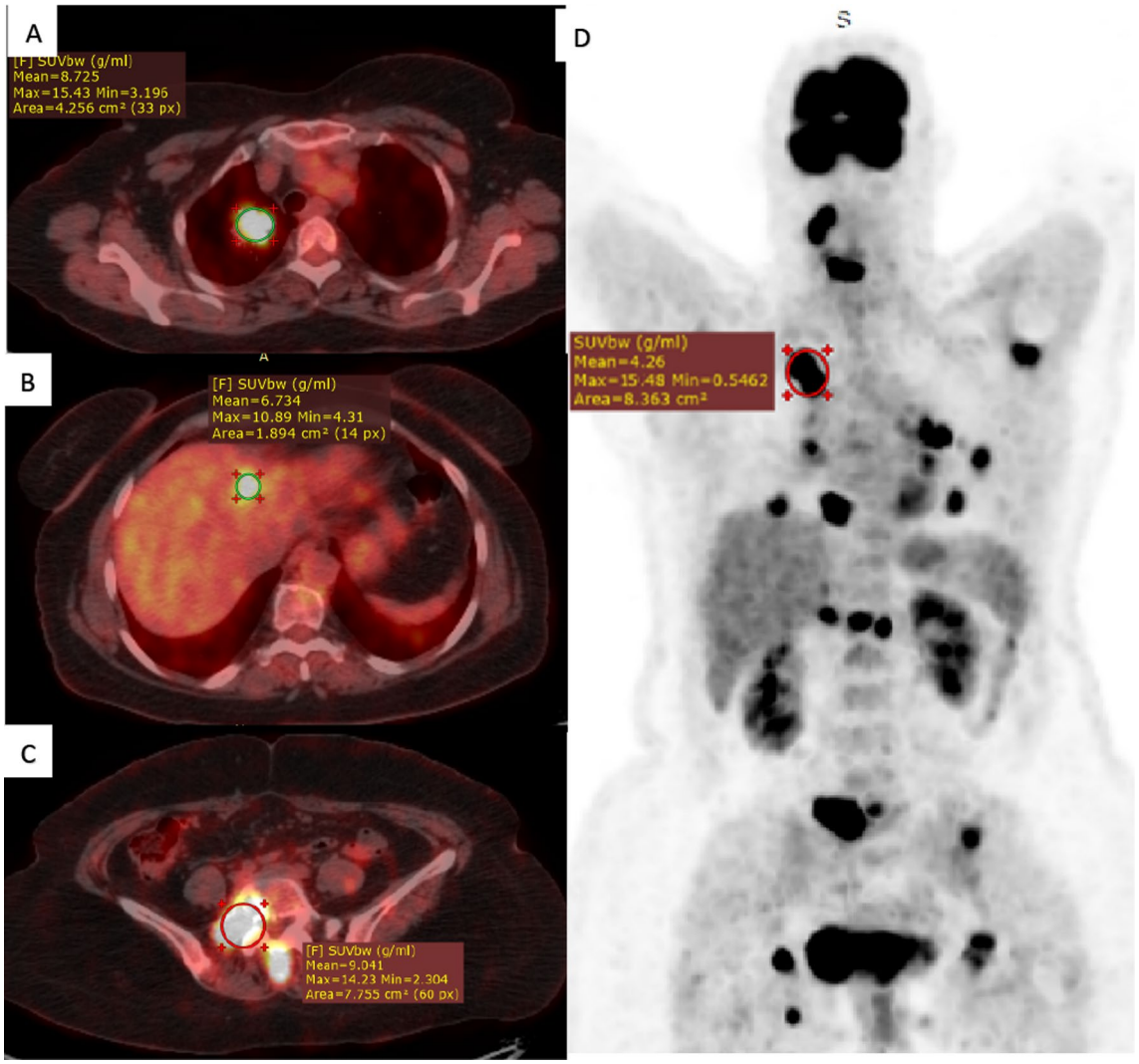

Fig. 3 A 61-year-old female patient who presented with hemoptysis and bony aches, underwent (FDG) PET/CT imaging. (Fig. 3). **A**–**D** (FDG) PET/CT. **A** Axial view: Right apical spiculated metabolically active pulmonary mass lesion measuring 3.6 × 3.5 cm with max.SUV ~ 15.4. **B** Left hepatic lobe (segment IVa) lesion showing max.SUV 10.8. **C** Multiple lytic metabolically active osseous lesions in bilateral pelvic bones with SUV ~ 14.2. **D** Full-body coronal MIP PET showing the primary lung mass and metastasis to lungs, liver, adrenal, osseous deposits. The tissue sampling was obtained via CT guided lung biopsy proved to be bronchogenic adenocarcinoma

Agreeing with the results of previous studies by Sunnetcioglu et al. [8] and Ozgul et al. [9], this study revealed no significant association between the primary tumor max.SUV and the age or gender of the patients. Alternatively, Qiang et al. [7] and Lee et al. [10] found that max.SUV was significantly higher in male patients, while Duan et al. [11] reported that max.SUV was significantly higher in patients over 60 years.

Multiple prior studies reported a significant correlation between the primary lung tumor size and its max.SUV. Dooms et al. [12] described a strong significant association between tumor size and max. SUV in patients with (NSCLC). In another study by Um et al. [13], the authors showed a significant correlation regarding the primary lung tumor max.SUV and its size, with the tumors measuring ≤ 3 cm eliciting a significantly lower max.SUV than tumors larger than 3 cm. Moreover, in a retrospective study of 85 patients with pulmonary lesions, Lu et al. [14] found a positive correlation between the size of a malignant tumor and max.SUV. More recently, Ozgul et al. [9] observed that tumors larger than 5 cm in size had a significantly higher max.SUV than smaller tumors. Similar results were also confirmed by Zhu et al. [4], Duan et al.

