Pulmonol. 2020;xxx(xx):xxx–xxx

PULMONOLOGY

www.journalpulmonology.org



ORIGINAL ARTICLE

Can PET-CT predict diagnostic success in ultrasonography-guided transthoracic fine needle aspiration biopsies in lung cancers?

C. Doğan[a,*,1], A. Fidan[a], S.Ş. Cömert[a], N. Kıral[a], B. Salepçi[a], E.T. Parmaksıza[a], B. Çağlayan[b]

[a] *Department Of Chest Diseases, Dr. Lütfi Kırdar Kartal Training and Research Hospital, Istanbul, Turkey*
[b] *Departmentof Chest Diseases, Koç University, Istanbul, Turkey*

Received 26 February 2019; accepted 19 December 2019

KEYWORDS
Lung cancer;
Positron emission tomography;
Transthoracic fine needle aspiration biopsy;
Ultrasonography

Abstract
Objective: To examine any correlations between tumor maximum standard uptake values (SUVmax) in positron emission tomography-computed tomography (PET-CT) and homogeneous/heterogeneous tumor FDG uptake in PET-CT, and the diagnostic success of the procedure in thoracic ultrasonography (US)-guided transthoracic fine needle aspiration biopsy (TFNAB).
Methods: The files of patients who underwent thoracic US-guided TFNAB between 2013 and 2018 were examined. Patients who underwent thoracic US-guided TFNAB and were diagnosed as having primary lung cancer were considered as the US-TFNAB diagnostic group. Patients whose disease was diagnosed as primary lung cancer using a different diagnostic method (e.g. CT-guided biopsies, fiberoptic bronchoscopy) due to a lack of diagnosis despite undergoing thoracic US-guided TFNAB were allocated to the US-TFNAB non-diagnostic group. The clinical and radiologic characteristics and PET-CT parameters of the two groups were compared.
Results: A total of 104 patients were included in the study; 79 (76%) patients whose disease was diagnosed using US-guided TFNAB, and 25 (24%) patients whose primary lung cancer could not be diagnosed with US-guided TFNAB. The mean SUVmax value of the US-TFNAB diagnostic group was 19.5 ± 10.1, whereas it was 15.1 ± 8.9 in the US-TFNAB non-diagnostic group ($p = 0.016$). Whether a lesion showed homogeneous or heterogeneous FDG uptake did not effect diagnostic success ($p = 0.289$). SUVmax value was the only effective independent factor in the diagnostic success of the procedure ($p = 0.035$).
Conclusions: High SUVmax values in PET-CT in lung cancers may increase the diagnostic success of US guided-TFNAB procedures.
© 2020 Sociedade Portuguesa de Pneumologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

* Corresponding author.
E-mail address: coskund24@hotmail.com (C. Doğan).
[1] Present address: Neslişah sokak. Teknik yapı Up city sitesi. B2 blok D 40 36877. Uğur Mumcu mahallesi. Kartal Istanbul-Turkey.

https://doi.org/10.1016/j.pulmoe.2019.12.005
2531-0437/© 2020 Sociedade Portuguesa de Pneumologia. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Thoracic ultrasonography (US)-guided transthoracic fine needle aspiration biopsy (TFNAB) performed on peripheral lung tumors is a diagnostic method with proven reliability and effectiveness, and has been used for a long time. Much work has been done on factors affecting the diagnostic success of US-guided TFNAB. These studies investigated the effects of factors on diagnostic success, including the size of the lesion, its internal structure, its location in thorax, the selected biopsy method such as FNAB or Tru-cut, the type of needle used, the use of color Doppler during the procedure, the type of US probe preferred for the procedure, and rapid on-site evaluation (ROSE).[1–6]

Studies have shown that US-guided TFNAB and computed tomography (CT)-guided TFNAB have similar diagnostic success in peripheral tumors of the lung. However, US-guided TFNAB has advantages over CT-guided procedures because it can be performed at the patient's bedside, it is a real-time procedure, and it does not require exposure to radiation.[7]

Positron emission tomography (PET) is a metabolic imaging technique in which isotopes emitting positrons are used. Metabolism is rapid due to the rapid cell proliferation and increased protein synthesis in malignant tumor cells. Therefore, glucose metabolism is also increased. The uptake of 18-fluoro-labeled FDG (18F-FDG), a glucose analogue, is proportional to glucose use in malignant tissues, and FDG is taken up into the cell like glucose, but not metabolized. In these tumor cells, metabolic imaging can be performed using FDG, which is held in the cell without being metabolized.[8,9] FDG uptake intensity is positively correlated with proliferative activity, cell differentiation, and the aggressiveness of tumor, and negatively correlated with prognosis.[10] It is also known that necrotic areas in tumor exhibit less FDG uptake, and are regarded as false-negative areas in PET-CT images.[11,12]

Studies have demonstrated that in biopsies of mediastinal lymph nodes in lung cancers, high standard uptake values (SUVmax) correlated with diagnostic success of biopsy procedures, and that in the case of high SUVmax values, diagnostic success increased.[13,14] When the literature was examined, no study investigating the relationship between PET-CT parameters and thoracic US-guided TFNABs performed in peripheral tumors of the lung was found. In the current study, correlations between tumor SUVmax values in PET-CT and homogeneous/heterogeneous tumor (presence of necrotic component) FDG uptake in PET-CT were investigated, and the diagnostic success of the procedure was assessed in peripheral lung tumors on which we performed thoracic US guided-TFNAB.

Material and method

Patient population and demographic findings

We used a retrospective and cross-sectional study design. We retrospectively reviewed hospital records of patients who had peripheral lesion localization in the lung parenchyma as detected using thoracic US due to its contact with visceral pleura, and had undergone thoracic US-guided TFNAB in the US unit of our Chest Diseases Clinic between January 2013 and May 2018.

