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ORIGINAL RESEARCH

The Effect of Hounsfield Unit Value on the Differentiation of Malignant/Benign Mediastinal Lymphadenopathy and Masses Diagnosed by Endobronchial Ultrasonography

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Aim: In cases where standardized maximum uptake (SUVmax) values in positron emission tomography (PET-CT) were not sufficient to differentiate mediastinal lymphadenopathy and masses from malignant or benign, the contribution of Hounsfield unit (HU) values in thorax computed tomography to the diagnosis was evaluated.

Material Method: The study was conducted by evaluating the data of 182 patients between 2019 and 2023. HU values on non-contrast thorax computed tomography and PET-CT SUV_{max} values of biopsied masses and lymph nodes were compared with histopathological diagnoses.

Results: Patients, 58 females (31.9%) and 124 males (68.1%), who underwent EBUS were included in the study. Biopsies were taken from 233 stations (199 lymph nodes, 34 masses) from 182 patients. A total of 135 of the biopsies taken from 233 stations were histopathologically malignant and 98 were benign. While PET-CT SUV_{max} values of cases with benign histopathology were 4.5 ± 3.5, it was 7.6 ± 4.2 in patients with malignant pathology ($p<0.05$). The HU value on non-contrast thorax tomography in patients with benign histopathology was 43.1 ± 15.7, and in patients with malignant histopathology it was 40.5 ± 13.7 ($p>0.05$). When HU was compared according to lung cancer type, it was found to be significantly higher in non-small cell lung cancer ($p=0.035$). A weak ($r=0.182$) positive and significant relationship ($p<0.01$) was found between PET-CT values and HU values in thorax computed tomography.

Conclusion: While positron emission tomography maintains its importance in the differentiation of mediastinal lymphadenopathy and masses from malignant to non-malignant, it was concluded that HU values in computed tomography are not sufficient to distinguish malignant/non-malignant.

Keywords: Hounsfield unit, positron emission tomography, SUV_{max}, benign, malignant, mediastinal lymphadenopathy

Introduction

Mediastinal lymphadenopathy and mass lesions are diagnosed earlier and more frequently due to advances in radiological imaging methods. Endobronchial ultrasonography (EBUS) is a minimally invasive method that allows the diagnosis of hilar and mediastinal lymphadenopathies and mass lesions adjacent to the bronchial wall with its proven high diagnostic value.[1,2]

Positron Emission Tomography-Computed Tomography (PET-CT) is used quite frequently in the diagnosis and staging of lung and mediastinal malignancies. With the introduction of PET/CT in the differentiation of malignant and benign lung and mediastinal lesions, the number of unnecessary biopsies and unnecessary surgical interventions has decreased. PET-CT attempts to distinguish malignant or benign pathologies by measuring the maximum uptake values (SUV_{max}) standardized with fluoro-2-deoxy-glucose (FDG) in mediastinal and mass lesions. It is known that increased FDG uptake has high sensitivity (81.3%) and specificity (79.4%) for malignancy.

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However, in benign conditions related to infection or inflammation, there is increased FDG uptake in PET-CT and gives false positivity.[3–5]

Hounsfield unit (HU) is a relative measurement calculated based on the X-ray absorption density of the tissue, used in the interpretation of computed tomography images and diagnosis of diseases. HU is used in the diagnosis of fatty liver, determination of bone density, adrenal tumors, prediction of meningioma growth, and evaluation of solitary pulmonary nodules or thyroid nodules.[6]

In recent years, radiomics has been used as a new method in the distinction between malignant and benign pathologies. PET/CT and PET/MRI radiomics, which have been extensively studied especially in lung cancer research, are promising in the diagnosis of the disease, evaluation of metastasis, prediction of molecular subtypes and prediction of patient prognosis.[7]

There were very few studies in the literature on the use of the Hounsfield unit (HU) in the differentiation of malignant and benign pathologies. For this purpose, we wanted to compare PET-CT SUV_{max} values and HU values of malignant and benign mediastinal lenadenopathy and masses histopathologically diagnosed with EBUS and evaluate whether HU values could be a usable parameter in the distinction between malignant and benign.

Material and Method

The study was conducted single center, retrospectively and cross-sectionally, between 2019 and 2023, by evaluating non-contrast thorax tomography and pathology data of 182 patients who were detected to be involved in PET/CT due to mediastinal lymphadenopathy or mass and had needle biopsy with EBUS, at the Chest Diseases Clinic of the Training and Research Hospital.