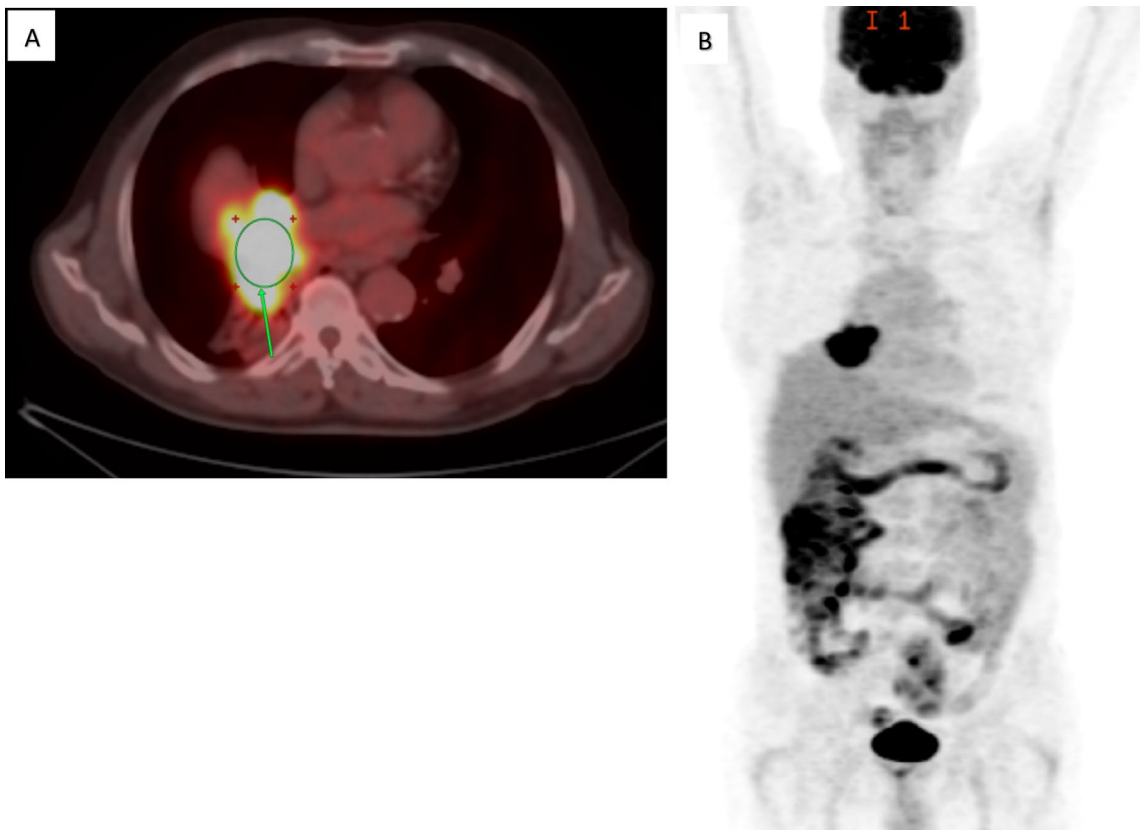

Fig. 4 66-year-old gentleman with recent bronchoscopy showing a right bronchial mass lesion. (Fig. 4). **A**–**B** (FDG) PET/CT. **A** Metabolically active large right lower lobe central peribronchial soft tissue mass lesion (arrow) is seen cuffing the left lower lobe bronchus with consequent narrowing of its lumen, the lesion measures about 74 × 44 mm and showing max.SUV ~ 17. **B** Full-body coronal MIP PET showing the primary lung mass with no other distant metastasis. The tissue sampling proved to be undifferentiated large cell carcinoma

Table 1 Descriptive data of the whole study population

	N	Mean	SD	Median	Min	Max	IQR
Age	40	62.95	10.013	63.5	35	88	13
Tumor Size (mm)	40	52.40	26.75	48.5	19	165	33
Tumor Max.SUV	40	12.351	5.446	15.55	4.5	25	7.9
LN size (mm)	40	20.4	19.463	17.5	0	85	11
LN SUV	40	8.99	8.746	7	0	45.5	10.3
Mets Size (mm)	40	38.233	39.951	25.5	0	134	43.5
Mets SUV	40	14.838	17.413	10.1	0	75	19.3

SD standard deviation, *IQR* interquartile rang

[11], Qiang et al. [7] and Budak et al. [2]. Likewise, a significant association between tumor size and tumor max.SUV was also noted in this study. These findings can be easily explained by the fact that larger tumors are associated with an increase in the number of glucose transporter-1 (GLUT-1) which is present on the cell membrane of tumor cells and is responsible for the uptake of FDG by malignant tumors [7].