Patients who underwent thoracic US-guided TFNAB and were diagnosed as having primary lung cancer were considered as the US-TFNAB diagnostic group. Patients whose disease was diagnosed as primary lung cancer using a different diagnostic method (e.g. CT-guided biopsies, fiberoptic bronchoscopy) due to a lack of diagnosis despite undergoing thoracic US-guided TFNAB were allocated to the US-TFNAB non-diagnostic group (Table 1). The demographic findings of the patients such as age, sex, and smoking history were recorded (Table 2).

Procedures

Computed tomography

A Hitachi Pratico (Pratico, Hitachi, Japan) device was used for thoracic CT scans. The CT examinations were performed in a caudal-cranial direction with a 1-mm slice thickness and full inspiration in the supine position. The window width was 1500 Hounsfield Units (HU) for the lung window and 400 HU for the mediastinal window. The window level was −700 HU for the lung window and 10 HU for the mediastinal window. The measurements were made in the axial plane; however, coronal and sagittal images were used if necessary. Intravenous contrast agents were used for all scans except for patients with acute or chronic renal insufficiency. The radiologic findings of the patients such as tumor size, localization, and tumor contour characteristics were recorded.

Thoracic ultrasonography in peripheral lung masses

In the US unit of our clinic, thoracic US is conducted by an experienced pulmonologist using a General Electric (GE) Logic 7 device (Healthcare, Waukesha, WI, USA)and a 3.5-MHz convex probe in the abdominal mode. With the patient in a sitting position (in the supine, oblique, lateral decubitus position if needed), the entire thorax is scanned, starting from the region where the lesion has been previously observed radiologically, by moving the probe across the intercostal spaces transversely and longitudinally, along the parasternal line, the medial and lateral clavicular line, the anterior — medial and posterior axillary line, lateral and medial scapular line, and the paravertebral line.[15]

Thoracic ultrasound-guided transthoracic fine needle aspiration biopsy procedure

In the USG unit of our clinic, prior to biopsy procedures, a complete blood count and biochemical tests and a coagulometric test results are examined. Informed consent forms of all patients are obtained before the procedure. Patients with a platelet count of <50,000/uL and INR > 1.3, and those who do not agree to US guided-TFNAB do not undergo the procedure. Prior to thoracic US guided-TFNAB procedures, no premedication or sedation is administered. Iodine-alcohol is used to sterilize the region where the procedure will be performed and the USG probe to guide the procedure. The biopsy procedure is performed in real time using a 22-G spinal needle attached to a 20-mL injector from the predetermined spot in which necessary measurements have been made and scanned using a power Doppler.

Please cite this article in press as: Doğan C, et al. Pulmonol. 2020. https://doi.org/10.1016/j.pulmoe.2019.12.005

Table 1 Inclusion/exclusion criteria.

Criteria for inclusion in the study
- Patients with peripherally localized lung lesions, which could be detectable by thoracic US for contacting with the visceral pleura.
- Patients without contraindication to TFNAB (number of platelets>50,000/uL, INR < 1.3).
- Patients who agreed to undergo TFNAB.
- Patients whose PET-CT reports were available.
- Patients diagnosed with primary lung cancer.
- Patients whose final histopathological diagnoses were available.

Criteria for exclusion from the study
- Patients with contraindication to TFNAB (number of platelets <50,000/uL, INR > 1.3).
- Patients who did not agree to undergo TFNAB.
- Patients without any PET-CT scan.
- Patients whose PET-CT reports were not available.
- Patients with suspected metastasis to lung.
- Patients whose final histopathological diagnoses were not available.

CT: Computed tomography; PET-CT: Positron emission tomography-computed tomography; TFNAB: Transthoracic fine needle aspiration biopsy; US: Ultrasonography.

Table 2 Clinical, radiologic, radiometabolic (PET/CT) features of the patients.

	US-TFNAB diagnostic group (n = 79)	US-TFNAB non-diagnostic group (n = 25)	p value
Age (Mean ± SD)	62.6 ± 9.6	62.6 ± 10.1	0.961
Sex (F/M)	13/66	5/20	0.763
Smoking history (Yes/No)	75/4	22/3	0.355
Tobacco (Pack-year ± SD)	30.1 ± 11.4	29 ± 13	0.492
Radiologic characteristics(CT)			
Tumor size (mm) (mean ± SD)	7 ± 2.8	7 ± 2.5	0.831
Tumor localization			
Right upper lobe (n, %)	27/16.5%	14/56%	0.052
Right middle lobe (n, %)	–	1.4%	0.240
Right lower lobe (n, %)	15/19%	2/8%	0.351
Left upper lobe (n, %)	23/29.1%	5/20%	0.371
Left lower lobe (n, %)	13/16.5%	3/12%	0.756
Tumor contour properties			
Regularly contoured (n, %)	10–12.6%	4-16%	0.739
Lobular contoured (n, %)	20–25.3%	6-24%	0.895
Irregularly contoured (n, %)	49–62.1%	15-%60	0.856
Mean SUVmax ± SD in PET/CT (mean ± SD)	19.5 ± 10.1	15.1 ± 8.9	0.016
Heterogeneous FDG uptake in PET/CT (n, %)	41 (51.8%)	16 (64%)	0.289
The mean number of TFNABs per patient (mean ± SD)	1.1 ± 0.3	1.04 ± 0.2	0.345

CT: computed tomography; F: Female; FDG; fluorodeoxyglucose; M: Male; SD: standard deviation; SUVmax: maximum standard uptake; PET-CT: positron emission tomography-computed tomography; TFNAB: transthoracic fine needle aspiration biopsy; US:ultrasonography.

