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Role of PET/CT in Differentiating Synchronous Second Primary Lung Masses from Lung Metastases

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Abstract

Background: In case of multiple pulmonary and extrapulmonary lesions, it is difficult to determine if the lung mass was primary lesion or metastasis from a distant organ, even in multiple pulmonary lesions. it is difficult to determine sit of primary one.

Aim of Study: We retrospectively measure the SUV_{max} and Δ_{SUVmax} in pulmonary and extrapulmonary lesions and identify if there is a cutoff value of $_{SUVmax}$ between pathologically proved synchronous second primary and metastatic lesions.

Patients and Methods: 65 patients (50 male and 15 female with age ranged from 35 to 70 years) who had multiple pulmonary and extrapulmonary lesions were evaluated by PET/CT, all patients were evaluated by oncology physicians, patients were selected after histopathological evaluation, patients with lung metastasis taken as a control group. SUV_{max} and Δ_{SUVmax} were measured in both groups.

Results: A significant $(\Delta SUV)_{max}$ difference between both included groups: Metastatic lung cancers and second primary lung tumours with a cutoff value of 35% while no significant ΔSUV_{max} between the studied cases in the same groups, as below this level approved for metastatic lesion and above this cutoff values consistent with the synchronous second primary tumour, this help in better staging and management of lung cancer.

Conclusion: PET CT is considered as a functional non-invasive technique, we recommended that all patients with multiple pulmonary and extrapulmonary lesions to add this investigation, before taking the decision of management, it can differentiate between multiple primaries and metastatic lesion depending upon the FDG activity.

Key Words: *Second primary lung masses – Lung metastases – PET/CT – ΔSUV_{max}.*

Introduction

INCIDENCE of mortality from lung cancer increasing rapidly due to increase commerciality of cigarette smoking, lung cancer is now a popular disease that needs early diagnosis and understands to improving its staging and early management that improve the overall survival **[1,2]**.

Primary lung cancer send metastasis to different organs in the body mainly to lungs, brain, breast colon, and genitourinary tract. Synchronous primary lung cancer means two primaries in the same time or within at least 6 months after discovering the first one, one primary in the lung and the other one may be in the lung or any other distant organ. The incidence of a simultaneous second primary lung cancer is about 1-8% from all cases of lung cancer **[3]**.

The presence of two or more lesions within the lung or outside is a big dilemma about where is the primary. Two primaries are a common developing problem with increasing its detection rate due to advance in early detection techniques as CT and PET/CT and advance in cancer therapy. Differentiation between multiple lesions as synchronous or metastatic will influence the strategy of treatment and determined the survival rate. In case of multiple primaries surgical removal was the best choice for treatment while, metastatic lesions chemo and radiotherapy were the choices for treatment and the survival rate of multiple primaries is better than that of metastatic lesions **[4]**.

Tumours had the same clonal origin often behave in a similar way and have the same histological features, Dijkman B.G., et al., hypothesized that the SUVs of clonally related masses (i.e. metastases) would be closely resembling than those of

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Abbreviations:

PET : Positron Emission Tomography.
CT : Computerized Tomography.
SUV : Standardized Uptake Value.
FDG : Fluoro-Deoxy-Glucose.
SCLC : Squamous Cell Lung Cancer.

tumours with a different clonal origin. Consequently, they hypothesized that the SUVs of metastases nearing the SUV of the primary tumour they originate from and that the SUVs of two primary tumours differ markedly.

Imaging of lung cancer and its metastasis using conventional CT is still the main imaging modality to detect the morphological criteria of the masses including: Site, size, density, outlines, lymph nodes and metastasis to different organs but it lacked proper delineation of actual outlines of mass from nearby consolidation or collapse, differentiation between the different pathological and metastatic processes which will improve TMN staging, detection of the most active site for a biopsy which improves the outcome of surgical operation if indicated, and actual detection of residual or recurrent mass from post-operative sequel **[5,6]**.

Newly functioning imaging tools used for accurate TMN staging as whole-body diffusion-weighted-MRI (WB diffusion WI-MRI) and PET/CT. Wb diffusion WI carried the advantage of no ionizing radiation exposure and less coast than PET/CT **[7]**.

PET/CT played an important role in diagnosis, staging and follow-up of patients with lung masses. It anticipated the metastasis even small lesions moreover both metastases, as well as synchronous primary tumours, can be visualized.

Lung cancer divided into small-cell and non-small cell, the small-cell includes the adenocarcinoma, large cell carcinoma and squamous cell carcinoma, and adenocarcinoma considered to metastasis early and appeared as a peripheral mass **[8]**.

Few trials tried to investigate the role of SUV_{max} in differentiating between lung metastases and synchronous second primary lung tumours PET/CT had shown encouraging results as F-18 FDG PET imaging provided metabolic information, based on the increased glucose metabolism in malignant lesions. The CT component on integrated PET/CT had a limited role for correcting the attenuation and for anatomic localization in the past. The metabolic parameters on PET and the HU on the integrated PET/CT scan can be used together for the identification of nature of these multiple lesions. There is no consensus on the accurate diagnostic criteria for differentiation of lung metastases and synchronous second primary lung tumours with using these two parameters **[9]**.

Our study investigated the role of PET/CT in the diagnosis of the pulmonary and extrapulmonary lesions in case of multiple lesions trying to detect the second primary and differentiating it from metastasis and study the role of $SUVmax$ of both primary and metastasis this will help to improve early staging and management and overall survival rates.

Patients and Methods

Patients population:

Our retrospective study included 65 patients (50 males and 15 females with age ranged from 35 to 70 year, mean age was 52.4) with multiple pulmonary and extrapulmonary lesions (18 had second primary lung masses and 47 had lung metastases, total lesions=150), all patients referred from Oncology Department after histopathological analysis of lesions to PET/CT Unit of Tanta University hospitals either for staging or post-operative to assess the operative bed and re-staging, this study took three years of duration started from April 2016 to March 2019, this study was Approved by Ethical Committee of Tanta University Hospital as tabulated in Fig. (1).