Several studies indicated that max.SUV varies according to histologic subtypes of lung cancer. When De Geus-Oei et al. [15] compared the SUV values of adenocarcinomas, squamous cell carcinoma and large cell carcinomas in a total of 19 NSCLC patients, they found that the max.SUV was significantly higher in squamous cell carcinoma when compared to adenocarcinomas and large cell carcinomas, while no significant difference

Table 2 Comparison of max.SUV in patient groups designated according to the histopathology of the primary lung tumor

	Histopathology			*P* value
Max.SUV	SCC	Adenocarcinoma	LCC	*P* = 0.000009
Median	19.2	11.8	16.4	
IQR	17.55–21.95	7.98–15.5	8.68–16.9	
Range	1625	4.5–18.6	6.1–17	

SD standard deviation, *IQR* interquartile rang, *SCC* squamous cell carcinoma, *LCC* large cell carcinoma

Table 3 Comparison of max.SUV in patients with and without lymph mode metastasis

Max.SUV	−VE LN metastasis	+VE LN metastasis	*P*-value
Median	10	15.6	0.63
IQR	7.2–19.4	10.5–17.3	
Range	4.5–25	4.9–24	

SD standard deviation, *IQR* interquartile rang, *LN* lymph nodes

Table 4 Comparison of max.SUV in patients with and without distant metastasis

Max.SUV	+VE metastasis	−VE metastasis	*P*-value
Median	14.9	16.3	0.46
IQR	9.9–17.8	8.5–17.3	
Range	4.5–25	7.6–24	