In all US-guided TFNAB procedures, after the hypoechoic mass lesion is detected using US, anechoic, irregular hypoechogenicities or areas observed as mixed echo-patterns in the lesion, if any, are assessed as necrotic foci. A biopsy procedure is performed by avoiding these areas.[16]

Integrated positron emission tomography/computed tomography findings

Patients with a fasting time of at least 8 h and a normal blood glucose level were included in the procedure. The PET-CT scans were as performed on a Philips Gemini TF ultra-speed integrated PET-CT imaging system (Philips Healthcare, Best, The Netherlands). SUV was calculated based on the ratio of the tissue radioactivity concentration and all administered doses at the time of injection divided by body weight. Patients whose PET-CT revealed different levels of FDG uptake in different areas of the tumor due necrotic areas mainly constituted by tumor cells that had lost their vitality were recorded as patients with heterogeneous FDG uptake (presence of necrotic component), and patients whose PET-CT revealed similar levels of FDG uptake across the entire tumor were recorded as patients with homogenous FDG uptake (absence of necrotic component).[8,17,18] The PET-CT findings of the patients were examined. From the PET-CT

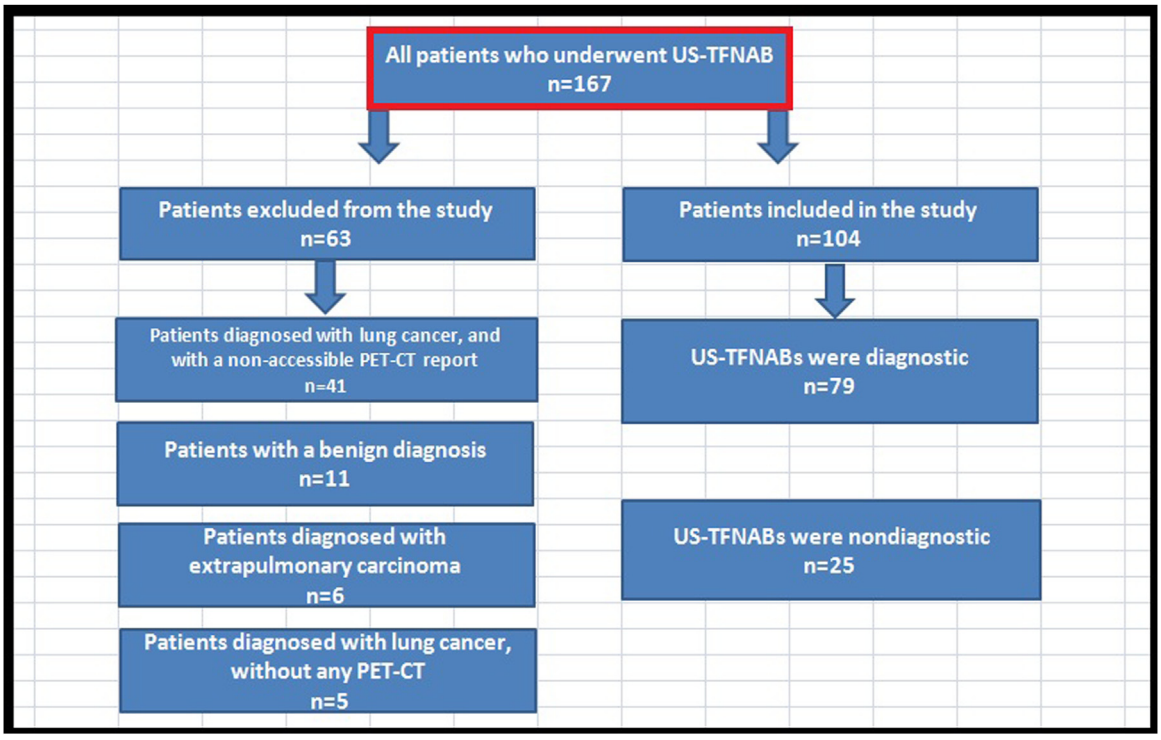


Figure 1 Flow diagram of included/excluded patients.

reports, the SUVmax value of the main mass lesion biopsied and homogeneous or heterogeneous FDG uptake features of that lesion were recorded. Patients were excluded from the study if a PET-CT report was not available or a PET-CT scan had not been performed.

Pathologic examination histopathologic results

We did not have an on-site pathologist at the time of the procedures. After the cytologic specimens were prepared using both alcohol fixation and air-drying techniques, the remaining material was separated and sent in an appropriate manner to the pathology laboratory for the preparation of a cell block. In the pathology laboratory, slides fixed in 95% alcohol are stained with the Papanicolaou stain, and air-dried slides are stained with the May-Grunwald-Giemsa stain. Three-micron-thick paraffin sections obtained from the cell blocks are stained with hematoxylin andeosin. Immunohistochemical examination is applied to cell block sections in the required specimens. Patients with a definitive diagnosis of extra pulmonary cancer metastases or benign lesions and patients without a definite histopathologic diagnosis were excluded from the study.

The size of lesions detected using CT, number of TFNABs per lesion, diagnoses of patients identified using US-guided TFNAB, final diagnoses of patients whose disease could not be diagnosed using US-guided TFNAB, and final diagnosis methods were recorded. We compared the clinical, radiologic and radiometabolic (SUVmax values and homogeneous FDG uptake of the main lesion by PET-CT/heterogeneous FDG uptake) characteristics of patients between the US-TFNAB-diagnostic and US-TFNAB non-diagnostic groups.

