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Original Research Article

The Role of PET-CT in the Assessment of Lung Masses in a Tertiary Care Centre: A Prospective Study

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Abstract

Objective: To investigate the diagnostic value and precision of PET-CT in assessing lung masses in the subjects of our study.

Methods & Materials: From 1 April-30 August 2022, the Department of Radiodiagnosis and Department of Nuclear Medicine at Patna Medical College Hospital in Patna, Bihar undertook this prospective cross-sectional study. Included were patients who were suggested and referred for the assessment of lung masses found on chest X-ray or by CT. During the study period, all patients who were referred for a lung mass examination were included. This investigation was conducted on a Siemens Biograph Sensation 16 device.

Results: The study population's mean and SD ages were 61.233 and 10.101. There were 30 patients, of which 10 (33%) were female and 20 (67%) were male.

Conclusion: PET CT is sensitive for spotting osseous involvement and subclinical adenopathy.

Keywords: Lung cancer, PET CT, S.U.V., Standardized Uptake Values.

Introduction

In the entire world, lung cancer is the top cause of mortality for both men and women. Lung cancer claims the lives of almost 1.6 million people annually, and the overall 5-year survival rate is barely 15% [1, 2]. The majority of lung cancers are found when they are already advanced. The patient may acquire a second malignancy, such as lung cancer, during or after undergoing therapy for the first. The mean survival duration is 31 months in patients with synchronous multiple primary lung cancer (MPLC) and contraindications to surgical therapy [1, 2, 3]. Distinguishing between intrapulmonary metastases and a new primary cancer may be difficult. It may be even more difficult to discriminate between a subsequent primary lung tumor and an intrapulmonary metastatic tumor if the former develops at a location previously treated with radiotherapy, due to the morphological changes that have taken place there. In recent years, the incidence and mortality of lung cancer are always ranked as the highest among all neoplasms. Lung cancer's main symptom is a mass, and getting the disease diagnosed is crucial for treating it. Lung cancer therapy depends on an early and precise diagnosis.

Lung cancer prevention is far more crucial than lung cancer screening. Receiving a

chest radiograph did not extend the survival of patients with lung cancer, according to randomised controlled trials. Recent research, however, has shown that patients with a history of severe nicotine dependency benefit from annual lung cancer screening with chest computed tomography (CT). For the past decades, Computed Tomography (CT) has been the gold standard imaging method in oncology. It has been used for initial staging, tumor evaluation after treatment, and follow-up of patients with cancer. The method depicts intricate morphological changes with the use of intravascular contrast, abnormal contrast enhancement, and blood flow due to pathological circumstances. The distinction between benign and malignant tumours is not always easy to make using this traditional imaging method.

The CT transmission scan can be utilised to produce an attenuation map that can be used to correct this attenuation effect in addition to providing anatomical information. The CT attenuation coefficients are scaled to represent the attenuation of the high-energy 511keV emission photons first due to the CT Xrays' lower photon energy (100–140kVp). Once scaled, they can be applied to the emission data to obtain the attenuation corrected image. This correction process is essential for quantitative assessment (S.U.V. standardized uptake values) as well as improved image quality. Because artifacts can be introduced during this process, any suspected findings can be verified by seeing if the abnormality was present on the uncorrected emission image. If it was present on the uncorrected image as well, then it is likely a true focus of increased uptake. The emission PET scan is often acquired after the CT transmission scan. The patient stays on a single scanning table and in the same position for both phases of the scan because the scanners are in the same gantry. As seen on the fusion image, they are inherently registered.

The functional status of a suspicious lesion can be depicted using the non-invasive molecular imaging technology known as positron emission tomography (PET), which uses a variety of radiolabelled chemicals to visualise metabolic changes between tissues. PET was developed in the early 1970s and was approved in the United States for limited use in the oncological clinical practice in 1998 [5,6]. The development of this method was based on the observation that malignant cells are associated with an increased glycolytic rate and increased cellular glucose uptake.