Inclusion Criteria

-Age ≥18 years All patients underwent EBUS.

Exclusion Criteria

Patients whose pathology results, PET-CT and non-contrast thorax tomography images cannot be accessed (n=80).

General Electric HiSpeed Dual Scanner (General Electric, Rosslyn, USA) device was used for HU measurement in non-contrast thorax tomography.

PET-CT SUVmax values were obtained using the PHILIPS MEDICAL SYSTEMS GEMINI TF device and the TOF device.

EBUS Operation

At least two biopsies were taken from each focus of the lymph nodes (4R, 4L, 7, 10R, 10L) and the mass with pathological involvement in PET/CT with a 22 G thick needle using the Fujifilm EB-530US device.

HU Evaluation

It was performed in cases of lymphadenopathy or mass that were involved in PET/CT and were biopsied. Mediastinal LAP and HU values of the mass on non-contrast thorax tomography were evaluated by two separate specialist physicians. The highest HU value detected by measuring all regions of the lymph node or mass was taken. HU was determined by taking the average of the highest HU values determined by both physicians.

The patients' demographic data, histopathological diagnoses, PET-CT SUV_{max} values, and HU values on non-contrast thorax tomography were compared.

This study was carried out with the approval of Samsun University Non-Interventional Clinical Research Ethics Committee (Date: 15,03,2023. Decision No: 2023/51). As patient consent to review their medical records was not required by the Samsun University Non-Interventional Clinical Research Ethics Committee due to the retrospective design of the study, the committee waived the requirement for informed consent. This decision was taken after a detailed review by the ethics committee. We ensured patient data confidentiality and compliance with the Declaration of Helsinki.

Statistical Analysis

All data were analyzed with the SPSS V 23 Windows program (SPSS Inc., Chicago, IL, USA). Frequencies and percentage values of categorical variables; mean and standard deviation values of numerical variables were calculated. Assumptions of normal distribution and variance homogeneity were made with Kolmogorov - Smirnov and Levene tests. Non-parametric tests were applied for variables that did not show normal distribution. Mann–Whitney *U*-test was applied for two independent groups, and Kruskal–Wallis test was applied for more than two groups. Correlation analysis was done with the Spearman correlation test. Sensitivity and specificity values were calculated, and the percentages were obtained. An optimum cut-off value for HU and SUV_{max} density was determined with receiver operating characteristic (ROC) curve analysis.

Results

A total of 182 patients were included in the study (Female: 58 31.9%, Male: 124 68.1%). The average age of the patients was 60.7 ± 11.3 years (Female: 61.4 ± 11.1, Male: 62.5 ±10.3). Biopsies were taken with EBUS from 233 stations (199 lymph nodes, 34 masses) from 182 patients. While 135 of the biopsies taken from 233 stations (Lymph node: 103 51.1%, Mass: 32 94.1%) had malignant pathology, 98 had benign pathology (Lymph node: 96 48.2%, Mass: 2 5.9%). The demographic data of the patients are shown in Table 1.

While the PET-CT mean SUV_{max} value of patients with benign pathology was 4.5 ± 3.5, it was 7.6 ± 4.2 in patients with malignant pathology ($p<0.05$). The HU value on non-contrast tomography in patients with benign pathology was

Table 1 Demographic Features

Age (Ort ± SD)	62.1±10.5
Sex n (%)	
Male	103 (54.5)
Female	86 (45.5)
EBUS n (%)	
Lymph Node / Mass	199 (85.4) / 34 (14.6)
Malignant	103 (51.1) /32 (94.1)
Benign	96 (48.2) / 2 (5.9)
MALIGNANT n (%)	
SCLC	27 (20)
NSCLC	93 (68.9)
Adenocarcinoma	42 (18)
Squamous cell carcinoma	25 (10.7)
Type indistinguishable	23 (9.9)
Large cell carcinoma	3 (1.3)
Metastasis	10 (7.4)
Breast carcinoma	4 (1.7)
Bladder carcinoma	2 (0.9)
Cervix carcinoma	2 (0.9)
Renal cell	2 (0.9)
Pleomorphic adenoma	1 (0.4)
Lymphoma	5 (3.7)
BENIGN (n, %)	
Benign cytology	52 (22.3)
Granulomatous diseases	33 (14.2)
Sarcoidosis	26 (11.2)
Tuberculosis	6 (2.6)
Silicosis	1 (0.4)
Anthracosis	13 (5.6)