Statistical analysis

Statistical analysis was performed using the SPSS 17.0 (IBM Inc.,Relased 2008. SPSS Statistics for Windows Chicago, USA) and Med-Calc version 8.1.1.0, (Med-Calc Software, Ostend, Belgium) programs. In descriptive statistics, continuous variables are expressed as mean ± standard deviation, and categorical variables as percentage. The data of the groups were evaluated using the Chi-square and Mann-Whitney U test, and receiver operating characteristic (ROC) curve analysis.

Multivariate logistic regression analysis was conducted with variables likely to affect diagnosis in order to find independent variables that influenced the diagnostic success of thoracic US guided-TFNAB procedures. Logistic regression analysis was performed using the forward likelihood ratio method, and $p < 0.05$ was considered as significant.

Findings

US guided-TFNAB procedures were conducted in a total of 167 patients in our US unit during the study period. A total of 104 patients, including 86 (82.7%) males and 18 (17.3%) females who met our inclusion criteria, were included in the study (Fig. 1). The mean age of the patients was 62.6 ± 9.6 (range, 42–84) years. Ninety-seven (93.3%) patients had a smoking history, and the average smoking story was 29.8 ± 11.8 pack-years. The most common thoracic CT finding was mass in 104 (100%) cases. The mean long axis diameter of masses and nodules detected in our patients was 7 ± 2.7(min 2, max 17) cm. An analysis of anatomic localization of masses and nodules showed that the tumor

Please cite this article in press as: Doğan C, et al. Pulmonol. 2020. https://doi.org/10.1016/j.pulmoe.2019.12.005

Table 3 Distribution of final histopathological diagnoses.

	US-TFNAB diagnostic group (n = 79)	US-TFNAB non-diagnostic group (n = 25)	p value
NSCLC with unidentifiable sub-type (n, %)	27–34.2%	13–52%	0.110
Squamous cell carcinoma (n, %)	30–38%	6–24%	0.201
Adenocarcinoma (n, %)	13–16.5%	4–16%	0.957
Small cell carcinoma (n, %)	6–7.6%	2–8%	0.947
LCNEC (n, %)	3–3.8%	–	0.323
Total	79	25	

LCNEC: large cell neuroendocrine carcinoma; NSCLC: non-small cell lung cancer; TFNAB: transthoracic fine needle aspiration biopsy; US: ultrasonography.

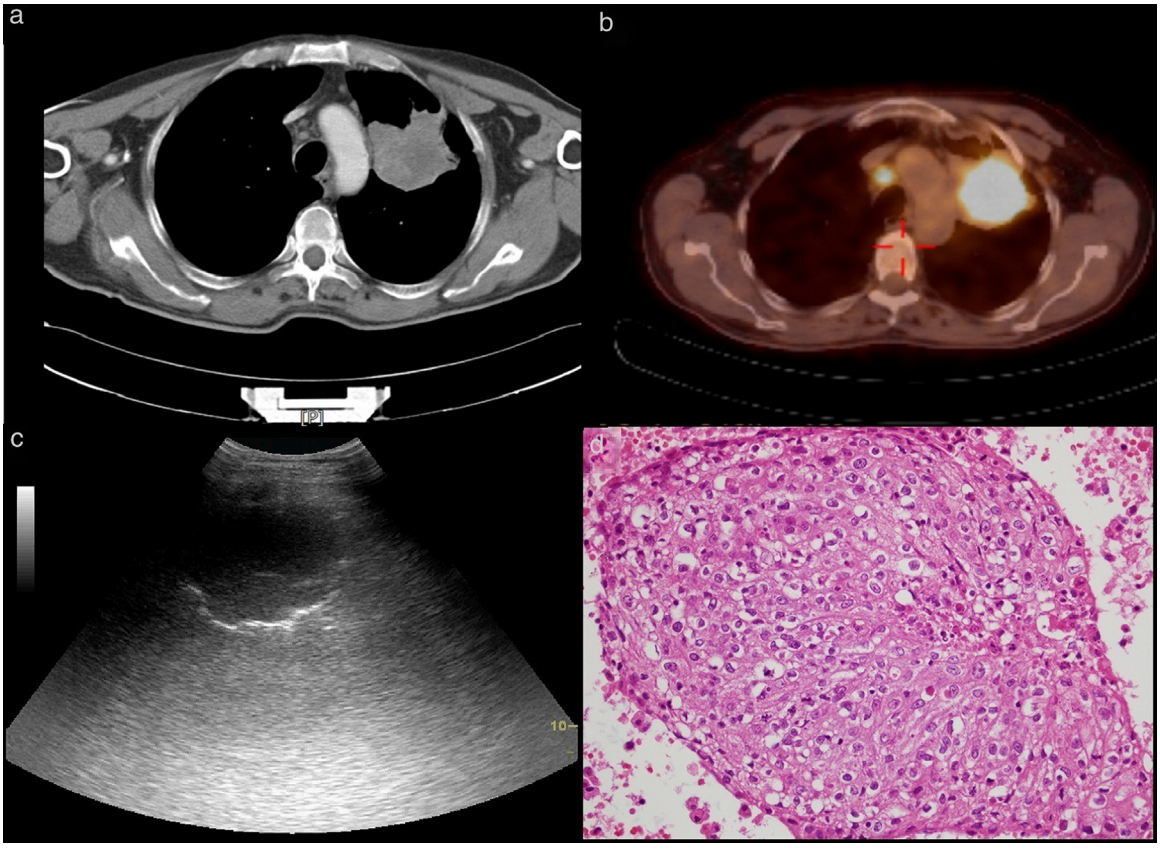


Figure 2 a) An approximately 5 × 5-cm mass in the left lung in thoracic CT. b) Homogeneous FDG uptake of the mass in PET-CT. c) Ultrasonographic image of the mass. d) Malignant tissue fragment (HEx400) whose structural and cellular details can be evaluated in the histopathologic preparation.

was most frequently localized in the right upper lobe in 41 (39.4%) patients (Table 2).