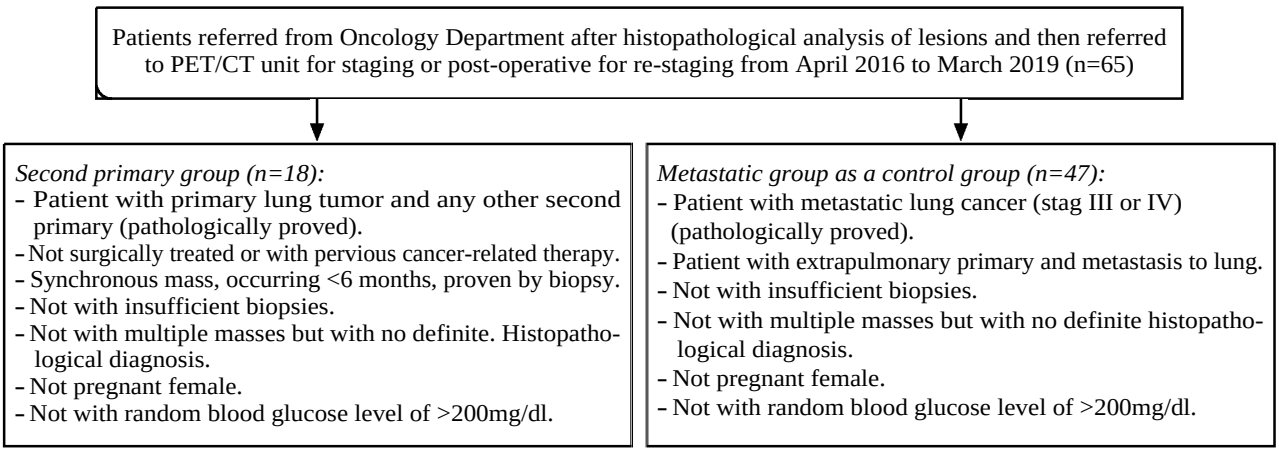

Fig. (1): Flowchart of included and excluded patient.

Inclusion criteria: Patients with multiple pulmonary and extrapulmonary lesions that underwent histopathological evaluation for both lesions (in case of multiple pulmonary lesions biopsy taken from the largest nodule which had malignant morphological criteria on conventional CT).

Exclusion criteria: Patients with previous cancer-related therapy, patient with multiple masses, but with no definite histopathological diagnosis. Pregnant female, patients with a random blood glucose level of >200mg/dl and patients with insufficient biopsies as shown in flowchart Fig. (1).

All patients referred for PET/CT unit for staging or post-operative assessment and detection of the hidden site for metastasis.

Methods:

A- A full history taking as regard to patient age, weight, height, sex, complaint, history of diabetes, smoking and smoking index.

B- MDCT was done for all patients as a first imaging modality, which gives us an idea about the anatomical and morphological data and detects infiltration and extension of the mass to nearby structures and detects distant metastasis. In case of multiple lesions, we depend on morphological criteria as a nodule with speculation, irregular outlines and nearby traction and fibrosis were favours of primary cancer. Presence of multiple lesions with round outlines and sharp border favours for metastatic lesions.

C- Histopathological analysis was done for both original and distant metastatic lesions.

D- Fused PET/CT:

Preparation: Combined PET/CT was done for all patients on a 16-multidetector scanner (Siemens). Patients should be fasted for at least 4 hours with the pre-scanning measuring of random blood glucose level, patients with high blood glucose level referred to internal medicine department to correct the glucose level, all metallic objects should be removed, patients wear a specific gown and IV cannula was inserted, patients asked to limit their movements and avoid stressful condition to avoid physiological uptake.

Patient's weight and height should be measured to calculate the dose of FDG, the patients put in a suitable warm environment to avoid brown fat stimulation, patients also instructed to ingest diet high-fat, low in carbohydrate and protein 24h before the examination. 10mCi (1ml/10kg) 18-F-FDG was injected manually 45-60min before starting the examination in the previously inserted IV cannula. This period is known as the uptake phase which is the time for the 18-FDG to be adequately bio distributed to the patients' cells. Patients were asked after isotope administration to rest in a quiet isolated room.

Non enhanced CT scanning was performed from the base of the skull with arm extended above the head, parameters of CT were 125-kv. Pitch of 1.5, reconstructed slice thickness of 4mm and 16 slice acquisition, average duration about 20sec. the attenuation correction of CT data done with suspended breath-hold this followed by CT scan with contrast with the same previous CT parameters, contrast material was administrated by injector by a rate of 2ml/sec, PET emission scan was acquired with a spatial resolution of 4.8mm and with slice thickening of 3mm.

PET images were reconstructed with (FORE) fourier rebinning and attenuation-weighted subset's expectation-maximization and all PET/CT images were displayed on a work station in axial, sagittal and coronal reformatted images, image analysis was done by two experienced radiologists in PET/CT analysis of at least 5 years of experience, the result was recorded and analyzed.

PET/CT image interpretation and reference stander: Qualitative evaluating of the pathologically proved primary mass/masses by measuring its dimensions, extension and nearby infiltration of surrounding organs the nearby lymph nodes for size, site and distant metastasis, quantitative analysis of the area of abnormal uptake was done followed by measuring of $_{SUVmax}$ by putting the Region of Interest (ROI) on primary and metastatic lesions at site of maximum uptake with taking the liver $_{SUVmax}$ as a stander with its $_{SUVmax}$ of 3. Followed by calculations of ΔSUV_{max} for both primary/primaries and metastatic lesions.

Statistical analysis:

All the PET and PET/CT finding of pulmonary and extrapulmonary results were recorded and analyzed using mean, standard deviation, minimum, median and maximum as quantitative data by using count (frequency) and relative frequency (percentages) for analyzing the data. Correlations between quantitative variables were done using Spearman correlation coefficient (Chan, 2003b). Sensitivity, specificity and accuracy with positive predictive values and negative predictive value were calculated, true positive considered when the result of PET or PET/CT were compatible with histopathology, and negative cases considered when result was not matched, *p*-values less than 0.05 were

considered significant. The calculation was done by using a statistical software package (Medcalc version 18.116, Chicago, IL). $_{SUVmax}$ and Δ SUV $_{max}$ were tabulated for both primary and metastatic lesions and by using the (ROC) curve with calculating area under the curve for determining the cutoff value between the primary and metastatic lesions.

Standardized uptake value:

SUV max defined as the maximum value of FDG uptake per pixel of tumour volume in the area of interest (VOI), SUV was normalized to patient weight and injected activity, $_{SUVmax}$ calculated for both primary and metastatic lesions in case of multiple metastases we chose the largest one, Δ SUV was measured as the difference between the $_{SUVmax}$ of primary and secondary masses and expressed as a percentage (high SUV_{max} - low SUV_{max})/high $_{SUVmax}$ X 100. We assessed the causes of false positive and false negative results of both PET and PET/CT.