SD = standard deviation, IQR = interquartile rang, LN: lymph nodes

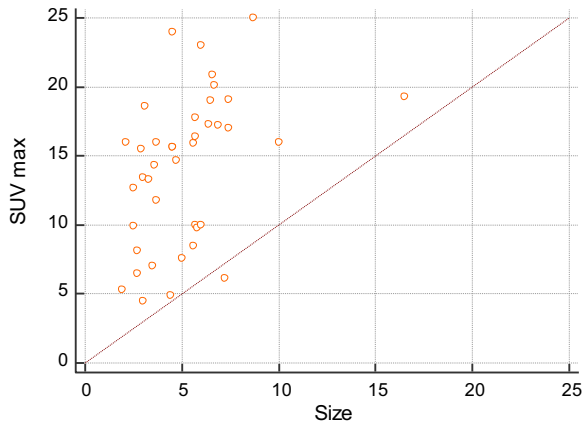

Fig. 5 Scatter diagram displaying the positive correlation between tumor max.SUV and tumor size in all patients

between adenocarcinomas and large cell carcinomas was identified. Moreover, Sun et al. [16] found that the mean max.SUV of patients with lung adenocarcinoma was significantly higher with the increase in its T stages. In a similar respect, Vesselle et al. [17] stated that the

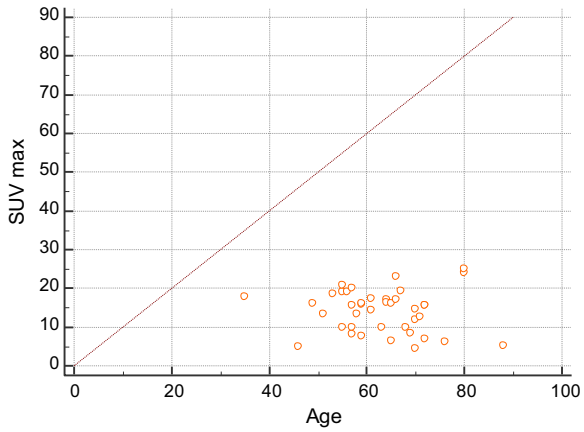

Fig. 6 Scatter diagram displaying insignificant correlation between tumor max.SUV and the age of patients

max.SUV of broncho-alveolar carcinoma was less than all other subtypes, with the (non-broncho-alveolar carcinoma) adenocarcinomas having a less max.SUV values than SCC. Wang et al. [18] reported the max.SUV of the primary tumor was significantly higher in the SCC group (11.0 ± 4.1) than in the adenocarcinoma group (7.4 ± 4.4). Consistent findings were also described by Duan et al. [11], Lee et al. [10], Sunnetcioglu et al. [8] and Qiang et al. [7]. In keeping with the published results, this study also demonstrated that the max.SUV of SCC was significantly higher than both adenocarcinomas and LCC, whereas no significant difference existed between adenocarcinomas and large cell cancers although the max.SUV of the LCC group was higher than adenocarcinoma group. Several factors could explain the difference in the FDG uptake between adenocarcinomas and SCC. Ito et al. [19] observed that GLUT-1 expression was lower and accordingly max.SUV was also lower in adenocarcinomas than in squamous cell carcinomas. Furthermore, GLUT-1 is mainly located on the membrane of tumor cells in squamous cell carcinomas, making it more effective in FDG uptake than that located in the cytoplasm of tumor cells [20]. Additionally, max.SUV is correlated with lung cancer cell proliferation and tumor volume doubling time [21]. It is a well-documented fact that adenocarcinoma has a significantly slower growth rate than squamous cell carcinoma and the median volume doubling time of adenocarcinoma is 249–258 days, much longer than that of squamous cell carcinoma (81–131 days) [22, 23]. Nevertheless, the difference between SUV values of squamous cell carcinomas and adenocarcinomas was not detected by all studies. Budak et al. [2] noted that no statistically significant difference was identified between adenocarcinoma (16.8 ± 13.5) and SCC (17.9 ± 5.6), as did Ozgul et al. [9]. The reasons for these controversial findings are