There were 79 (76%) patients in the US-TFNAB diagnostic group and 25 (24%) in the US-TFNAB non-diagnostic group. When the final diagnostic methods of these 25 patients (US-TFNAB non-diagnostic group) were examined, it was observed that 13 (52%) patients' final diagnosis was achieved using CT-guided Tru-cut biopsies, 9 (36%) with fiberoptic bronchoscopy (FOB), and 3 (12%) with thoracic US-guided Tru-cut biopsies. The distribution of the final histopathologic diagnoses of the patients is given in Table 3. The mean number of TFNABs per patient was 1.09 ± 0.28.When the PET-CT reports of the patients were examined, the mean SUVmax in PET-CT scans was 19.5 ± 10.1 in the US-TFNAB diagnostic group, whereas it was 15.1 ± 8.9 in the US-TFNAB non-diagnostic group (p = 0.016) (Fig. 2). When heterogeneous FDG uptake and homogeneous FDG uptake characteristics in PET-CT of biopsied mass lesions of the patients were examined, heterogeneous FDG uptake was reported in 41 (5) patients in the US-TFNAB diagnostic group and in 16 (64%) patients in the US-TFNAB non-diagnostic group (Figs. 2a–d) (Figs. 3a–d). There was no statistically significant relationship between lesions showing homogeneous or heterogeneous FDG uptake and the diagnostic success of the US guided-TFNAB procedure (p = 0.289) (Table 2).

The cut-off value obtained by ROC analysis made in order to determine the optimal SUVmax cut-off value in PET-CT

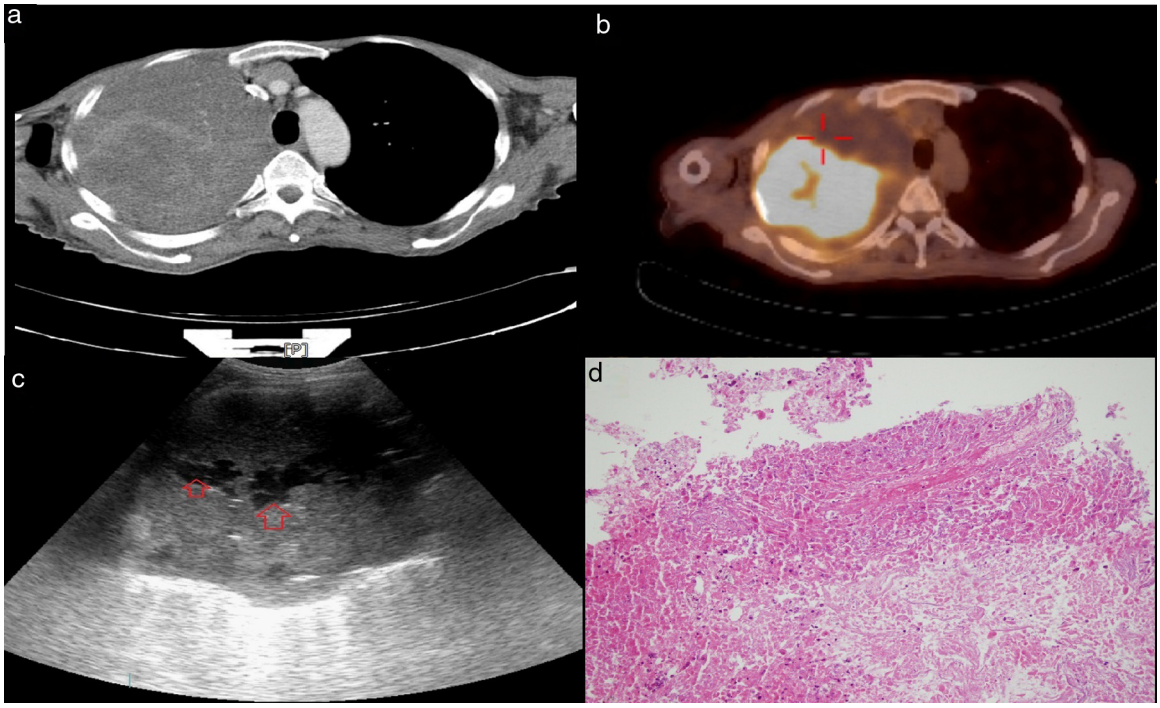


Figure 3 a) An approximately 15 × 10-cm mass in the right lung in thoracic CT. b) Heterogeneous FDG uptake with observed necrotic areas inside the mass in PET-CT. c) Anechoic necrotic foci in the ultrasonographic image of the same mass. d) Necrotic tissue specimen (HEx200) whose structural and cellular details cannot be evaluated in the histopathologic preparation.

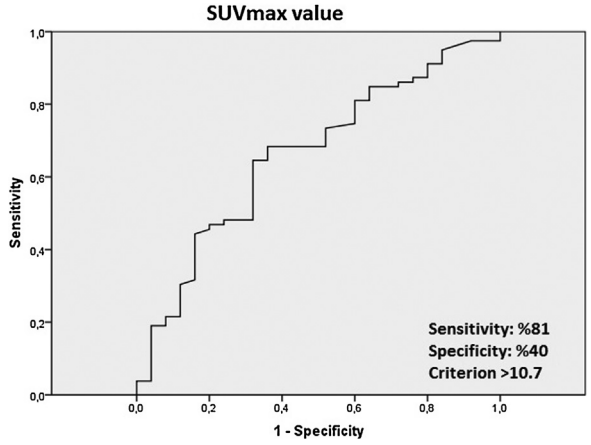


Figure 4 ROC analysis curve showing the SUVmax cut-off value of the patients.

was 10.7 (AUC: 0.661). Where SUVmax was above 10.7 in PET-CT, the sensitivity and specificity of US guided-TFNAB were calculated as 81% and 40%, respectively (Fig. 4).

