The Egyptian Journal of Hospital Medicine (July 2018) Vol. 72 (4), Page 4264-4269

Role of PET/CT in Differentiating Bronchogenic Carcinoma from Inseparable Pseudo-Neoplastic Lesions

Mounir S. Girguis, Mohamed G., Ahmed M. Osman, Maged M. Sabry
Radiodiagnosis Department, Ain Shams University, Cairo, Egypt
Corresponding Author: Maged M.S. Abdel-Aziz, **Email:** drmagedsabry@live.com, **Tel.:** 01006264155

ABSTRACT

Background: Bronchogenic carcinoma is the single most important cause of cancer-related deaths with approximately 1.5 million cases worldwide every year. Computed tomography (CT) scanning can only estimate the proximal extent "with difficulty in visualization the real borders" of a tumor. The role of MRI in local staging of bronchogenic carcinoma is limited by the signal loss secondary to respiratory motion and heterogeneity of the magnetic field caused by the tissue/air interfaces. Positron Emission tomography combined with CT (PET/CT can accurately delineate the viable tumor from surrounding atelectasis and collapse/consolidation, This information cannot only demarcate the size and extent of the tumor for accurate T staging, but also provide guidance for biopsies if histological confirmation is required

Purpose: It was to emphasize the role of PET/CT in differentiation the bronchogenic carcinoma from its inseparable pseudo-neoplastic lesions for better staging and increase the accuracy of follow up by ruling out the pseudo progression as well as pseudo regression.

Patients and Methods: The study involved 32 patients proved histo-pathologically to have bronchogenic carcinoma and referred for PET/CT scanning. Each patient included in the study was subjected to full history taking, reviewing medical sheet and PET/CT examination. The study was done in private center (Techno-scan holding center, Heliopolis branch using PET-CT machine (GE Discovery VCT 64 PET/CT, USA); in which PET-CT examination was followed by diagnostic contrast enhanced CT examination and processed at Ain Shams University, Radiology department.

Results: In this study we found presence of inseparable pseudo neoplastic lesions among 20 patients out of 32 patients and the mean diameter of the bronchogenic mass lesion was 6.89 +/- 3.65 SD as measured by CT, while it was 5.77 +/-3.38 SD as measured by PET/CT in centimeters.

Conclusion: The combined PET/CT using 18F-FDG is the best oncologic imaging modality with valuable role in local staging and follows up in patients of bronchogenic carcinoma.

Keywords: Bronchogenic carcinoma–PET/CT– Pseudoneoplastic lesions.

INTRODUCTION

Bronchogenic carcinoma is the single most important cause of cancer-related deaths with approximately 1.5 million cases occurring worldwide every year [(1)].

A number of imaging modalities have been used in staging lung cancer. These include (CT), magnetic resonance imaging (MRI) and fluorine-18-dexy-D-glucose positron emission tomography (FDG/PET) [(2)].

CT scanning can only estimate the proximal extent "with difficulty in visualization the real borders" of a tumor. It also has difficulty in differentiation between pleura-pericardial or chest wall invasion and anatomic contiguity or desmoplastic reaction [(3)].

The use of FDG tracer made PET contribution to oncological imaging matchless by any other functional imaging modality [(3)].

PET/CT can accurately delineate the viable tumor from surrounding atelectasis and collapse/ consolidation. This information cannot only demarcate the size and extent of the tumor for accurate T staging, but also provide guidance for biopsies if histological confirmation is required or prior biopsy attempts have led to inconclusive pathological results [(4)].

AIM OF THE WORK

To emphasize the role of PET/CT in differentiation the bronchogenic carcinoma from its inseparable pseudo-neoplastic lesions for better staging and increase the accuracy of follow up by ruling out the pseudo progression as well as pseudo regression.

PATIENTS AND METHODS

A cohort study involved 32 patients with histopathologically proved bronchogenic carcinoma and referred for PET/CT scanning. This study carried out in the period from March 2016 to July 2017. All patients were histopathologically proven to have bronchogenic carcinoma either by endoscopic transbronchial or CT guided biopsies. The study was done in private center (Techonscan holding center, Heliopolis branch) using PET-CT machine (GE Discovery VCT 64 PET/CT, USA); in which PET-CT examination was followed by diagnostic contrast enhanced CT examination and processed at Ain Shams University, Radiology department.

Received:20/4/2018
Accepted:29/4/2018

In the day prior to exam, the patients were instructed to refrain from all strenuous activity and home blood glucose was checked.

In the day of exam: All the patients were asked to fast six hours prior to scan.