43.1 ± 15.7, and in patients with malignant pathology it was 40.5 ± 13.7 (p>0.05). While a statistically significant difference was detected in the PET-CT average SUV_{max} values of the patients depending on whether the lesion was malignant or benign, no statistically significant difference was detected in the HU values. Malignant and benign PET-CT SUV_{max} and thorax tomography HU according to pathology subtypes are shown in Table 2. When HU was compared according to lung cancer type (NSCLC/SCLC), HU was found to be significantly higher in NSCLC (p = 0.035).

Spearman correlation analysis was used to determine the relationship between PET-CT SUV_{max} values and HU. A weak (r=0.182) positive and significant relationship (p<0.01) was found between PET-CT SUV_{max} values and HU. This relationship is shown in Table 3 and Figure 1.

In receiver operating characteristic (ROC) curve analysis (area under the curve: 0.552), when the cut-off HU value was determined as 39.9, the sensitivity for malignant etiologies was 55.6% and the specificity was 52%. ROC curve analysis (area under the curve: 0.735), when the cut-off PET CT SUV_{max} value was determined as 4.25, the sensitivity for malignant etiologies was 80% and the specificity was 58.2% (Table 4, Figures 2 and 3).

Table 2 Malignant and Benign PET-CT SUV_{max} and Thorax Tomography According to Pathology Subtypes HU Values

Benign Pathology		**N**	**Mean**	**P**
Thorax CT HU	Benign cytology	52	41.5 ± 16.7	0.068
	Granulomatous diseases	33	47.6 ± 14.2	
	Anthracosis	13	37.7 ± 12.8	
PET CT SUV	Benign cytology	52	3.6 ± 2.4	0.003
	Granulomatous diseases	33	6.2 ± 3.9	
	Anthracosis	13	3.7 ± 3	
Malignant Pathology				
Thorax CT HU	NSCLC	93	42.1 ± 15	0.354
	SCLC	27	35.6 ± 8.7	
	Metastasis	10	41.4 ± 10.6	
	Lenfoma	5	37.1 ± 11.4	
PET CT SUV_{max}	NSCLC	93	8.1 ± 4.3	0.006
	SCLC	27	7.1 ± 4.1	
	Metastaz	10	6.4 ± 2.1	
	Lymphoma	5	2.6 ± 1.3	

Table 3 Relationship Between PET-CT SUV_{max} and HU

PET/CT SUV_{max}		BT HU
	Spearman's r	0.182*
	p	0.005
	n	233

Note: *Correlation is significant at p<0.01 level.