When a logistic regression model was established for the variables (number of TFNABs performed, size of tumor, location of tumor, SUVmax value, presence of homogeneous/heterogeneous FDG uptake) likely to influence the diagnostic success of thoracic US guided-TFNAB, the SUVmax value was found to be the only independent factor effective in the diagnostic success of the procedure ($p = 0.035$, OR: 1.08, 95% CI: 1.0–1.1). The diagnostic success was not influenced by the number of TFNABs ($p = 347$), tumor size ($p = 0.359$), anatomic location of tumor ($p = 0.240$), or homogeneous/heterogeneous character of FGD uptake ($p = 0.095$).

Discussion

In the present study, which aimed to evaluate the impact of PET-CT findings in thoracic US-guided TFNAB on diagnostic success in primary lung cancers, US-guided TFNAB allowed us to make a diagnosis in 79 of 104 (76%) patients, whereas it failed in 25 (24%) patients. SUVmax was statistically significantly lower in patients whose disease could not be diagnosed using US-guided TFNAB. Although FDG involvement was mostly heterogeneous (64%) in mass lesions in those who could not be diagnosed, no statistically significant difference was found between the type of FDG involvement (homogeneous/heterogeneous) and diagnostic success. Furthermore, SUVmax value was the only independent factor which was effective in diagnostic success of the procedure.

Glucose affinity is increased in malignant tumor cells. The main reason for increased glucose affinity is carrier proteins such as the glucose transporter (GLUT1-GLUT3), which is increased in tumor cell membranes. Previous studies reported that tumors with extremely increased GLUT 1- GLUT 3 production, hence high FDG uptake, had poor prognosis.[19] It is known that tumors with high FDG uptake are metabolically more active.[20] The greater the glucose affinity of the tumor, the higher the FDG uptake. Aggressive tumors with high cell differentiation and proliferative activation have high FDG uptake.[10] In a study investigating the diagnostic efficiency of conventional transbronchial needle aspiration biopsies, Öztürk et al.[21] established a statistically significant correlation between SUVmax values of lymph nodes in PET-CT and diagnostic efficiency ($p < 0.05$), and concluded that the diagnostic success of the procedure increased with high SUVmax values in PET-CT. In that study, the authors performed transbronchial biopsy on 127

Please cite this article in press as: Doğan C, et al. Pulmonol. 2020. https://doi.org/10.1016/j.pulmoe.2019.12.005

lymph nodes, and reported a cut-off SUVmax value of 4.8, a procedure sensitivity of 71.7%, and a specificity of 51.4%. That study is an important study because it associates high SUVmax values with the diagnostic properties of biopsies. Studies have shown a strong correlation between tumor growth and invasion and high FDG uptake.[22–24] Umeda et al.[25] published a paper on the hypothesis that there might be a relationship between SUVmax and the diagnostic efficiency of transbronchial biopsies performed with virtual bronchoscopic navigation in peripheral lung lesions.[25] In that study, 201 peripheral lung lesions were evaluated and it was concluded through multivariate analysis that high FDG uptake and positive bronchial signs were the only statistically significant determinants of diagnostic efficiency (SUVmax $\geq$2.8 OR: 3.57). Based on their results, the authors concluded that different diagnostic methods such as CT-guided biopsy or surgical biopsy, which increase diagnostic efficiency, would be more useful in lesions with low SUVmax values. In their series consisting of 140 patients who underwent transbronchial biopsies on mediastinal lymph nodes by bronchoscopy, Seijo et al.[26] investigated the effects of FDG uptake in biopsies and reported that a cut-off SUVmax value of 3 or more increased diagnostic efficiency. When a cut-off SUVmax value was 3, the sensitivity of the procedure was 98% and the specificity was 45%. In that study, of 27 patients with an SUVmax value less than 3, 26 could not be diagnosed despite a sample adequacy of 74%, adequate needle passage (3.7), and adequate lymph node size (14.4 mm). The authors concluded that FDG uptake was the only and most important variable in transbronchial biopsies of malignant mediastinal lymph nodes based on multivariate analysis.

The above-mentioned studies and many similar previous studies[13,14] demonstrated that a high SUVmax value in PET-CT affected diagnostic procedures in malignant diseases and the diagnostic characteristics of the procedures correlated with SUVmax values. Our study is in good agreement with these results. In our study, the diagnosis rate of thoracic US-guided TFNAB in patients with high SUVmax values was higher than in patients with low SUVmax values ($p = 0.016$). In multivariate regression analysis, SUVmax values were found to be the only independent factor effective in the diagnostic success of the procedure ($p = 0.035$). We associate this relationship with the fact that tumors with high FDG uptake are metabolically more active, more proliferative, and have more cell differentiation.[10,20]

