

Correlation and Predictive Value of the FDG uptake within Primary Mass in Non-small Cell Lung Carcinoma and Incidence of Distal Metastases

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A B S T R A C T

Introduction: Identification of tumour anatomic and functional features may allow us a better understanding of cancer dissemination. Here, we investigated how 18-Fluorine -Fluoro-2-Deoxyglucose [FDG] uptake influences the incidence of distal metastases.

Material and Methods: We retrospectively evaluated 18-Fluorine -Fluoro-2-Deoxyglucose Positron emission tomography integrated with computed tomography [FDG-PET/CT] of 35 patients with Non-Small cell carcinoma [NSCLC], who had come for pre-treatment staging of the disease.

Results: The mean FDG uptake of the tumour was maximum Standardized Uptake value [SUV max] of 10.73. 21 of the 35 patients had metastases. Metastases to the bone was the most frequent. The Pearson correlation between the FDG uptake and incidence of metastases was 0.013, suggesting negligent linear correlation between the two.

Conclusion: Non-small cell lung carcinoma tumour have a favoured spread to the bones. FDG uptake cannot be taken as an independent parameter to predict the incidence of metastases in NSCLC

Keywords: Non-Small Cell Lung Carcinoma, FDG-PET/CT, SUV Max, Metastases.

INTRODUCTION

Lung carcinoma is the second most common cancer in both men and women. In men, prostate carcinoma is most common, while in women, breast carcinoma is the most common. Of all cancers, lung carcinoma accounts for about 14 percent of all new cancers and 19 percent of cancer related deaths.¹ Lung carcinoma is divided into Non-Small cell carcinomas and Small cell carcinomas. The use of these terms is however being challenged.² Squamous cell carcinoma is commonest histological subtype.³ Presence and site of metastases is important to the clinical course and outcome of the patients.

Metastases to distal organs occurs by cancer cell migration and subsequent survival and proliferation. Distribution of metastatic spread is a not matter of chance but rather due to biological compatibility between the migrating cancer cells and receiving organ, according to the "seed" and "soil" hypothesis.⁴ Distal metastases is present in 18-36 percent of the cases at the time of diagnosis.⁵ Adrenal glands, bones, liver and brain are the common sites of metastases.

FDG-PET/CT is widely used for the evaluation of malignant tumours⁶, where FDG uptake serves as a marker of increased glycolytic activity. FDG-PET/CT provides

quantitative and semiquantitative measurement of glycolytic activity over the tumour volume in a simple, non-invasive and reproducible manner, unlike histopathological tests. Maximum Standardized Uptake value [SUV max] is a semiquantitative method of measuring the tumour glucose metabolism and reflects the tumour aggressiveness.

In this study, we thus investigated whether there exist a correlation between the FDG uptake in primary tumour and the incidence of distal metastases and also if the FDG uptake can be used an independent predictor of distal metastases.

MATERIAL AND METHODS

We retrospectively analysed the FDG-PET/CT of 35 patients with histopathologically proven patients Non-Small Cell Lung Carcinoma who came had come to our institution [Sri Ramachandra Medical Centre, Chennai, India] for pre-treatment staging. Patients who had prior neoadjuvant chemotherapy or radiotherapy were excluded from our study.

FDG-PET/CT imaging

Patients were asked to fast at least 6 h before the FDG-PET-CT scan. All patients had a glucose level below 180 mg/dl and were injected intravenously with 0.22 mCi (8.14 MBq)/kg (5-8 mCi/260-320 MBq) FDG. At 60-90 min

after the injection, data were acquired from the vertex to the upper thigh. The first CT scan was performed using 120 kV, 130mA, and a 3-mm section thickness. Immediately after CT, a PET scan (Siemens Biograph Horizon; Siemens Medical Solutions, Inc., Malvern, PA, USA) was performed for about 7 mins, with seven to eight bed positions and 1 min/position. PET images were reconstructed iteratively with CT data for attenuation correction, using an inline integrated Siemens Esoft Workstation system.