Good history taking and verify indications from the patient. The weight of the patient is measured.

10 - 20mCi (370 MBq; approximate dose to patient, 3-5MBq/Kg) of 18F-FDG was administered to each patient 45–90 minutes before examination, then they were asked to rest in a quiet room, devoid of distractions, and they also asked to keep their movements, including talking, at an absolute minimum. This minimizes physiologic uptake of FDG into skeletal muscle, which can confound interpretation of the scan.

Inclusion criteria:- Patients with pathologically proven bronchogenic carcinoma were included in this study.

Exclusion criteria:- Pregnant females (for the risk of radiation on the fetus). Patients with blood glucose level >300 mg/dl at the time of the study (for misinterpretation after 18F-FDG uptake). High serum creatinine > 2mg/dl is contraindication for non-ionic contrast media injection.

Technique: Technique was done using PET-CT machine (GE Discovery VCT 64 PET/CT). A typical whole body PET -CT study (neck, chest, abdomen, and pelvis) was done, scanning began at the level of the skull base and extended caudally to the level of the upper thighs. The total length of CT coverage was equal to an integral number of bed positions scanned during acquisition of PET data. The study was performed with the patient breathing quietly. The CT images, PET images and fused PET-CT images will be evaluated regarding the primary tumour size, site and extension, the presence of lymph nodes and distant metastases, comparison with previous studies as well as the effect of the results on patient's management.

Ethical and approval statements: The study was approved by the Ethics Board of Ain Shams University and an informed written consent was taken from each participant in the study.

Statistical analysis: Data were coded and entered using the statistical package SPSS (Statistical Package for the Social Sciences) version 24. Data was summarized using mean, standard deviation, median, minimum and maximum in quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. For comparing categorical data, Chi square (χ^2) test was performed. Exact test was used instead when the expected frequency is less than 5 (Chan, 2003a). Correlations between quantitative variables were done using Spearman correlation coefficient (Chan, 2003b). P-values less than 0.05 were considered as statistically significant.

RESULTS

The study involved 22 male and 10 female patients between 34 and 77 years old. Comparison between CT largest diameter of the masses and their active PET/CT sized was done. p-value for results was less than 0.001. Pie chart was done for relation between smokers and non smokers at our study population and there was positive relation between smoking and incidence of bronchogenic carcinoma, as 69% of the study population gave positive history of smoking. Right Upper Lung lobe (RUL) was the commonest site to be involved by the malignant lesion among our study population with incidence of 34.4%. The most frequent pathological type among our study population was adenocarcinoma with incidence of 46.8%. The mean diameter of the bronchogenic mass lesion was 6.89 +/- 3.65 Standard deviation (SD) as measured by CT, while it was 5.77 +/-3.38 SD as measured by PET/CT in Centimeters. When comparing the follow up results between CT and PET/CT there were:

Nine patients show regressive course by follow up CT while by combined PET/CT those patients shows: Six patients of them presented actual regression of activity and size. While the last three patients presented progressive course as regards activity which is called Pseudo Regression.

Three patients show progressive course by follow up CT while by combined PET/CT those patients shows: One patient of them presented actual progression of size and Maximum standardized uptake value (SUV max). Another patient presented central inactivity. While the last patient presented regressive course.

One patient show residual mass by follow up CT while by combined PET/CT this show total resolution of activity.

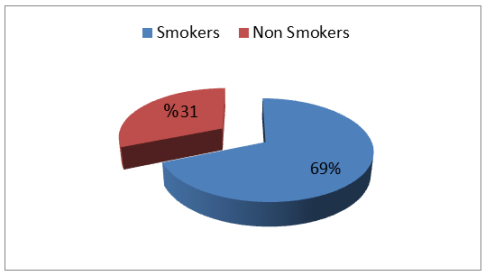

Figure (1): Pie chart showing the relation between smokers and non smokers at our study population.

Table (1): Types, numbers and percentage of the tumor's pathology of the patient in the study.