The presence of various ratios of FDG uptake in various areas in PET-CT (heterogeneous FDG uptake) allows differentiation of necrotic areas, granulation tissues, and viable tumor tissues inside tumoral tissue. Clinical trials have shown that PET-CT can better assess proliferative activity in tumoral tissue and is useful in distinguishing viable tumor tissue from fibrotic tissue.[27–30] In a study by Cataluna[31] that evaluated factors affecting the diagnostic accuracy of bronchial biopsies, the degree of cell differentiation and the absence of necrosis in pathologic specimens were shown to be the most influential factors on diagnostic accuracy. They demonstrated that in the absence of necrosis in a pathology specimen, diagnostic accuracy was 5.2 times higher. Further, Greses et al.[32] found diagnostic sensitivity to be 69.6% in their series of 151 patients, and demonstrated that one of the variables that significantly affected diagnostic accuracy in biopsy procedures was the presence of necrosis in the biopsy material. They reported that the diagnostic success was 2.6-times higher when there was no necrosis in the biopsy material. In spite of a higher rate (64%) of patients whose PET-CT revealed heterogeneous uptake due to the presence of a necrotic component than in the US-TFNAB non-diagnostic group, no statistically significant difference was found between the two groups ($p = 0.289$). As is widely known, US is very sensitive in the differentiation of necrotic areas in tissues.[16] Necrotic areas with thoracic US are seen as focal heterogeneous echo-densities within a hypoechoic mass lesion[33] (Fig. 3c). We thought that mass lesions with a necrotic component in PET-CT might negatively affect diagnostic success; however, we found no statistically significant relationship. This may be associated with the low number of patients and real-time nature of US-guided TFNABs. In real-time procedures, needle movements can be tracked within the lesion. The direction of the needle can be determined by the operator. Therefore, during biopsy, necrotic regions may be identified and biopsy of those necrotic regions can be avoided.

A limitation of our study is that it was a retrospective study conducted with a limited number of patients. It reflects experiences related to this subject from a single center; therefore, the results cannot be generalized. Another limitation is that we did not evaluate the interrater differences for thoracic US procedures and SUVmax values. Furthermore, the number of patients in some sub-groups, particularly in cancers with a relatively low FDG involvement such as well differentiated adenocarcinomas, was small. It may be worth conducting controlled studies with adequate numbers of participants in cancers with a relatively lower FDG involvement such as well-differentiated adenocarcinomas and evaluating the diagnostic role of PET-CT and US-guided biopsy in cancers with a low FDG involvement.

Conclusion

With this study, we showed that high SUVmax values in PET-CT in lung cancers increased diagnostic success of US guided-TFNAB procedures, and that a lesion with a necrotic component in PET-CT was not a factor that affected the diagnostic success of TFNAB procedures. Based on the results of this study, we believe that, in patients with low SUVmax values in PET-CT — especially in cases of urgent need for diagnosis – alternative diagnostic methods for early diagnosis should be kept in mind instead of US-guided TFNAB.

Conflict of interest

Coşkun Doğan, Ali Fidan, Sevda Şener Cömert, Nesrin Kıral, Banu Salepçi, Elif Torun Parmaksız, and Benan Çağlayan and declare that they have no conflict of interest.

There are no financial or other relations that could lead to a conflict of interest

The manuscript has not been submitted to more than one journal for simultaneous consideration.

The manuscript has not been published previously, unless the new work concerns an expansion of previous work.

Please cite this article in press as: Doğan C, et al. Pulmonol. 2020. https://doi.org/10.1016/j.pulmoe.2019.12.005

Ethical statements

All procedures were conducted in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. The study was approved by the local ethics committee.