Results

A total of 65 patients with multiple intra and extrapulmonary lesion (50 male and 15 female) their age ranged from 35 to 75 with mean age 53.25 years, patient's variables including smoking, site of primary lung cancer and metastatic lung cancer and degree of differentiation were tabulated in (Table 1) with no significant difference between the patient with primary lung cancer and those with metastatic lung lesions (*p*-value 0.05).

The involved patient divided into two groups: The first group was metastatic group control) which included 47/65 (72.3%). Patients with bronchogenic carcinoma and metastasis either in the lung or in different organs, the second group was synchronous second primary group included 18/56 (27.6%), divided to 6/18 with synchronous second primary cancer in distant organ and 12/18 with synchronous lung masses, the total number of lesions 160 masses. As shown in (Table 1).

Based on the histopathological data cases were; 47 (72.3%) metastatic lung Cancer and 18 (27.6%) second primary cancer with either synchronous in the lung or different sites at different organs.

Metastatic lung cancers (47) were found to be 34 non-small cell lung cancer NSCLC (72.3%) and 13 small cell lung cancer SCLC (27.6%) distributed as follow: 11 LUL (23.4%), 5 RLL (10.6%), 12 RUL (25.5 %), 6 LLL (12.7%), 3 LML (6.3%), 5 RT hilum (10.6%) and 5 LT hilum (10.6%) the degree of differentiation were mainly of well and moderately differentiation.

Synchronous second primary lung cancers (18) were distributed as follow: 5 SCLC (27.7%), 7 NSCLC (38.3%), 1 case breast cancer (5.5%), two cases of laryngeal cancer (11.1%), 1 case of liver cancer (5.5%), 1 case of renal cancer (5.5%) and one case of colon cancer (5.5%) while the degrees of differentiation were mainly of poor and undifferentiated as tabulated in (Table 1).

Table (1): Demographic data in both studied groups.

Patients variables	Metastatic lung cancers	Second primary tumors	*p*-value
Number	47 (72.3%)	18 (27.6%)	
Age	35-57 (mean 52.25)	25-72 (mean 53.7)	0.26
Sex	6 female (12.7%)	7 female (38.8%)	0.41
Smoking	25 (55.3%)	14 (77.7%)	0.001
Final diagnosis (histopathology)	- 34 NSCLC (72.3%) - 13 SCLC (27.6%)	- 7 NSCLC (38.8%) - 5 SCLC (27.7%) - 1 invasive ductal carcinoma of breast (5.5%) - 1 mucinous carcinoma of breast (5.5%) - 1 renal cell carcinoma (5.5%) - 1 hepatocellular carcinoma (5.5%) - 2 laryngeal squamous cell carcinoma (11.1%)	
Characteristic of primary:			
Site	11 LUL (23.4%) 5 RLL (10.6%) 12 RUL (25.5%) 6 LLL (12.7%) 3 LML (6.3%) 5 RT hilum (10.6%) 5 LT hilum (10.6%)	3 LLL (16.6%) 2 RML (11.1%) 3 RUL (16.6%) 4 LUL (22.2%) 1 breast (5.5%) 2 laryngeal (11.1%) 1 liver (5.5%) 1 renal (5.5%) 1 colon (5.5%)	
Differentiation:			0.007
Well	- 25 (53.1%)	- 2 (11.1%)	
Moderately	- 12 (25.5%)	- 2 (11.1%)	
Poor	- 6 (12.7%)	- 2 (11.1%)	
Very poor	- 3 (6.3%)	- 8 (44.4%)	
Undifferntiated	- 1 (2.1%)	- 4 (22.2%)	

The mean ΔSUV_{max} between the metastatic lung cancer (47 cases) was lower than the second primary lung disease (18 cases) at 25%-75% as seen in (Tables 2,3) with a *p*-value of (0.007). Although the ranges of the groups show 50% overlap, the majority (75%) of patients with metastatic disease had a ΔSUV_{max} below 16.6% (median 20%) as showed in Figs. (2,3), whereas the ΔSUV_{max} exceeds 60.6% (median 68%) for the majority of the second primary cancer as showed in Figs. (6,7).

Table (2): 95% percentiles accuracy of ΔSUV_{max} in metastatic lung cancer.

Percentiles		95% confident level
25	50.0000	35.8471 to 57.7809
75	68.7500	60.0000 to 80.0000

Table (3): 95% percentiles accuracy in ΔSUV_{max} in second primary lung cancer.

Percentiles		95% confident level
25	8.0400	5.5000 to 11.1000
75	20.0000	16.6440 to 25.0000
90	26.8160	22.0032 to 47.8882