		Count	%
Pathology	Adenocarcinoma	15	46.8%
	Squamous cell carcinoma (SCLC)	8	25.0%
	Undifferentiated Carcinoma	6	18.8%
	Small Cell Carcinoma (SCC)	3	9.4%

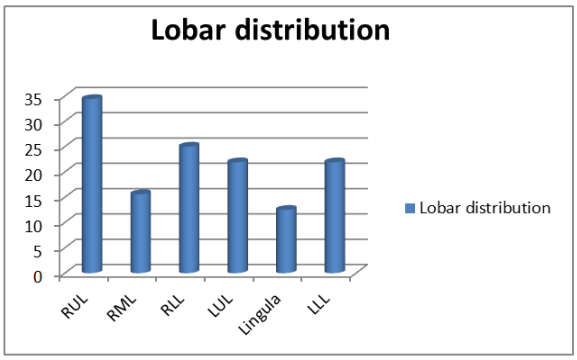

Figure (2): Lobar distribution of the tumor: Right Upper Lung lobe (RUL), Right Middle Lung Lobe (RML), Right Lower Lung lobe (RLL), Left Upper Lung Lobe (LUL) and Left Lower Lung Lobe(LLL).

Table (2): Interval changes of the appearance and size of tumor by follow up CT and combined PET/CT.

		Count	%
Follow up CT	Not done	19	59.4%
	Progressive	3	9.4%
	Regressive	9	28.1%
	Residual	1	3.1%
Follow up PET/CT	Not done	19	59.4%
	Progression (Pseudo Regression)	3	9.4%
	Progressive	1	3.1%
	Progressive with central inactivity (Pseudo Progression)	1	3.1%
	Regressive	6	18.8%
	Regressive (Pseudo Progression)	1	3.1%
	Total regression of activity	1	3.1%

CASES

Case 1

Clinical data: A 72 years old female patient with history of Right lung UL adenocarcinoma. Her staging PET/CT done in Dec. 16 reported T4N2M1a Disease. She has been put on immunotherapy. PET/CT is requested for Therapy Monitoring

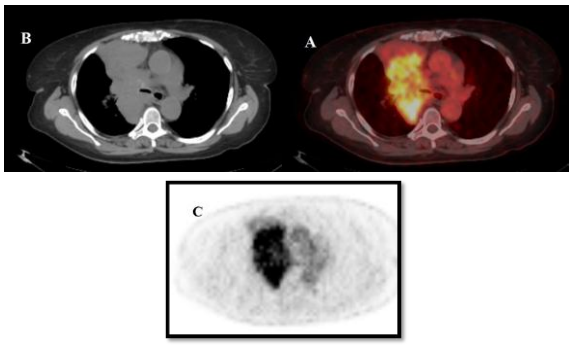

Figure (3): A: Combined PET/CT image of the mass, B: contrast enhanced CT only of the mass, C: PET images only of the mass.

Comment:

Large right upper lung mass lesion (10x6x7.5 cm); inseparable from Rt. aspect of mediastinum, encasing the Rt. main bronchus up to the carina and eliciting denser tracer fixation; SUVmax reaching 10.5 with inseparable anteriorly related inactive consolidative patch.

Case 2

Clinical data:

A68 years old female patient with history of Lt. lung mass and Lt. supra-clavicular LN.s, nodal biopsy revealed metastatic SCC.

PET/CT done for status evaluation and therapy monitoring.

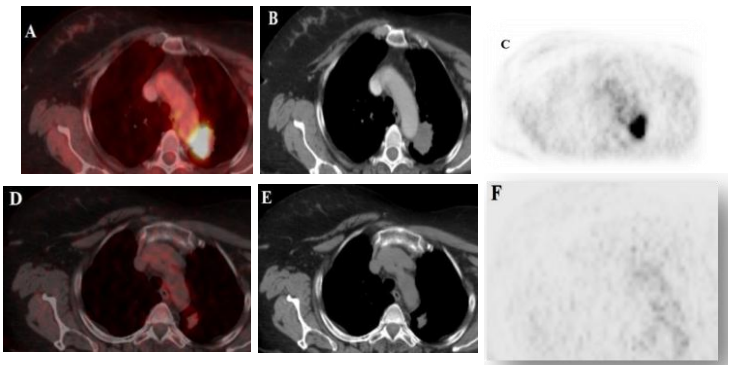

Figure (4): Follow up images of the same patient, figures (A,B and C) dated December, 2016 while figure (D,E and F) dated March, 2017. A and D: Combined PET/CT image of the mass, B and E: contrast enhanced CT only of the mass, C and F: PET images only of the mass.

Comment:

After three months interval time when comparing the old to new CT images of the patient, apparent small residual nodule is seen yet after combined PET/CT study it seems that it is inactive nodule with total regression of activity.

Case 3

Clinical data:

A 78 years old male patient with history of Rt. SCLC received chemotherapy.

PET/CT study was done for status evaluation and therapy monitoring.