References

[1]. Suzuki N, Saitoh N, Kitamuro S. Tumor invason of the chest wall in lung cancer: Diagnosis with US. Radiology. 1993;187:39–42.
[2]. Yang PC, Lee LN, Luh KT, Kuo SH, Yang SP. Ultrasonography of Pancoast tumor. Chest. 1998;94:124–8.
[3]. Liao WY, Chen MZ, Chang YL, Wu HD, Yu CJ, Kuo PH, et al. US–guided transthoracic cutting biopsy for peripheral thoracic lesions less than 3cm in diameter. Radiology. 2000;217:684–91.
[4]. Laurent F, Montaudon M, Latrabe V, Bégueret H. Percutaneous biopsy in lung cancer. Eur J Radiol. 2003;45:60–8.
[5]. Elmalı M, Can B. Transthoracic Lung Biopsies. J Exp Clin Med. 2005;22:61–6.
[6]. Chen CH, Cheng WC, Wu BR, Chen CY, Chen WC, Hsia TC, et al. İmproved diagnostic yield of bronchoscopy in peripheral pulmonary lesions: combination of radial probe endobronchial ultrasound rapid on site evaluation. J Thorac Dis. 2015;7:418–25.
[7]. Yamamoto N, Watanabe T, Yamada K, Nakai T, Suzumura T, Sakagami K, et al. Efficacy and safety of ultrasound (US) guided percutaneous needle biopsy for peripheral lung or pleural lesion: comparison with computed tomography (CT) guided needle biopsy. J Thorac Dis. 2019;11:936–43.
[8]. Cox BL, Mackie TR, Eliceiri KW. The sweet spot: FDG and other 2-carbon glucose analogs for multi-modal metabolic imaging of tumor metabolism. Am J Nucl Med Mol Imaging. 2014;5:1–13.
[9]. Yilmaz M, Adli M, Celen Z, Zincirkeser S, Dirier A. FDG PET-CT in cervical cancer: relationship between primary tumor FDG uptake and metastatic potential. Nucl Med Commun. 2010;31:526–31.
[10].Sönmezoğlu K. The use of FDG-PET scanning in lung cancer. TuberkToraks. 2005;53:94–112.
[11].Paul R, Johansson R, Kellokumpu-Lehtinen PL, Soderstrom KO, Kangas L. Tumor localization with 18F-2-fluoro-2-deoxy-D-glucose: comparative autoradiography, glucose6-phosphatase histochernistiy, and histology of renally implanted sarcoma of the rat. Res Exp Med. 1985;185:87–94.
[12].Mac Manus MP, Hicks RJ, Matthews JP, McKenzie A, Rischin D, Salminen EK, et al. Positron emission tomography is superior to computed tomography scanning for response assessment after radical radiotherapy or chemoradiotherapy in patients with non-small-cell lung cancer. J ClinOncol. 2003;21:1285–92.
[13].Borekci S, Elbek O, Bayram N, Uysal N, Bakir K, Zincirkeser S, et al. Combined transbronchial needle aspiration and PET/CT for mediastinal staging of lung cancer. TuberkToraks. 2011;59:55–61.
[14].Fortuny MS, Gallego M, Berna LI, Monton C, Vigil L, Masdeu MJ, et al. FDG-PET parameters predicting mediastinal malignancy in lung cancer. BMC Pulm Med. 2016;16:177.
[15].Wrightson JM, Maskell NA. Thoracic ultrasound for beginners: utility and training issues for clinicians. Br J Hosp Med. 2011;72:325–30.
[16].Pan JF, Yang PC, Chang DB, Lee YC, Kuo SH, Luh KT. Needle aspiration biopsy of malignant lung masses with necrotic centers. Improved sensitivity with ultrasonic guidance. Chest. 1993;103:1452–6.
[17].Basu S, Kwee TC, Gatenby R, Saboury B, Torigian DA, Alavi A. Evolving role of molecular imaging with PET in detecting and characterizing heterogeneity of cancer tissue at the primary and metastatic sites, a plausible explanation for failed attempts to cure malignant disorders. Eur J Nucl Med Mol Imaging. 2011;38(6):987–91.
[18].Murakami S, Saito H, Sakuma Y, Mizutani Y, Ishikawa Y, Kondou T, et al. Correla-tion of 18F-fluorodeoxyglucose uptake on positron emission tomography withKi-67 index and pathological invasive area in lung adenocarcinomas 30 mm orless in size. Eur J Radiol. 2010;75:62–6.
[19].Younes M, Brown RW, Stephenson M, Gondo M, Cagle PT. Over-expresion of Glut 1 and Glut 3 in stage1 nonsmall cell carcinoma is associated with poor survival. Cancer. 1997;80:1046–51.
[20].Ahuja V, Coleman RE, Herndon J, Patz EF. The prognostic significance of fluorodeoxyglucose positron emission tomography imaging for patients with nonsmall cell lung carcinoma. Cancer. 1998;83:918–24.
[21].Öztürk Ö, Sandal A, Karahan S, Er B, Önder S, Köksal D, et al. Diagnostic yield of conventional transbronchial needle aspiration biopsy (C-TBNA) without an on-site cytopathologist: Experience of 363 procedures in 219 patients. TuberkToraks. 2016;64:137–43.
[22].Murakami S, Saito H, Sakuma Y, Mizutani Y, Ishikawa Y, Kondou T, et al. Correlation of 18F-fluorodeoxyglucose uptake on positron emission tomography withKi-withKi-67 index and pathological invasive area in lung adenocarcinomas 30 mm orless in size. Eur J Radiol. 2010;75:62–6.
[23].Demura Y, Tsuchida T, Ishizaki T, Mizuno S, Totani Y, Ameshima S, et al. 18F-FDG accumulation with PET for differentiation between benign and malignantlesions in the thorax. J Nucl Med. 2003;44:540–8.
[24].Vesselle H, Schmidt RA, Pugsley JM, Li M, Kohlmyer SG, Vallires E, et al. Lung cancer proliferation correlates with [F-18]fluorodeoxyglucose uptake by positronemission tomography. Clin Cancer Res. 2000;6:3837–44.
[25].Umeda Y, Demura Y, Anzai M, Matsuoka H, Araya T, Nishitsuji M, et al. 18F-FDG uptake predicts diagnostic yield of transbronchial biopsy in peripheral lung cancer. Lung Cancer. 2014;85:47–52.
[26].Seijo LM, Campo A, Torres JP, Lozano MD, Martino E, Bastarrika G, et al. FDG uptake and the diagnostic yield of transbronchial needle aspiration. J Bronchol Intervent Pulmonol. 2011;18:7–14.
[27].Shin CH, Paik SH, Park JS, Kim HK, Park SI, Cha JG, et al. Primary pulmonary T-cell lymphoma: a case report. Korean J Radiol. 2010;11:234–8.
[28].Buchpiguel CA, Alavi JB, Alavi A, Kenyon LC. PET Versus SPECT in Distinguishing Radiation Necrosis from Tumor Recurrence in the Brain. J Nucl Med. 1995;36:159–64.
[29].Kubota R, Kubota K, Yamada S, Tada M, Ido T, Tamahashi T. Microautoradiographic study for the differentiation of ıntratumoral macrophages, granulation tissues and cancer cells by the dynamics of fluorine- 18-fluorodeoxyglucose uptake. J Nucl Med. 1994;35:104–12.
[30].Minn H, Joensuu H, Ahonen A, Kiemi P. Fluorodeoxyglucoseimaging: a method to assess the proliferative activity of human cancer in viwo. Cornparison with DNA flow cytornetiyin head and neck tumors. Cancer. 1988;61:1776–81.
[31].Cataluna JJ, Perpina M, Greses JV, Calva V, Padilla JD, Paris F. Cell type accuracy of bronchial biopsy specimens in primary lung cancer. Chest. 1996;109:1199–203.
[32].Greses JV, Soler JJ, Perpiñá M, Sanchís J, Vera F. Factors related to diagnostic reliability of bronchial biopsy in primary bronchogenic carcinoma. Arch Bronconeumol. 1997;33:556–60.
[33].Koenig SJ, Narasimhan M, Mayo PH. Thoracic ultrasonography for the pulmonary specialist. Chest. 2011;140:1332–41.

Please cite this article in press as: Doğan C, et al. Pulmonol. 2020. https://doi.org/10.1016/j.pulmoe.2019.12.005