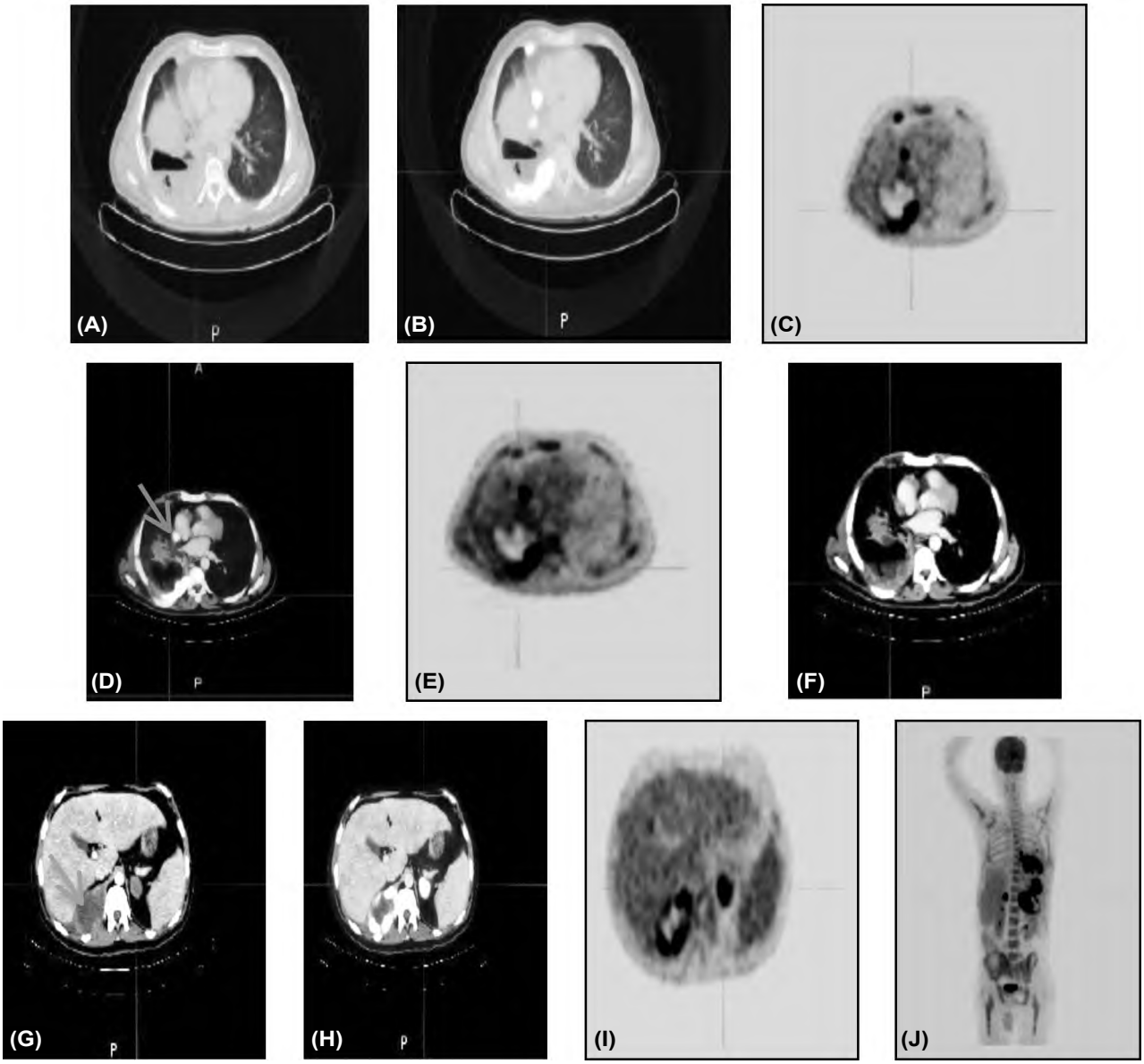

Fig. (2): Male patient aged 50 years old underwent right lower lobectomy of lung mass, histopathology proved it to be bronchogenic carcinoma (squamous cell carcinoma), he referred to PET unit for assessment of pulmonary operative bed and distant metastasis. (A, B,C) (CT, fused PET CT and PET respectively) show operative bed cystic lesion with thickened irregular wall and air fluid level extending to the right retrocural region with $_{SUVmax}$ 15 with multiple enlarged mediastinal lymph nodes with $_{SUVmax}$ 10 (blue arrows), there is a small rounded active lesion seen in right upper lung lobe with $_{SUVmax}$ 9 (orange arrow), (G, H, I, J) There is also bilateral enlargement of supernal gland more at right side with $_{SUVmax}$ 9.6 (blue arrows), biopsy from metastatic site revealed metastasis from lung cancer with ΔSUV_{max} 15% that consistent with pathology to be metastatic from lung cancer.