The biological process is seen using radiolabelled 18F-fluorodeoxyglucose (18FFDG). An analogue of glucose called FDG is taken up by cells similarly to glucose but is biologically held inside of cells after being phosphorylated by enzymes to form FDG-6-phosphate. Therefore, FDG can be used to quantify glucose metabolic rates [7,8]. The PET-CT scanners are essentially full ring coincidence detectors, the P.E.T. portion, physically mounted together with CT systems of various types. The PET tomographs are fitted with various crystals that are used to detect the emission photons and convert them to light signals. This scintillation event is converted to an electric signal that can be displayed on a monitor.

Lung tumours

Lung tumors are mainly divided into Small cell and non-small cell tumours. Histologic Classification of Non-small Cell Lung Cancer:

- Squamous Cell (Epidermoid) Carcinoma
- Adenocarcinoma
  - Acinar
  - Papillary
  - Bronchoalveolar
  - Solid tumor with mucin

- Clear cell adenosquamous carcinoma undifferentiated carcinoma
- Large cell carcinoma giant cell

The major distinction in terms of both staging and therapy is between small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC).

FDG Uptake in Lung Cancer

FDG is significantly present in lung cancer. Due to the relatively modest uptake in the nearby aerated lung compared to other soft tissues, this uptake stands out even more. About three times as much activity may be seen in non-aerated lung as in aerated lung. As lung tissue is less "dense", an area of atelectasis would have relatively higher uptake per volume of tissue compared to surrounding normal lung. This would hold true for a lung nodule as well. Therefore nodules should not be compared to surrounding aerated lung, but rather to other solid soft tissue to assess for relatively increased uptake. Comparison typically can be made with mediastinal soft tissues or blood pool.

SUV criteria

Standardized Uptake Value takes into account the differences between normalizing for body weight, for lean body mass, or for surface area.

SUV calculation

SUV = [mCi/ml (decay corrected) in tissue] / [mCi of tracer injected/body weight (grams)]

- "Cut off" value between benign and malignant single pulmonary nodules is in the range 2.0-2.5.
- Value decreases for smaller lesions due to partial volume effects
- Indirect comparison can be made to the mediastinal blood pool (generally in the range of 2.5).
- A positive nodule will demonstrate uptake greater than the mediastinal blood pool.
- Using this internal control can help avoid errors in the SUV calculation
- Quantified SUV facilitates comparison with the mediastinal blood pool on the display

Advantages of FDG-PET in Lymph Node Staging

FDG-PET has the ability to identify positive nodes that are smaller than the standard CT pathologic enlargement criteria of one centimeter as well as identify larger size nodes that are negative. PET imaging with anatomically fused images is advantageous in being able to identify the exact location of mediastinal nodes near the midline.

Methods

The patients in this prospective cross-sectional study were suggested and referred for the evaluation of lung masses found on chest x-ray or by CT between the dates of 1 April- 30 August 2022. This investigation was conducted on a Siemens Biograph Sensation 16 device.

Sample population and sampling method: All the patients who were referred for lung masses evaluation, within the study period were included through the purpose or convenient sampling method.

Inclusion criteria: All patients with a nodule/ mass lesion in lung parenchyma on chest radiography or CT scan were included

Exclusion criteria: All pregnant patients, patients with abnormal glucose levels on the day of test, breast feeding mothers were excluded.

Ethical consideration: Institutional Ethical committee permission was taken prior to the commencement of the study.