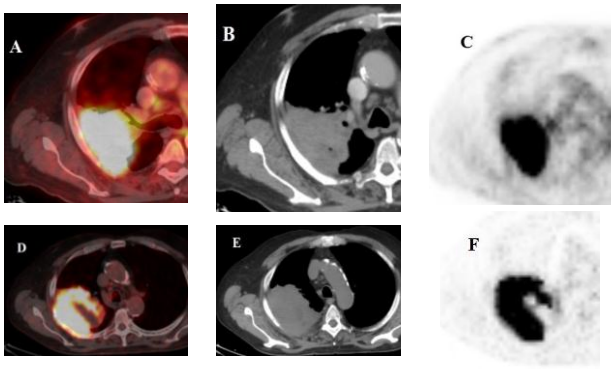

Figure (5): Follow up images of the same patient, figures (A,B and C) dated December, 2016 while figure (D,E and F) dated May, 2017. A and D: Combined PET/CT image of the mass, B and E: contrast enhanced CT only of the mass, C and F: PET images only of the mass.

Comment:

After four months interval time when comparing the old to new CT images of the patient, apparent progression is seen termed by increased of the size of the mass, yet after combined PET/CT study it seems that it is pseudo-progression because the active mass of the patient shows large central area of inactivity.

DISCUSSION

Occasionally, it is difficult to determine the exact tumor location and extent on CT scan due to surrounding atelectasis. In such situations, FDG PET/CT can accurately delineate the viable tumor from surrounding atelectasis and collapse/ consolidation. This information can not only demarcate the size and extent of the tumor for accurate T staging but also provide guidance for biopsies if histological confirmation is required or prior biopsy attempts have led to inconclusive pathological results [4].

Our study involved 32 patients (22 male and 10 females) proved to have bronchogenic carcinoma referred for PET/CT scans for staging or therapy follow up.

There was positive relation between smoking & incidence of bronchogenic carcinoma with 69% of the study population gave history of smoking. This is consistent with ***Furrukh*** [5], who stated that smoking has the most consistent causative agent for developing the disease.

Fifteen patients among the 32 of our study representing 46.8% were pathologically proved adenocarcinoma this coincides with ***Colby et al.*** [6] who stated that Adenocarcinomas are the most frequent subtype of bronchogenic carcinoma.

In our study both upper lung lobes were the most frequent sites of bronchogenic carcinoma (18 of 32) patients being more frequent invading right upper lung lobe (34.4% of cases). This is in agreement with ***Jamnik et al.*** [7] who stated that bronchogenic carcinomas are predominantly found in the upper lobes.

We found a significant difference between the mean diameter of the malignant mass measured by CT and mean diameter measured by PET/CT images with P value <0.001 being relatively lower in PET/CT (6.89+/- 3.65cm) compared to (5.77+/- 3.38 cm) in CT. This is may be explained by the presence of nearby inseparable lesions which was wrongly estimated as part of the mass in CT due to absence of morphological difference while in PET/CT we measured the mass diameter depending on the mass showing positive activity. This also noticed by ***Aydin et al.*** [8] who stated that the maximum measurement of the tumors on the CT scan showed a lower concordance (mean difference -0.3) than that obtained from CT.

In our study the biological active masses evidenced by high SUVmax values were inseparable from other non neoplastic (Pseudoneoplastic lesions) in 20 of 32 patients in form of consolidations, atelectasis, pleural effusion and thickening as in agreement with ***Hochhegger et al.*** [9]. Integrated PET/CT allowing the differentiation between tumor and post-obstructive atelectasis, which can present challenges when the T staging of NSCLC is performed with CT alone. Also ***Sahiner et al.*** [10] who stated that PET/CT can allow a more detailed characterization and evaluation of pleural effusions as differentiation between benign and malignant effusion is important in determining the respectability and use of radiotherapy. Pleural

thickening or nodularity on CT may be suggestive for metastatic pleural disease. CT is not conclusive of the benign or malignant nature of the pleural disease. And Our study agreed with ***De Wever et al.*** [11] in that PET/CT allowed better discrimination between the tumor and surrounding consolidative changes. This differentiation helped in proper assessment of the actual size and extensions of the tumor and this is very important for staging and treatment option decision if the patient will have operation or radiotherapy and also very important during patients follow up.

Combined PET /CT could change of biopsy site decision in 9 of our 32 patients, directing it to the active mass only. In agreement with ***Yousefi-Koma et al.*** [12] who stated that exact localization of biopsy site is easy and more accurate with PET/CT fusion image.