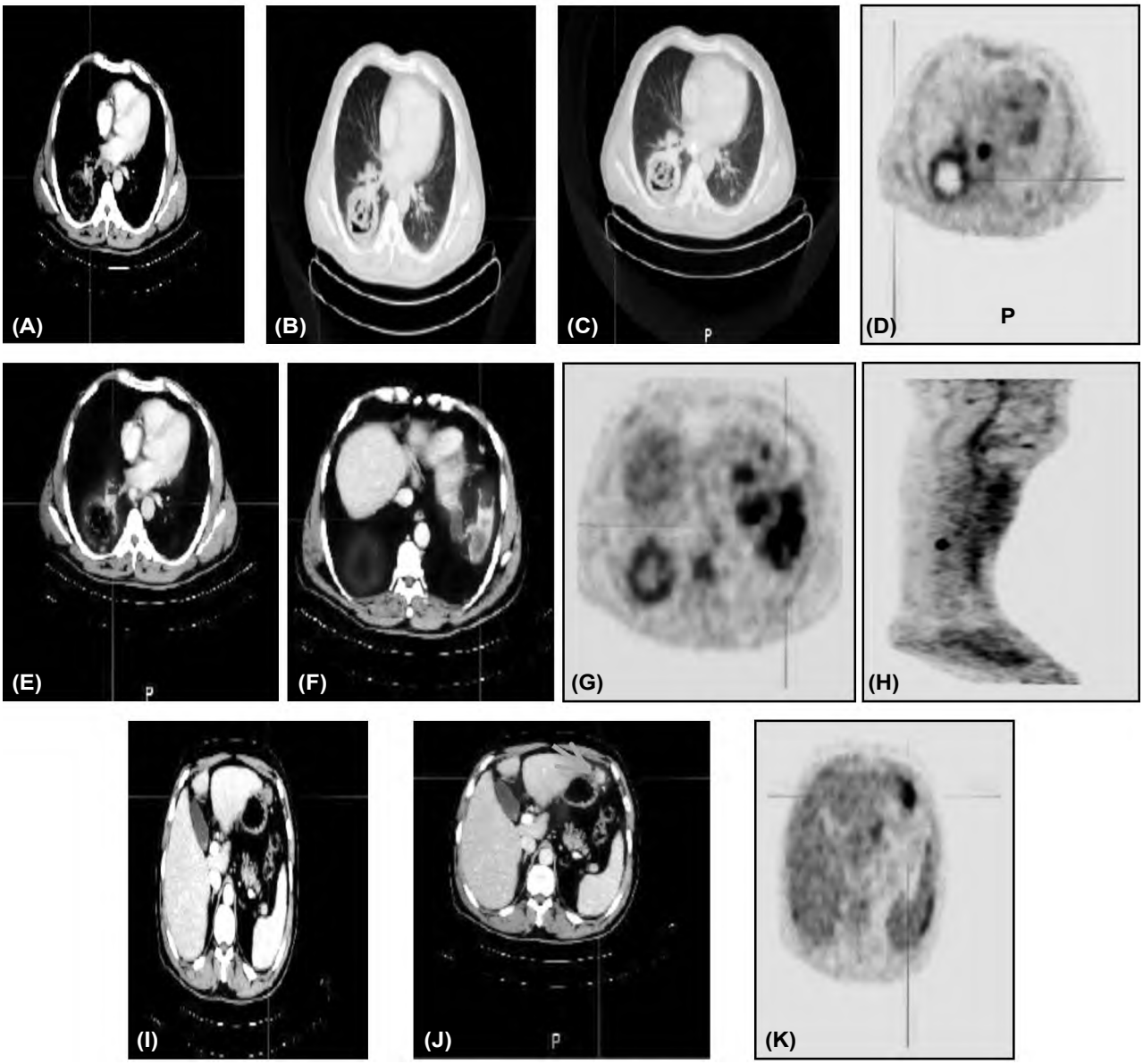

Fig. (3): A male patient aged 52 years complaining from dyspnea 3 months ago, CT chest with contrast was done and revealed right lower lobe cavitary lung lesion with air bronchogram (A & D), he did PET (E), fused PET CT (B,C) which showed a well-defined cavitary mass in the apical segment of right lower lung lobe measuring 6.2 X 7cm with thick nodular wall and high metabolic activity of $_{SUVmax}$ 7, with multiple enlarged mediastinal lymph nodes the largest measured 3 X 3cm with SUV_{max} 11.5 (arrow), multiple metastatic lesion in form of peritoneal and omental deposits at outer aspect of stomach with SUV_{max} 8.8 (I, G, K), large sub phrenic collection with $_{SUVmax}$ 12.4 (H), multiple subcutaneous and intramuscular areas of metabolic activity in the thigh with $_{SUVmax}$ 8.7, histopathology confirm necrotic adenocarcinoma of the lung with metastatic deposits Δ_{SUVmax} measured 20.45% consistent with metastatic.

Table (4): Sensitivity and specificity of the Δ_{SUVmax} for both metastatic and secondary primary masses.

Area under the ROC curve (AUC)	0.848
Standard error a	0.0618
95% confidence interval b	0.740 to 0.924
Z statistic	5.634
Significance level *p* (area=0.5)	<0.0001
Optimal criterion a	>44.4
Sensitivity	81.82
Specificity	85.71

p-value ΔSUV_{max} were non-significant between different cases of metastatic lung lesions and different cases of secondary primary cases with *p*-value of 0.96 and 0.63 respectively while *p*-value was significant between metastatic and secondary primary *p*-value <0.001.

Sensitivity and specificity of the ΔSUV_{max} for both metastatic and secondary primary lesions were 81.8% and 85.71% as showed in (Table 4).

Area under the curves and cutoff values:

This study measured area under the curve from (ROC) for both groups aiming to determine cutoff value. *p*-value ΔSUV_{max} were non-significant between different cases of metastatic lung lesions and different cases of secondary primary cases with *p*-value of 0.96 and 0.63 respectively while *p*-value was significant between metastatic and secondary primary *p*-value <0.001 as shown in (Table 5) and Fig. (4).

Table (5): Data of ROC for ΔSUV_{max} in both groups ($\Delta SUV\text{-}_{maxm}$ and $\Delta SUV\text{-}_{maxs}$).

ROC data	First group (ΔSUV-maxm) metastatic	Second group (ΔSUV-maxs) synchronous second primary lesions
• Area under the ROC curve (AUC)	0.504	0.569
• Standard error a	0.0954	0.146
• 95% confidence interval b	0.351 to 0.657	0.319 to 0.795
• Z statistic	0.0466	0.471
• Significant *p* (area=0.5)	0.9628	0.6377

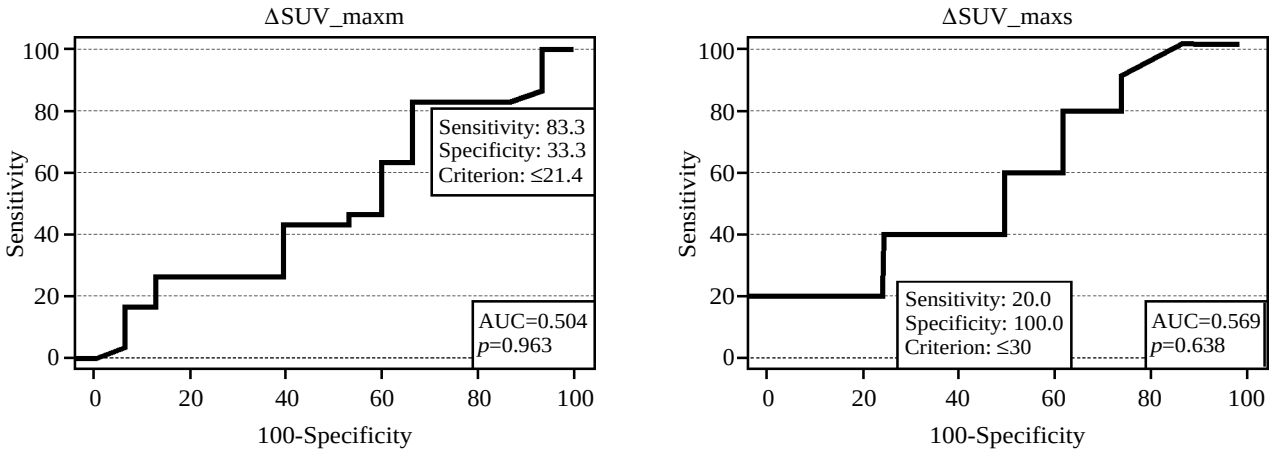

Fig. (4): ROC curve for metastatic lesions (ΔSUV-maxm) and for synchronous second primary lesions (ΔSUV-maxs).

The Area Under the Curve (AUC) for ΔSUV_{max} was for secondary primary lesions (ΔSUV^{-}_{maxs}) 0.56 (95%, CI: 0.31-0.79, *p*=0.63) and that for metastatic lesions $_{(\Delta SUV\text{-}maxm)}$ 0.50 (95%, CI: 035-0.65, *p*=0.96), while that of both (ΔSUV_{max}-both) was 0.94 (95%, CI:0.85-0.98. *p*<0.0001) Fig. (4), which represents a moderately high discriminating ability of the ΔSUV_{max}. The left upper corner of the ROC curve chosen as the optimal cutoff, which correspond to a ΔSUV_{max} of <35%. This cutoff was associated with sensitivity and specificity of 93.3, 91.1 respectively as shown in (Table 6) and Fig. (5).