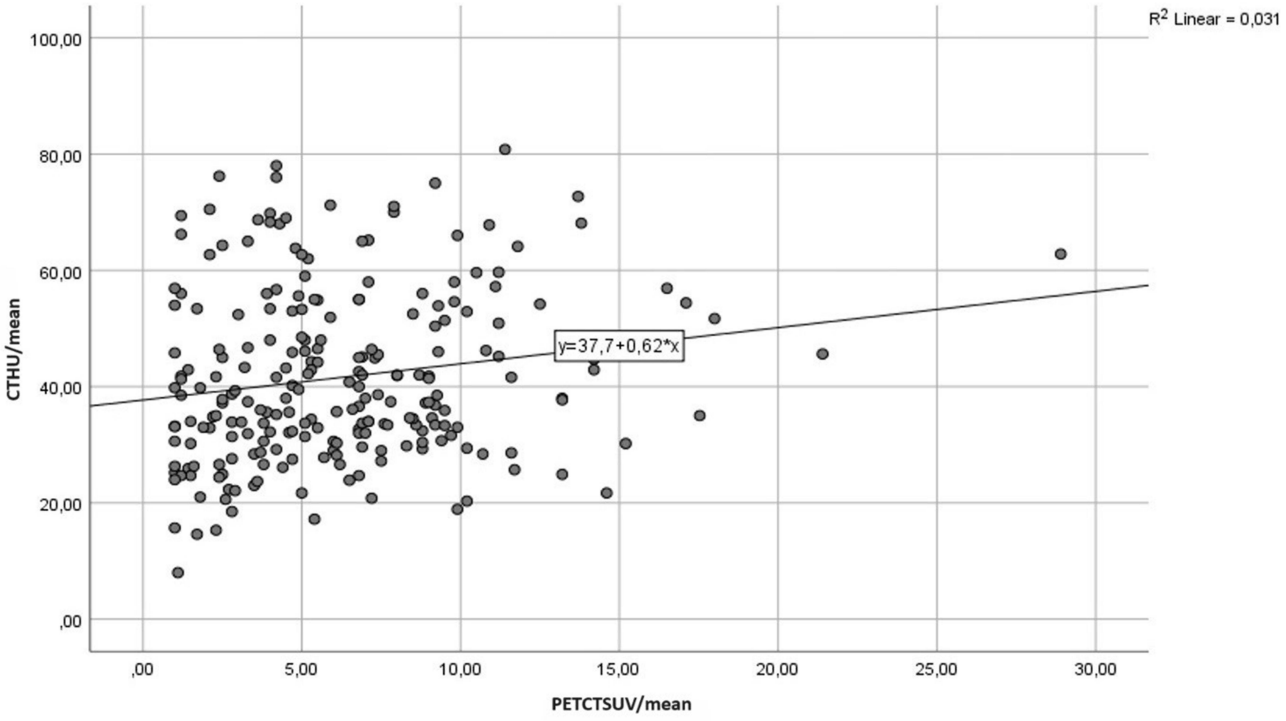

Figure 1 Spearman Correlation analysis.

Discussion

In our study, we found that the PET-CT average SUV_{max} value had 80% sensitivity and 58.2% specificity in the distinction between malignant and benign, and HU value had 55.6% sensitivity and 53% specificity. In addition, the PET-CT mean SUV_{max} value is high in granulomatous diseases, and although there is a weakly positive and significant relationship between PET-CT SUV_{max} values and HU, the HU value is an unsuccessful parameter in the distinction between malignant and benign, and HU is not used for lung cancer type in patients diagnosed with lung cancer. We found that the values are significant.

Studies show that PET-CT still has an important place in the differentiation of malignant/benign masses and mediastinal pathologies. However, it has been observed that this method can give misleading results and it is difficult to find definitive evidence that the lesions may be malignant or benign without biopsy. Increased FDG uptake is observed on PET CT, especially in benign conditions related to infection or inflammation. Granulomatous diseases are among these benign conditions. For this reason, it is indispensable to use minimally invasive methods such as EBUS for staging and diagnostic purposes.[8,9] In our study, consistent with the literature, SUV_{max} values on PET-CT were found to be high in granulomatous diseases.

Although the HU value for mediastinal lymphadenopathy and mass has been evaluated as promising in the distinction between malignant and benign in several studies, it has been emphasized that the HU value alone is not sufficient for the distinction between malignant and benign and that its sensitivity and specificity increase when confirmed by PET-CT and biopsy.

Table 4 ROC Curve Analysis

Malignant-Benign	AUC (%95)	Cut off	p	Sensitivity %	Specificity %
Thorax CT HU	0.552 (0.476–0.628)	39.9	0.039	55.6	52
PET CT SUV_{max}	0.735 (0.669–0.800)	4.25	0.000	80	58.2

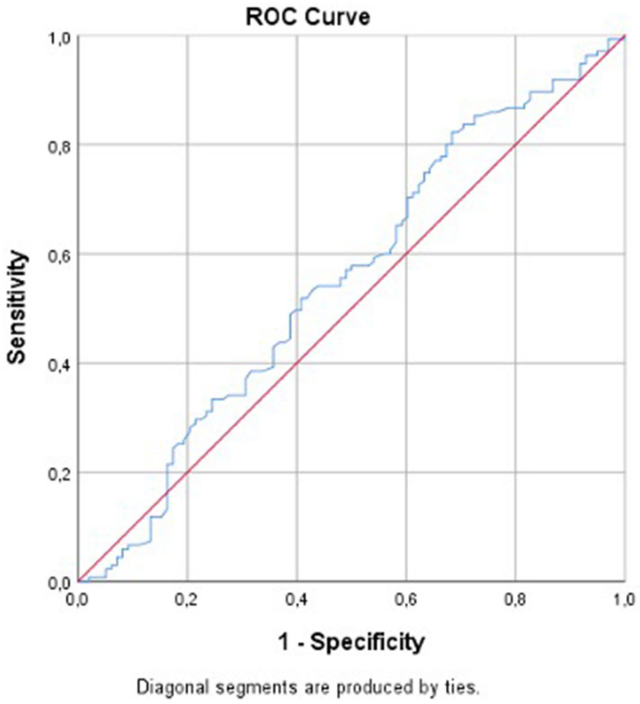

Figure 2 HU ROC curve analysis.