We agree with ***Nabil et al.*** [13] who concluded that integrated PET/CT imaging, which combines both functional and morphologic imaging in a single examination, has shown how the initial staging and subsequent follow-up of patients with chest tumors can supersede the traditional methods of evaluation in terms of diagnostic accuracy and has an impact on the management. The follow up for 13 of 32 patients in the study revealed that:-

Nine patients presents regressive course by CT while by PET/CT three of them shows progressive course (pseudo regression). This may be attributed to reduction of size of the inseparable consolidation and therefore the mass-consolidation complex and progression of the actual mass size.

Three patients presents progressive course by CT while by PET/CT two of them shows regressive course (pseudo progression).This may be explained by that the enlargement in size was in the inactive inseparable consolidation.

One patient show residual mass by follow up CT while by combined PET/CT this show total resolution of activity because the residual mass wasn't active tumor pathology.

This is consistent with ***Bogot et al.*** [14] who stated that post-surgical findings and radiation effects may simulate tumor recurrence on imaging and FDG-PET imaging has a role in distinguishing persistent or recurrent tumor from post-treatment scarring or fibrosis and is more sensitive than chest CT in detecting recurrent tumor.

CONCLUSION

The combined PET/CT is better than CT imaging alone for staging and follow up assessment of patients with bronchogenic carcinoma as well as pre biopsy assessment and more accurate in differentiating true mass lesions from inseparable pseudo neoplastic lesions as well as can rule out pseudo regression or pseudo progression of the mass in follow up.

REFERENCES

1. **Ningappa R, Ashwini C and Deepak S (2015):** Role of MDCT in the evaluation of Bronchogenic carcinoma. SSRG international Journal of Medical Science, 2(3):21-23.
2. **Ravene JG and Erasmus J (2013):** Azygoesophageal recess. Journal of Thoracic Imaging,17:219-226.
3. **Cano A, Hidalgo HL, Moreno AE, Correa PC and De Vega MV (2012):** Role of imaging techniques in the TNM classification of non-small cell bronchogenic carcinoma.Radiologia, 54(4):306-20.
4. **Purandare NC and Rangarajan V (2015):** Imaging of lung cancer: Implications on staging and management.The Indian Journal of Radiology & Imaging, 25(2):109-120.
5. **Furrukh M (2013):** Tobacco Smoking and Lung Cancer: Perception-changing facts. Sultan Qaboos University Medical Journal, 13(3):345-358.
6. **Colby TV, Noguchi M, Henschke C, Vazquez MF, Geisinger K, Yokose T, Ohori P, Jambhekar NA, Rami-Porta R, Petersen I, Franks T, Takahashi T, Kawai T, Shimosato Y, Meyerson M, Matsuno Y, Khoor A, Hanash SM, Westra WH and Jen J (2004):** Adeno carcinoma In W. D. Travis, Brambilla E., Müller-Hermelink H. K. and Harris C. C.(eds): Pathology and Genetics of Tumours of the Lung, Pleura, Thymus and Heart. IARCS Press.
7. **Jamnik S, Uehara C and D Silva VV (2006):** Location of lung carcinoma in relation to the smoking habit and gender.J Bras Pneumol., 32(6): 510–14.

8. **Aydin F, Dertsiz L, Budak ES, Yildiz A, Ozbilim G and Gungor F (2013):** Measurements of tumor size using CT and PET compared to histopathological size in non-small cell lung cancer.Diagnostic Intervention Radiology, 19(4):271-8.

9. **Hochhegger B, Alves G,Irion K, Fritscher C, Fritscher LG, Concatto NH and Marchiori (2015):** PET/CT imaging in lung cancer: indications and findings. Jornal Brasileiro de Pneumologia, 41(3):264-274.

10. **Sahiner I and Vural GU(2014):** Positron emission tomography/computerized tomography in lung cancer. Quantitative Imaging in Medicine and Surgery,4(3):195-206.

11. **De Wever W, Stroobants S, Coolen J and Verschakelen JA (2009):** Integrated PET/CT in the staging of non small cell lung cancer: technical aspects and clinical integration. Eur Respir J., 33(1):201-12.

12. **Yousefi-Koma A, Panah-Moghaddam M and Kalff V (2013):** The Utility of Metabolic Imaging by 18F-FDG PET/CT in Lung Cancer: Impact on Diagnosis and Staging.Tanaffos,12(1):16-25.

13. **Nabil H, Maher M and Mahdy S (2014):** Follow up in chest tumors: Value of integrated PET/CT. The Egyptian Journal of Radiology and Nuclear Medicine,45(3): 679-688.

14. **Bogot N, Naama R, and Quint LE (2004):** Imaging of Recurrent Lung Cancer.Cancer Imaging,4(2): 61–67.