Table (6): ROC data for (ΔSUV_{max}-both) in both studied groups.

Area under the ROC curve (AUC)	
Standard error a	0.0344
95% confidence interval b	0.859 to 0.987
Z statistic	12.994
Significance level *p* (area=0.5)	<0.0001

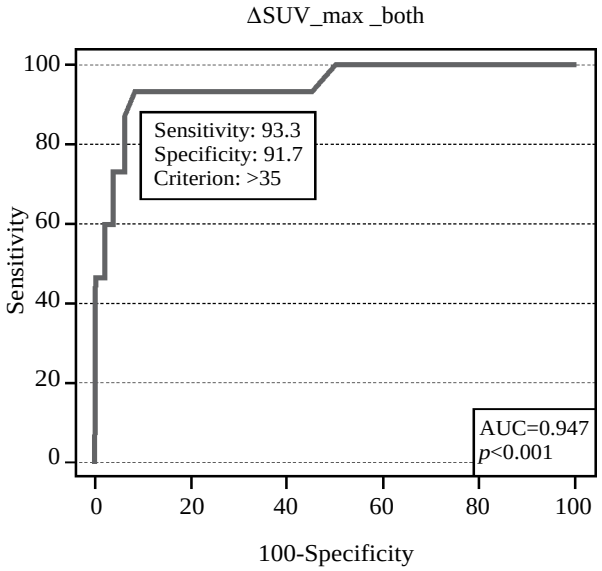

Fig. (5): ROC curve for ΔSUV_{max}- both for both included study groups.

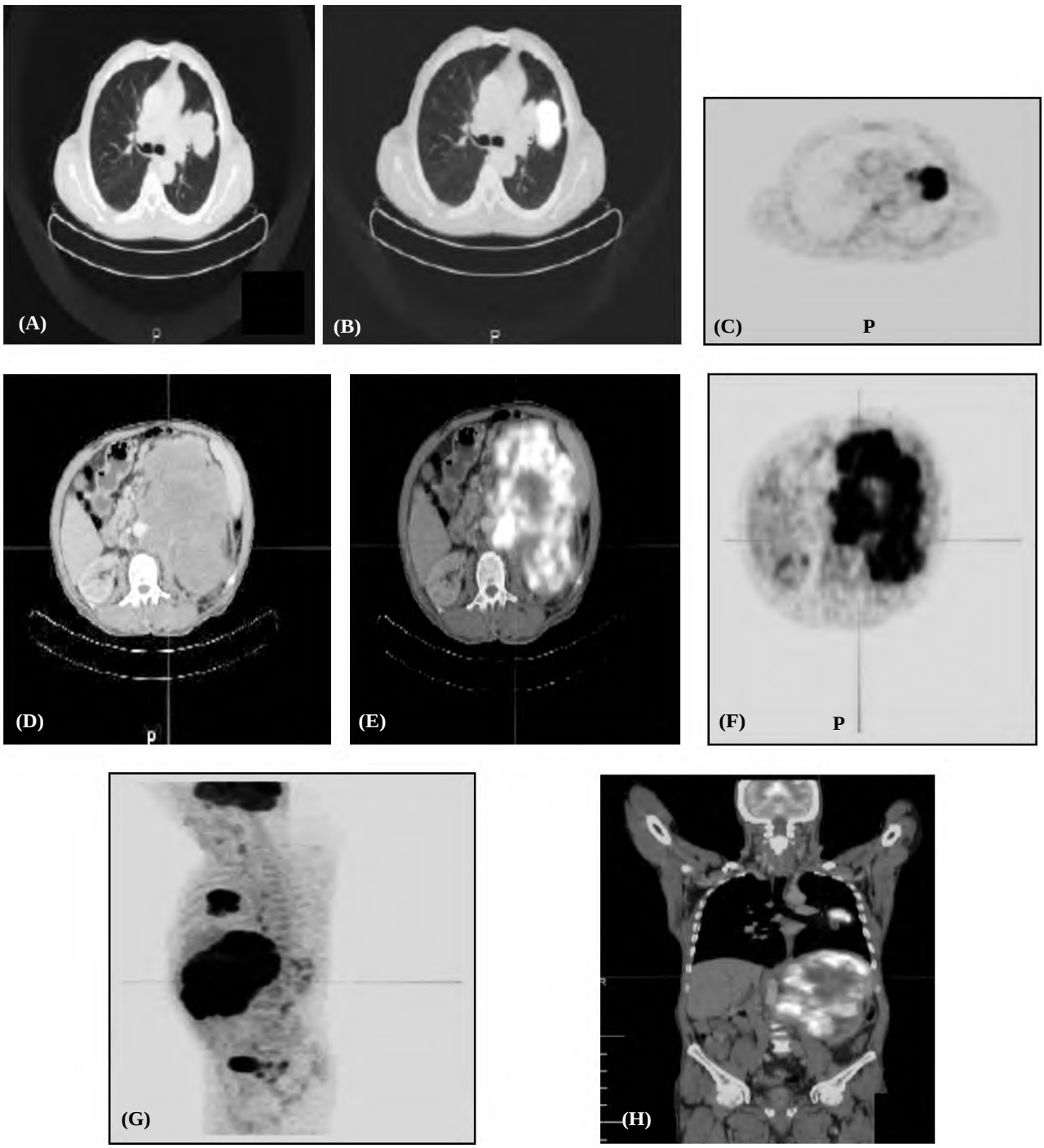

Fig. (6): A male patient aged 64 years old complaining of left loin pain for 6 months ago and did U/S which revealed large necrotic retroperitoneal soft tissue mass arising from the left kidney, (D, E, F) CT, fused PET CT and PET respectively showed a large necrotic metabolically active left retro-peritoneal soft tissue mass arising from the upper and middle pole of the left kidney and non-separable from left supra-renal gland, spleen and greater curvature of the stomach as well as the left psoas muscle with $_{SUVmax}$ 20.5. Another well-defined (A, B, C) speculated soft tissue mass seen at left upper lung lobe extending to lingual with central extension to mediastinum with $_{SUVmax}$ 6.5. Histopathological biopsy revealed the left retro-peritoneal mass as a necrotizing anaplastic adenocarcinoma while that of lung taken by bronchoscopic biopsy as adenocarcinoma of lung. (G, H) sagittal and coronal showed both masse, the ΔSUV_{max} 68.59% confirmed to be synchronous malignant primary pulmonary mass and malignant retroperitoneal mass at the same time.