Data collection procedure: Following institutional ethical approval, the patients were informed of the study's goals and their agreement was obtained in this regard. Prior to the PET/CT examination, the patients were fasted for at least 6

hours. On the test day, patients had their blood sugar levels checked, and once they were found to be normal, they received 2 mci/kg of 18F-FDG. Prior to having a PET/CT scan, patients rested for roughly 50-60 minutes. acquisition of images An integrated PET/CT device is used for image acquisition (Siemens Biograph Sensation 16). A standard approach was used to do CT from the head to the pelvic floor (120 KV, 80 mA with a slice thickness of 5 mm). PET images in early display were acquired using 3D mode for the same scanning range as CT. The acquisition time for PET was 3 minutes per bed position and 5-6 continuous positions were scanned. Delayed images of chest were acquired at 2 hours after injection of 18F-FDG. PET images datasets were reconstructed iteratively using an ordered subset expectation maximization algorithm and were corrected with measured attenuation correction. The selected ROI's SUVmax in lesions was computed. A post processing facility was used to obtain axial, sagittal, and coronal CT, PET, and PET/CT infusion pictures. Analytical HPLC was used to confirm that 18F-FDG had radiochemical purity (>95%).

Data Analysis

The SUV max, as well as the pattern of activity (focal/diffuse), and the existence of photopenia without necrosis, were all taken into account in the image interpretation of the scintigraphy characteristics of the lesion. The existence of additional lesions such as lymphnodal activity, soft tissue or skeletal lesions, CT characteristics of the lesion correlating to the areas of aberrant tracer concentration, and FDG activity in the margins of the lesion (sharp margins/smeared out). In few of the cases a 2hr delayed imaging findings also taken into consideration, lesions with an increase in SUV value after 2hrs are considered as malignant. The cut off value in characterization of lesions as malignant vs benign was taken as 2.5. We tried to characterize the nature of lung masses in unknown cases taking SUV max cut off as 2.5,SUV max < 2.5 as benign and >2.5 as malignant.

Statistical Analysis

The collected data was entered in Microsoft excel 2007 and analysed using SPSS version 20 software, trial version. Data was described in terms of mean ± standard deviation, frequencies as appropriate. Chisquare and t-test will be used to find out the associated significance wherever applicable. The results were presented in the form of charts, graphs, etc. The statistical significance level was fixed at $P < 0.05$.

Results

Following complete written patient consent, 30 patients were evaluated while adhering to the inclusion and exclusion criteria. There were 30 patients, of which 10 (33%) were female and 20 (67%) were male. The study's participants ranged in age from 33 to 81. The study population's mean and SD ages were 61.233 and 10.101. Out of 30 subjects, 17 (56.66%) subjects had no previous malignancy where 13 (43.4%) subjects had past history of diagnosis of malignancy. Out of 13 following table reveal the details of previous malignancies. Of the 30 subjects, 11(36.6%) had solitary pulmonary nodule and rest of the 19(63.4%) had multiple nodules.

The lesion had a mean size of 2.7, with the greatest measuring 10 cm and the smallest 0.5 cm. Out of 30 individuals, 18 had lesions with spicules, and the others had lesions with smooth margins. 11 of the 30 individuals had lung parenchymal lesions that were necrotic. 28 of the 30 individuals had aberrant tracer activity due to lung prenchymal nodules or masses (ATA). Rest of the 2 subjects had lung parenchymal nodule/mass lesion which did not show any abnormal tracer activity. Mean value of the SUV max for the lung parenchymal lesions was 8.28. Maximum

suv max value is 31.4. Photopenic areas s/o necrosis are seen in the parenchymal lesion in 11 subjects. We tried to characterize the nature of lung masses in unknown cases taking SUV max cut off as 2.5, < 2.5 as benign and >2.5 as malignant. Out of the 17 subjects with unknown malignancy, 14 subjects had lung nodules with SUV max >2.5.

Out of the 14 subjects in whom suv max was >2.5, in 12 subjects the lesions turned out to be primary lung carcinomas. And in two subjects the lesion turned out to be metastatic lung nodule, one with primary in the breast and other with primary in the prostate which also showed intense tracer uptake. One case with lung lesion with SUV max of 1.67 turned out to be Bronchoalveolar carcinoma on HPE.