Image Analysis

Images were then transferred to Workstation (Siemens Syngovia workstation, Siemens Medical Solutions, Inc., Malvern, PA, USA). Computerized tomography integrated positron emission tomography fusion images in transaxial, sagittal, and coronal planes were evaluated. Maximum

standardised uptake values [SUV max] were based on the hottest pixel within the region of interest [ROI] drawn around the primary tumour on an attenuation-correction/PET-CT fused image. Presence or Absence of distal metastases was recorded as binarily.

STATISTICAL ANALYSIS

Data was exported on to a Microsoft excel sheet. The mean of the measurement data was expressed as mean \pm standard deviation [mean \pm SD]. Analysis of the data was done using Pearson's correlation coefficient. Statistical analysis was done using SPSS 17.0 [Chicago, Illinois, USA].

RESULTS

Of the 35 patients included in the study, 25 were male and 10 were female. Age varied from 35 to 77 years. The lowest

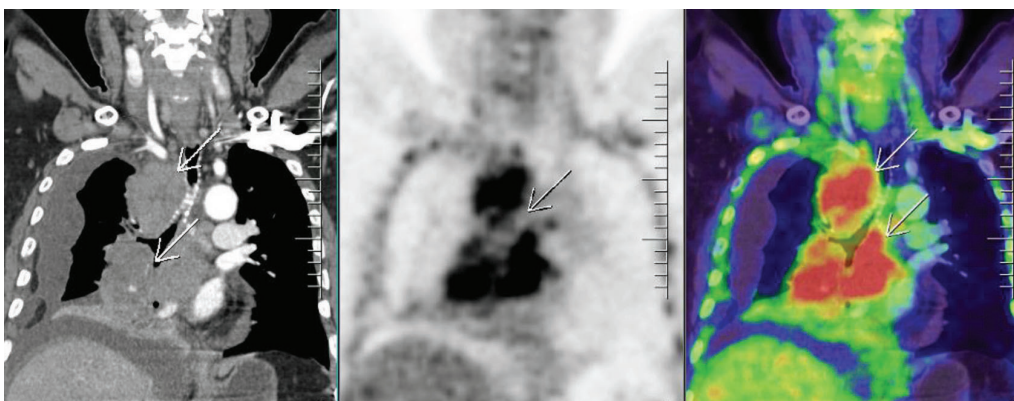


Figure-1: Coronal CT, PET and PET/CT fusion images showing FDG Avid masses in the right Lung.

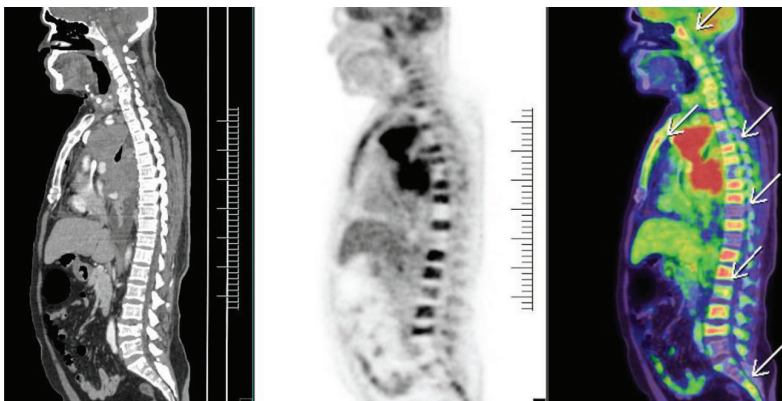


Figure-2: Sagittal CT, PET and PET/CT fusion images showing FDG avid metastases in multiple vertebrae.