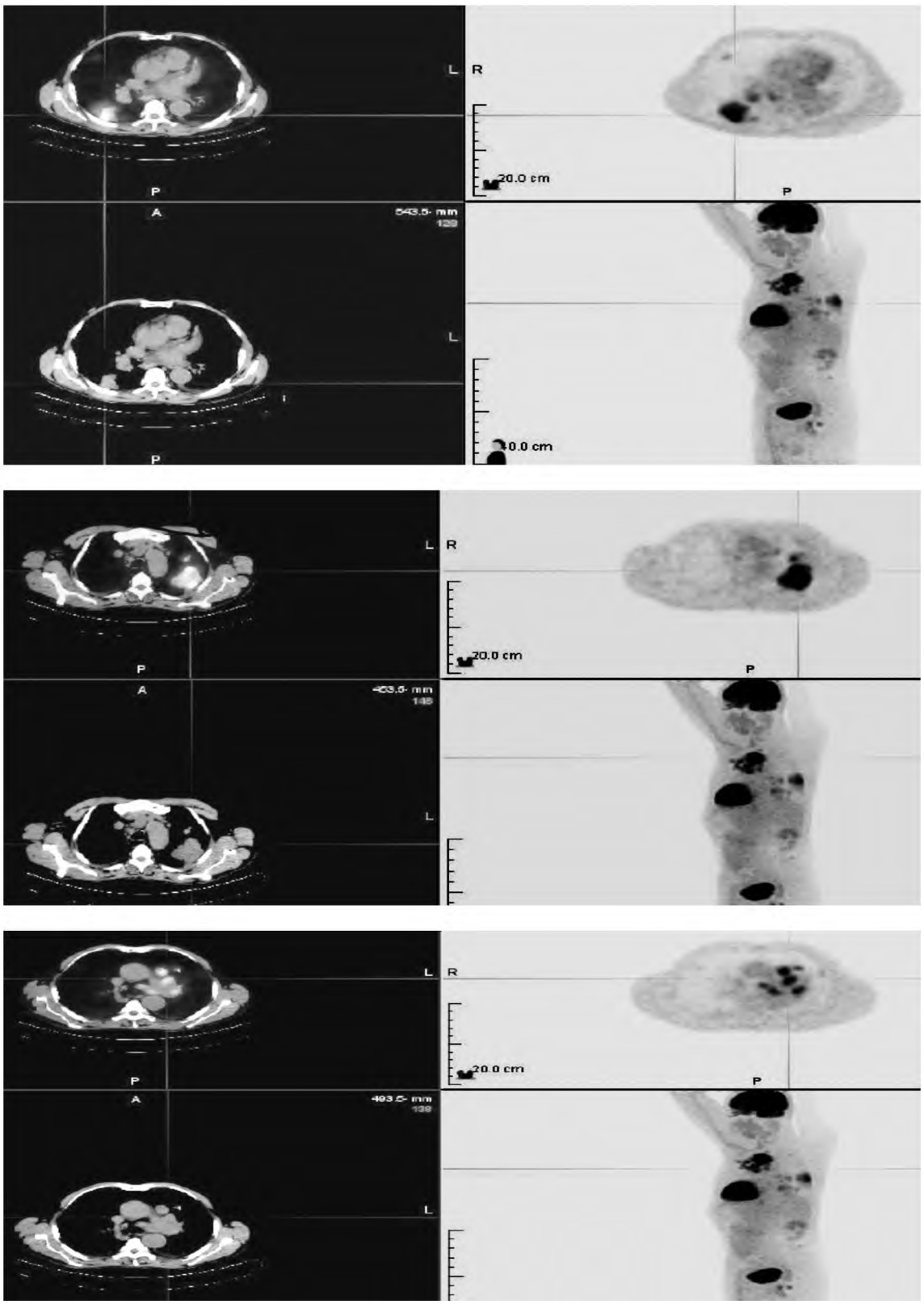

Fig. (7): A female patient aged 38 years old suffered from chest pain, loss of weight and dyspnea for 6 months ago. She did CT with contrast and revealed multiple pulmonary lesions and referred for PET CT unit for further assessment, (A, B) CT, PET, and fused PET CT showed two large irregulars speculated pulmonary soft tissue masses, one in the left apical segment of the lung with $_{SUVmax}$ 8 (A), another one in the right lower lung lobe with $_{SUVmax}$ 18 (B) with multiple metabolically active pre-vascular and mediastinal lymph nodes (C). (D) The coronal image showed two metabolically active pulmonary masses. Histopathological biopsy revealed left one as adenocarcinoma and the right one as synchronous squamous cell carcinoma with ΔSUV_{max} 55.5%.

Discussion

Multiple pulmonary and extrapulmonary masses are a common problem we faced in oncology work and when we see two or more lesions in the lung or any different organ, we considered it as metastasis for the first possibility, nowadays incidence of synchronous primary tumours exploding because of a revolution in imaging modalities and advanced cancer therapy and prolonged survival rate of the cancer patient, synchronous primary tumour defined as the tumour occurred at the same time or within 6 months of the occurrence of the first primary tumour and discovered during the period of chemo or radiotherapy or on follow-up.

Little previous studies and case reports tried to explain the coexistence of two primaries detected by FDG and involving mainly the lung due to immunologic or genetic defects, prolonged exposure to carcinogens, radiation and chemotherapy for primary cancer, and field cancerization **[10-14]**.

Few previous types of researches study the role of PET CT in differentiating between multiple lesions as synchronous primary or metastatic **[9]**.

Our study included 65 cases, most of them were metastatic with no significant sex or age predominance. There was significant correlation between the smoking and incidence of pulmonary and extrapulmonary lesions with a *p*-value of 0.001, this matched with the result of Furrukh M. **[15]**, who accused smoking as a causative factor for lung cancer in developing countries.

58,4% of our studied cases were pathologically proved as Non-Small Cell Lung Cancer (NSCLC), this result was consistent with the result of W.D. Travis **[16]**, who considered NSCLC as the most frequent type of lung cancer.