Diagnostic Accuracy

In this investigation, the sensitivity and specificity for classifying a lesion as malignant using the SUV maximum cutoff of 2.5 are 92.8% and 66.67%, respectively. Seven out of the thirteen participants who had a history of a known primary showed a strong tracer uptake on PET and were later found to have metastatic disease on HPE. The lesions in the remaining 6 cases were discovered to be granulomatous in 4 subjects and fibrosis on HPE in the other 2 subjects. The sensitivity and specificity PET- CT evaluating metastatic lung lesions taking SUV max value of 2.5 as cut off are 100% and 83.3%. All the parenchymal lesions which turned out to be adenocarcinoma on HPE showed abnormal tracer activity. The man SUV max for adeno carcinomas is 13.58. All Parenchymal lesions which turned out be squamous cell carcinoma on HPE showed abnormal tracer activity. The mean SUV max for squamous cell carcinoma is 8.36. Tracer activity was aberrant in one parenchymal lesion, which turned out to be a tiny cancer. This has a maximum SUV of 15.20. Additionally, the tumours that on HPE revealed to be infected or inflammatory granulomas displayed aberrant tracer activity. Suv max is 1.67 on average for these lesions.

Discussion

When assessing and staging lung lesions, the hybrid PET-CT equipment is a useful tool. By displaying both functional and morphological traits at once, combined PET and CT adds a marginal clinical benefit. Thirty patients, including 13 with confirmed cancer, had lung nodules or masses found on X-rays or CT scans for our study. In our study we used a SUV max of 2.5 as a threshold value for characterizing the lesion, lesions with SUV max > 2.5were considered as malignant and lesions with SUV max, 2.5 as benign similar to a study done by Orino k etal in showing efficacy of F-18 fluoro deoxy glucose PET scans in characterization of pulmonary nodules [5-10].

In our study the sensitivity and specificity in characterizing lesion as malignant taking suv max of 2.5 as cut off is 92.8% and 66.67%. Computed tomography and 18F-FDG-PET/CT result in a reduction of radiological artifacts due to cardiac and respiratory movements with a detection rate between 1 and 5 mm. Moreover, the latter positively contributes to the identification of sub-centimeter pulmonary neoplasms because their low necrotic areas favor the SUV and thus overall specificity.

The 2015 BTS Guidelines for the evaluation and management of pulmonary nodules state that cancer can be detected by PET-CT with a sensitivity of 93.9% and specificity of 88.5%. Our study supported these recommendations. The mediastinal blood pool should be used as a reference point for a qualitative analysis to identify FDG uptake [9]. Ultimately, these guidelines emphasize the importance of a revision of the uptake cut-off, towards a qualitative dual-time assay rather the absolute SUV value. However, the high sensitivity has to be referred to a pooled cohort of patients with an adjusted stratified risk stratified according to a

predefined model, and then, although it would be in conflict with those reported in the general analysis from ACCP in a reduction of the occurrences of false positives and false negatives, stratified rates of occurrence are in agreement with those published in other large series.

Yi et al. [11] evaluated 119 SPNs patients with diameters between 6.2 and 30 mm who underwent both helical dynamic computed tomography (HDCT) and 18F-FDG-PET/CT. Cut-off malignancy index were an enhancement ≥25 Hounsfield Units (HU) for the previous and a SUVmax≥3.5 for the latter. Sensitivity, specificity, diagnostic accuracy, PPV and NPV were 81 versus 96%, 93 versus 88%, 85 versus 93%, 96 versus 94% and 71 versus 92%, respectively. Authors concluded that -FDG-PET/CT can be used as a first level diagnostic investigation (i.e. first-line evaluation tool) but HDCT remains a viable alternative according to its high specificity and acceptable diagnostic accuracy.