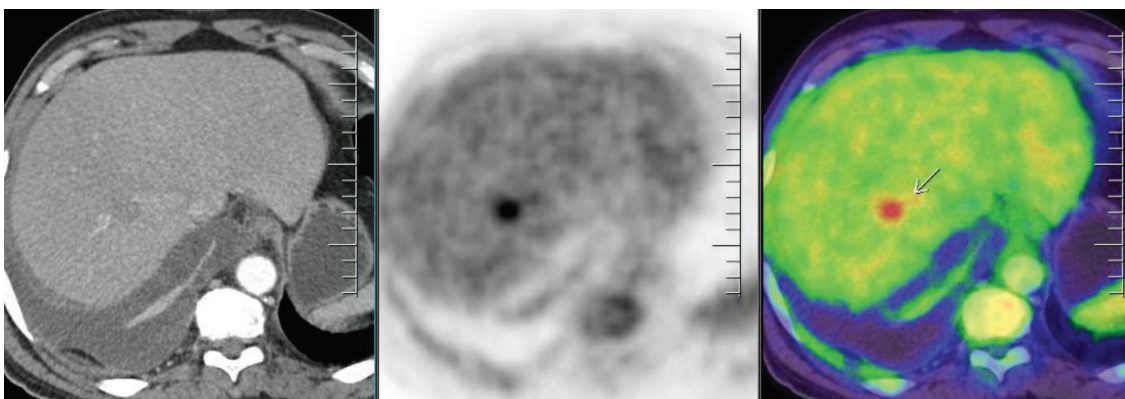


Figure-3: Axial CT, PET and PET/CT fusion images showing a FDG Avid Metastases in segment VIII of liver.

SUV max	Metastases (Y/N)
1.07	N
4.76	N
7.57	N
8.54	N
8.56	N
8.83	N
9.05	N
9.67	N
11.4	N
12.28	N
12.46	N
14.8	N
14.8	N
25.5	N
4.3	Y
4.93	Y
5.9	Y
6.19	Y
7.92	Y
8.29	Y
8.52	Y
8.53	Y
8.9	Y
9.97	Y
10.1	Y
10.67	Y
11	Y
11.1	Y
13	Y
13.2	Y
13.26	Y
15	Y
17.68	Y
18	Y
20.14	Y
Table-1:	

SUVmax was 1.07 and the highest SUV max was 20.14. The Mean SUVmax was 10.73 with a standard deviation of 4.80 (Figure 1). 21 of the 35 patients had distal metastases, with the bones being the most common site (Figure 2, Figure 3). The data is summarized in Table 1.

The Pearson Correlation Coefficient was 0.013, suggestive of negligible correlation.⁷

DISCUSSION

In this study, we examined the common sites of metastases and also if the FDG uptake correlates with the incidence of distal metastases.

Results revealed that the bone was the most frequent site of distal metastases. Carr LL. et al. found that adrenal gland was the commonest site, found in approximately 33% at autopsy.⁸ Radionuclide bone scan with ^{99m}Tc-methylene-diphosphonate was usually used for the detection of occult metastases, but, it had a high false-positive rate.⁹ FDG-PET/CT has an accuracy of 98 percent in detecting bone metastases as compared to 87 percent with bone scintigraphy.¹⁰ Meta-

analysis studies showed that the pooled sensitivity and specificity of FDG PET/CT for detecting distant metastasis from NSCLC were 0.87 [95 percent CI, 0.55–0.98] and 0.96 [95 percent CI, 0.93–0.98], respectively.¹¹ FDG-PET/CT has a high sensitivity [97 percent] and specificity [86 percent] for metastatic adrenal disease in NSCLC.¹² However, high glucose uptake by the gray matter and small size of the lesions restricts the diagnostic capability of FDG-PET/CT in the detection of brain metastases¹³, so MRI is the preferred modality of choice.

Our study also found no significant correlation between the FDG uptake in the primary tumour and in the incidence of metastases. Many studies have reported high FDG uptake with poorer prognosis^{14,15,16}, however, others have found that it is not an independent predictor of overall survival.^{17,18} FDG uptake was not recommended for risk stratification in the 7th edition of the American Joint committee on cancer staging manual.²⁰ In the National Comprehensive Cancer Network guidelines [version 3, 2014], it is not considered a prognostic biomarker.²¹ Study by Shou-Hui Zhu et al. inferred that higher FDG uptake by the primary tumour had a high extension and metastatic potential.²¹ Li et al. reported that FDG uptake of primary tumour was a potential indicator of metastases in T1 stage NSCLC.²²

Limitation of our study was that it was retrospective study, which could have caused selection bias, and also our sample size.

CONCLUSION

Although FDG uptake by a primary tumour is an indicator of the tumour metabolic activity and aggressiveness, the same cannot be used as an predictive indicator of the incidence of distal metastases. The favourable context of the bone appears to allow seeding of the tumour cells regardless of their FDG activity. Further investigations are required to assess the precise role of FDG uptake as an independent predictor of metastases.

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