In our study we found that the most common lobe affected were the upper lung lobe (61.1%) and this was the same result of Jamnik et al. **[17]** who stated that the upper lobes most commonly affected by the malignant process may be due to accumulation of toxin and carcinogens for long period due to lack of proper ventilation and lymphatic drainage as a result of less efficient delivery of protective materials through the circulation to upper lobes when compared to lower lobes, this occurs due to ventilation/perfusion ratio was greater in upper lobes than lower lobes especially in the smoker.

We found also in this study that the most of the lung metastatic masses were of a well and moderately differentiation (37/47) while that of the second primary tumour was of very poor and undifferentiated (12/18) with significant *p*-value 0.007 this due to the similarity in the cell of origin between the primary and metastasis unlike second primary tumours, where they were totally different in the type of cells and this consistent with Barletta JA et al. **[18]**.

In 65 studied cases, most of them were metastasis and showed lower ΔSUV_{max} than in the second primary group with moderately accuracy (0.94) as detected by AUC and higher sensitivity (81.8%) and specificity (85.7%) this indicate the high ability of ΔSUV_{max} in discrimination between the metastatic lesions and synchronous primary lesions.

Some researches (Dijkman et al.) **[19]** were matched with our result as the found ΔSUV_{max} was lower in metastatic than secondary primary lesions with both sensitivity and specificity 81% and determine cutoff value of 41%.

Huynh Quang Huy **[9]** who studied 81 patients with non-small cell lung cancer (44 metastatic and 37 second primary cancer) retrospectively and he evaluated $_{SUVmax}$ in both groups and found that the $_{SUVmax}$ was significantly higher in patients with a second primary tumour with *p*-value <0.001 that were matched with our results.

Nobuyuki Kosaka et al. **[20]**, who studied the role of SUV value differences between primary and metastatic lesions of patients with lung cancer and concluded that the SUVs of most metastatic lesions ranged from half to double those of primaries in lung cancer patients. When the SUV of a suspected metastasis was not in this range, other non-metastatic lesions should be considered. This highly matched with our results of higher SUV values in second primary tumours group.

Few studies supported our result about the ability of PET CT in differentiating between the metastatic group where they had the same origin and biological behaviour and those of separate origin (multiple primaries), FDG uptake by the lesion had been reported to be related to several tumour characteristics including the histological type and aggressiveness of the tumour **[21-23]**.

Several limitations faced our study, firs it was a retrospective study. We collected cases which already had taken a biopsy and confirmed histopathological diagnosis, if another study supports our hypothesis and cutoff value and depended upon it in diagnosis before biopsy, it may determine the actual nature of multiple lesions and determine the

most suitable one for biopsy according to SUV_{max}, and this will help in the improvement of diagnosis and management.

The second limitation was in case of multiple pulmonary lesions the biopsy was taken from the largest mass, which might be not the one matched with actual FDG PET activity result (not the largest one is the target) and patient considered falsely metastatic rather than considering second primary lung cancer.

The third limitation was once primary diagnosed, the other lesions considered metastatic and the diagnosis and management had been taken without any further assessment. This urging of rising awareness of physician about the increasing possibilities of synchronous second primary tumour should be raised.

Conclusion:

As the PET CT considered as functional non-invasive technique, we recommended it for all patients with multiple pulmonary and extrapulmonary lesions to improve diagnostic accuracy before taken the decision of management as it could differentiate between the multiple primaries and metastatic lesion depending upon the FDG activity. We recommend further prospective studies by doing PET CT firstly and chosen the lesions to be biopsied and compared the result with histopathology, this will improve the diagnosis and strategy of treatment.

Declarations:

1- *Ethics approval and consent to participate:* Informed consents taken from the patients and the study approved by Ethical Committee of Faculty of Medicine and University Hospital 2019-145.

2- *Consent for publication:* Authors accepted to publish the paper.

3- *Availability of data and material:* The author's confirm that all data supporting the finding of the study are available within the article and the raw data ad data supporting the findings were generated and available at the corresponding author on request.

4- *Funding:* No funding. Not applicable for this section.

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قيمة التصوير المقطعى بالانبعاث البيزترونى
تشخيص أورام الرئة المتزامنة الثنائية الأولية والثانويات

المقدمة: فى حالة تعدد الأورام داخل وخارج الرئة، من الصعب تحديد ما إذا كانت الرئة هى المكان الأول أو ثانويات خبيثة من مكان بعيد، حتى من الصعب تحديد أين الأورام الأولية.

الهدف من العمل: يمكننا قياس قيمة الامتصاص الموحدة العظمى فى الثانوى والثانويات المنتشرة فى حالة تعدد الأورام الرئوية وتحديد إذا كان هناك فرق قياس فى قيمة الأمتصاص الموحدة العظمى بين المجموعتين.

المرضى وطريقة البحث: فى دراسة شملت ٦٥ المرضى (٥٠ ذكور و ١٥ إناث تراوحت أعمارهم بين ٣٥ و٧٠ عاماً) يعانون من تعدد الأورام داخل وخارج الرئة وجميع المرضى تم تقييمها من أطباء الأورام، المرضى تم تقييمهم تشريحياً لاثبات نوعية الأورام التى يعانون منها وتم فحص وتقييم المرضى بواسطة التصوير المقطعى للانبعاث البيزترونى وتم قياس قيمة الامتصاص الموحدة العظمى للذين يعانون من أورام خبيثة على الرئة وخارجها كما اتخذت مجموعة أخرى من المرضى كمجموعة للمراقبة.

النتائج: هناك فرق بين قيمة دلتا الامتصاص الموحدة العظمى بين المرضى الذين يعانون من أورام خبيثة على الرئة وخارجها أو الذين يعانون من عدة أورام أولية وثانويات خارج الرئة مع تحديد قطع قيمة ٣٥٪، فى حين لا فرق كبير دلتا الامتصاص الموحدة العظمى بين الحالات فى نفس المجموعات وهذا يساعد فى تحسين العلاج اللازم لسرطان الرئة.

الخلاصة: تعتبر إضافة التصوير بالاشعة المقطعية بالانبعاث البيزترونى تقنية جديدة قد تساهم فى زيادة القدرة على التشخيص والقدرة على تمييز بين نوعية الأورام فقد أوصينا أن جميع المرضى الذين يعانون من أورام رئوية داخل وخارج الرئة إضافة هذا الفحص وهذا قد يساعد على تشخيص وعلاج أفضل للأورام.