not clear, but it is important to note that the degree of tumor differentiation, not just histopathology, has been shown to impact tumor max.SUV, meaning that the poor-differentiated neoplasms had significantly higher max.SUV than their well-differentiated counterparts [10, 11]. Furthermore, Suarez-Pinera et al. [24] established that within a cohort of lung adenocarcinomas, max. SUV differed according to the histological subtype of the adenocarcinoma.

Since FDG uptake on PET/CT is correlated with the aggressiveness of the primary NSCLC, it is not surprising that a number of studies have shown that the max.SUV of NSCLC was positively correlated to nodal status, where cases with nodal metastases displayed a significantly higher primary tumor max.SUV than cases without nodal metastases. Nevertheless, there is no consensus in the literature regarding this observation. Higashi et al. [21] showed that the incidence of lymphatic invasion and lymph node infiltration in NSCLC were associated with a considerable 18F-FDG uptake, concluding that tumoral uptake of 18F-FDG is a significant predictor of lymphatic system invasion. Nambu et al. [25] found that lymph node metastases were more prevalent in NSCLC cases with a higher tumor max.SUV. The frequency of lymph node metastases was 70% in patients with NSCLC with a primary tumor max.SUV greater than 12, whereas no lymph node metastases were found in patients with a tumor max.SUV less than 2.5 suggesting that lung cancer patients exhibiting a high tumor max.SUV may have an increased risk for lymph node metastases. Muto el al. [26] found that max.SUV varied significantly in primary lung adenocarcinoma with and without nodal metastases (max.SUV 4.9 vs. 2.2, respectively). However, they did not find a difference between max.SUV values obtained in *N*1 versus *N*2 involvement, thereby concluding that max.SUV is useful in predicting LN involvement but not in predicting the extent of disease. Other authors, however, described a trend of steady increase in max.SUV of primary NSCLC in N0 versus *N*1 as well as in *N*0 versus *N*2 [27]. Lately, Qiang et al. [7] reported that when max. SUV of the primary lung cancer was higher than 7, the possibility of lymph node metastasis was 22.5%, but the possibility of lymph node metastasis was only 4% when max.SUV was less than 7 indicating max.SUV of the primary tumor is a risk factor for nodal metastases. Despite these results, the current study revealed that there is no correlation between the max.SUV of the primary tumor and nodal status. Although tumor max.SUV was higher in patients with lymph node metastasis than in those without and increased steadily with an increase in nodal stage, that difference did not show a statistical significance. Similar results were published in studies by Ozgul et al. [9], Wang et al. [18] and Suarez-Pinera et al. [24] with the latter describing a patient with a primary tumor max.SUV of only 0.5 and N2 involvement which led them to disagree with Muto et al. [26], who recommended that lymph node dissection be omitted in cases where max. SUV of primary NSCLC was less than 1. Differences in sample sizes among the various studies may explain the variation in the results. Another factor which may play a role is that highlighted by Ozgul et al. [9] who observed that the frequency of lymph node metastasis was higher in adenocarcinomas (24%) than in squamous cell carcinomas (6%), suggesting that pathological subtype may be a significant factor associated with lymph node metastasis. Nevertheless, in contradiction, a prior study showed no difference in the frequency of lymph node metastasis between the two pathological subtypes [24]. A third reason is that in the absence of histopathological confirmation, solely relying on PET/CT to diagnose lymph node metastasis may itself yield inaccurate results. Though the sensitivity of 18F-FDG PET/CT in lymph nodes greater than 1 cm is high, the accuracy and specificity rates are low [27]. In a study by Detterbeck et al. [28], the false positive rate of PET in mediastinal lymph nodes was reported to be 13–22%, and the false negative rate as 5–8%. Indeed, as per Cerfolio et al. [29], FDG-PET-CT cannot omit the need for tissue biopsies for staging *N*1 or *N*2 lymph nodes, as the false positives and false negative results were noted in all stations of their study. Likewise, more recently, histopathologic lymph node evaluation was carried out in a study by Budak et al. [2] which revealed that the rate of patients incorrectly down-staged or up-staged by 18F-FDG PET/CT were 19% and 28%, respectively.