Kagna et al. [12] compared visual 18F-FDG-PET-low-dose chest CT (LDCT), semiquantitative 18F-FDG-PET/LDCT, and LDCT on 307 SPN patients, 93 of whom had a high risk of lung cancer. 38 percent of patients mentioned a malignancy-related histology diagnostic. Visual PET/LDCT analysis displayed sensitivity of 94%, specificity of 70%, accuracy of 80%, a PPV of 66%, and NPV of 95% compared to 77, 83, 81, 73 and 86% for semi-quantitative PET/LDCT and 97, 48, 66, 53 and 96% for LDCT respectively. Harders et al. [13] reported 168 patients with SPN ≤30 mm in order to verify multi-detector computed tomography (MDCT) and integrated PET clinical reliability in the detection of malignant lung lesions. 18F-FDG-PET/LDCT and MDCT showed a sensitivity of 97 versus 93%, a specificity of 47 versus 53%, a diagnostic accuracy of 81 versus 82%, a PPV of 89 versus 89% and a NPV of 79 versus 63%, respectively. Results appear to be marginally different from earlier results, particularly in terms of diagnostic acuity and sensitivity. With a sensitivity and specificity of 100% and 83.3%, respectively, our investigation included 13 people with a history of known primary using an SUV max of.2.5. Out of 8 subjects, 7 were found to be metastatic and one to have Kochs disease. Independent of the size of the nodes, our study demonstrated 100% sensitivity in picking up mediastinal nodes (even sub centimetre nodes). In our study PET CT shows 100% sensitivity in picking up adrenal metastasis. One case of Bronchoalveolar carcinoma showed low SUV max and turned to be the only false negative case in our study. In one case PET CT was able to show abnormal tracer activity in pelvic bones and D11 and L5 vertebral bodies likely to be metastasis which were not picked up on CT. In two cases with extensive necrosis, we are able to guide the site of biopsy by showing areas of intense uptake and the HPE turned out be positive. In our study we found that males are more affected than females. Non-small cell carcinoma was the most common primary malignancy of lung in our study and in that adeno carcinoma was more common.

Dabrowska et al. [14] reported 71 SPN patients with diameter between 8 and 30 mm. Radiological assessment was carried out by contrast-enhancement (CE) CT (enhancement cut-off of 19 HU) and 18F-FDG-PET/CT (SUVmax cut-off of 2.5), in order to assess the accuracy of the two radiological methods in characterizing benign or malignant lesion. Sensitivity was 100 versus 77%, specificity 37 versus 92%, diagnostic accuracy 0.58 versus 0.9, PPV 32 versus 83% and NPV 100 versus 89%. According to sensitivity and NPVs, the authors concluded that CECT should be preferred in low risk patients, while PET should be recommended in high-risk ones due to high specificity and PPV levels.

In their 2004 report on the International Association for the Study of Lung Cancer/American Society of Clinical Oncology consensus workshop, Travis et al. [15] warned that sub-solid nodules could be a manifestation of atypical adenomatous hyperplasia and hyperplasia in general (AAH). Between 10% and 23% of NSCLC patients have this later condition [16]. However, bronchioloalveolar carcinoma (BAC), which exhibits a lepidic growth-model along the inter-alveolar septa in the absence of stromal invasion, is frequently linked to the existence of a sub-solid lung nodule. Results were confident with Goudarzi et al. ones [17] The Authors, after an evaluation of 53 patients, underlined absence of a diagnostic role of PET/CT in the T-parameter staging process due to the low radiopharmaceutical uptake. In fact, in only 24% of lepidic or papillary adenocarcinomas, a significant and identifiable metabolic rate was detected; results which are inferior to other primitive tumor uptake values [18-21]

Conclusion

In our study, PET CT has a sensitivity and specificity of 92.8% and 66.7% in identifying the histopathological type of lung nodules/masses. When identifying nodules or masses seen in individuals with a history of cancer, PET CT offers a sensitivity and specificity of 100% and 83%, respectively. PET CT is capable of accurately identifying osseous involvement and subclinical adenopathy. Although 18F-FDG-PET/CT is the most sensitive noninvasive diagnostic procedure for prediction of malignancy of < 10 mm-solid solitary pulmonary nodules, CT alone cannot be considered superfluous due to its characteristics and peculiarities for a proper evaluation of these lesions.

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