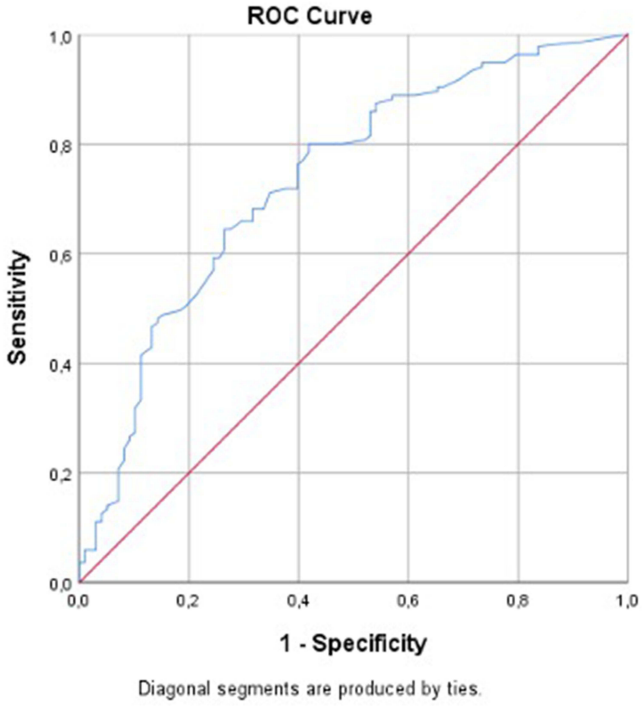

Figure 3 PET-CT ROC curve analysis.

Flechsig et al examined 248 lymph nodes in 122 lung cancer patients. A total of 118 of the lymph nodes were malignant and 130 were benign.

It was determined that HU was 32.4 in malignant lymph nodes and 9.3 in benign lymph nodes and was statistically significant.

It has been shown that 20 HU may be the cut-off value in distinguishing malignant/benign lymph nodes. It was stated that in cases of unclear lymph node involvement on PET CT, HU values can be used as an aid in the distinction between malignant and benign.

No significance was found in HU values across malignancy subtypes.[10] In another study by Flechsig et al, where they examined 60 lymph nodes (36 malignancies positive, 24 malignancies negative) in 45 patients diagnosed with lung cancer, the median CT density of positive lymph node (33.2 HU) was compared to negative lymph node (10.1 HU), found that it was significantly higher.[11]

Kim et al evaluated 2477 mediastinal lymph nodes in 674 patients in the mediastinal lymph node staging of non-small cell lung cancer using PET-CT in a country where tuberculosis is endemic. In the study, 275 lymph nodes were found to be malignant and when compared with PET-CT values, sensitivity was calculated as 61% and specificity as 96%. When HU values of lymph node samples were measured, it was emphasized that a value above 70 was considered malignant. It has been reported that the sensitivity and specificity will decrease, especially in regions where tuberculosis is endemic, considering that the false negative rate in PET-CT will be high.[12] In the study by Wang et al, in which 124 lymph nodes of 70 patients were correlated with PET-CT and EBUS TBNA, the HU value was found to be 33.07 ± 14.31 in inflammatory lymph nodes and 35.41 ± 9.78 in malignant lymph nodes, and it was used to distinguish between benign and malignant lymph nodes reported that there was no significant difference.[13] We obtained results similar to the study conducted by Wang et al. In our study, unlike other studies, we found a significant difference in HU values between NSCLC and SCLC, which are malignancy subtypes, in favor of NSCLC. Our study had some limitations. Our reasons were that our number of patients was small, the data were evaluated retrospectively, and although the HU value was evaluated by two separate experts, it may not have received a standard value because it was evaluated relatively. Another limitation was the evaluation of radiomics in our study due to technological inadequacies.

In conclusion, our study results showed that PET-CT SUV_{max} value maintains its importance in distinguishing malignant/benign. In addition, although it was determined that the HU value could not be used as a parameter alone, it was thought that it would lead to new studies that will be prospectively evaluated with larger patient numbers.

Disclosure

The authors report no conflicts of interest in this work.

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