Many previous studies focusing on the prognostic or predictive value of max.SUV agreed that a higher max. SUV was associated with a lower overall survival and relapse-free survival [7, 10, 29, 30]. An important point that remains to be discovered, however, is the reason for failure in these patients. One potential cause is earlier local recurrence of disease, suggesting that tumors with higher SUV values are more locally aggressive. Yet another possible mechanism is an increased tendency for distant metastasis [31]. Unfortunately, clinical studies that investigated the relationship between distinctive metastatic characteristics and max.SUV are few and controversial.

Although Lee et al. [10] found that the whole-body metastatic score had no correlation with max.SUV, they reported that unfavorable metastatic sites such as abdominal and pelvic metastasis were found to have an independent association with high max.SUV. Alternatively, Ozgul et al. [9] showed that tumor max.SUV was not significantly correlated with distant metastases, which could be attributed to increased 18 F-FDG uptake by some

subclinical inflammatory lesions as well as by malignant tumors. Similarly, in a study evaluating maximum SUV, average SUV, and ratios of tumor SUV to liver and aorta, Duan et al. [11] found that none of these parameters were useful in predicting NSCLC clinical stage. Likewise, no significant association between max.SUV and distant metastasis was depicted in this study. Further studies with a larger cohort of patients are required to shed light on the relationship, if any, between tumor max.SUV and the propensity for distant metastasis.

Limitations of the current study include the relatively small sample size which represents an important drawback in the interpretation of our results. Also, many factors such as environment, genetics, economic status and ethnicity, that were unaccounted for in this study, may affect the FDG uptake. Moreover, the unavailable analysis of number of parameters including tumor differentiation, total lesion glycolysis and SUV mean represents other limitations for this study.

Conclusions

To conclude, the primary tumor size and its histologic subtype can significantly influence their (FDG) uptake in lung cancer, meaning that the max.SUV is significantly higher in the patients with tumor larger than 4.85 cm and the max.SUV of the squamous cell carcinoma group is significantly higher than that of adenocarcinoma and large cell cancer groups. Therefore, these findings could be employed as indicators to predict the disease prognosis and therapeutic response. Nonetheless, max.SUV cannot be used as predictive of metastatic potential or lymph node involvement. In addition, there is no significant association between the primary tumor max.SUV and age or gender of patients in each histologic subtype. Larger prospective trials may potentially elucidate more significant relationships.

Abbreviations

18-F: 18 Fluorine; FDG: Fluorodeoxyglucose; GLUT-1: Glucose transporter-1; IQR: Interquartile ratio; LCC: Large cell carcinoma; LN: Lymph nodes; Max.SUV: Maximum standardized uptake value; Mbq: Megabecquerel; Mets: Stands for metastasis; NSCLC: Non-small cell lung cancer; PET/CT: Positron emission tomography/computed tomography; SCC: Squamous cell carcinoma; SD: Standard deviation.

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Author contributions

SMIYS collected data, analyzed findings, scientific writing, reviewed and organized context. AMRA contributed to scientific writing, reviewing content. MGM contributed to scientific writing, reviewing content, EAFD analyzed findings, scientific writing, reviewed content. All authors have read and approved the manuscript.

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Availability of data and material

The datasets (cases illustrative stacks, PET/CT images, CT images) used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Ethics Committee of Ain Shams Ethical Research Committee with Reference Number: FMASU MD 317/2019. An informed written consent from each patient was taken before enrollment into the study.

Consent for publication

An informed written consent to publish this information was obtained from study participants.

Competing interests

The authors declare that they have no competing interests.

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