Comparison of ventilation/perfusion scintigraphy and pulmonary CT angiography: Findings in the diagnosis of CTEPH and CTED

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Abstract

Objective: Despite the high sensitivity and specificity of ventilation/perfusion (VQ) scintigraphy in the diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH) and chronic thromboembolic disease (CTED), V/Q scintigraphy cannot distinguish whether the thrombus is acute or chronic. In our study, we aimed to compare pulmonary computed tomography angiography (CTA) findings with V/Q scintigraphy findings in CTEPH and CTED patients and to identify findings that would indicate chronic thrombus. **Subjects and Methods:** Eighteen patients diagnosed with CTEPH and CTED at our institution were included in the study between January 2020 and January 2024. Computed tomography angiography findings were recorded as V/Q findings [location (segmental, subsegmental, lobar), number, appearance (wedge or patchy) of mismatch perfusion defects], and the correlation of these findings was investigated. **Results:** The average age of 18 patients was 63.3±11.7, 66.7% were female and the majority of the patients were non-smokers, and no significant difference was detected between the CTED and CTEPH groups. Apart from the areas where chronic thrombus was localized on CTA, more widespread mismatch defects were observed by VQ scintigraphy. Most of the mismatch defects were wedge-shaped and there was similarity between groups. The presence of mosaic perfusion was detected in 62.5% of those with mismatch patchy defects (P=0.043). A negative correlation was detected between pulse oxygen saturation and the number of mismatch subsegmentary defects (r: -0.651, P=0.005). Systolic pulmonary artery pressure (sPAP) was found to be positively correlated with the number of mismatch defects (r: 0.523, P=0.026). **Conclusion:** Ventilation/perfusionscintigraphy is superior in the diagnosis of CTEPH/CTED. The presence of mismatch patch defects on V/Q scintigraphy in patients with clinical, echocardiographic, and CTA findings suggests that the presence of mismatch patch defects on V/Q scintigraphy may be a sign of chronic thrombus and the number of mismatch defects may be correlated with the severity of the disease

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Introduction

Thrombotic material remaining in the pulmonary arteries after acute pulmonary embolism (PE) can lead to occlusion of the pulmonary arteries and increased pulmonary vascular resistance, thus leading to chronic thromboembolic pulmonary hypertension (CTEPH) [1,2]. Sometimes it does not increase pulmonary artery pressure and is called chronic thromboembolic disease (CTED) [3]. The frequency of CTEPH after acute PE has been reported to be 0.4%-3.8% of patients in most series [4]. However, only about half of the patients diagnosed with CTEPH have a clinically known history of PE [5]. Due to the lack of a routine screening program to detect CTEPH after acute PE, most cases are diagnosed during the investigation of symptoms related to pulmonary hypertension. A delay in the diagnosis of CTEPH causes a progressive increase in pulmonary vascular resistance and ultimately right heart failure.

In patients with pulmonary hypertension, the diagnosis of CTEPH is made based on lung scintigraphy findings and/or specific evidence of arterial defects on computed tomography (CT), magnetic resonance imaging (MRI), or conventional pulmonary angiography [6]. Ventilation/perfusion(V/Q) scintigraphy is recommended for the examination of all patients with unexplained pulmonary hypertension (PH) [6] and is the procedure of choice for the evaluation of CTEPH [7]. Normal scintigraphic findings exclude the presence of chronic thromboembolic disease [8]. Not all patients with abnormal V/Q scintigraphy have CTEPH, and the differential diagnosis includes in situ thrombosis, pulmonary artery sarcoma, fibrosing mediastinitis, pulmonary vasculitis, and sarcoidosis. These diseases can be distinguished from CTEPH by some characteristic radiological fe-

atures that can be demonstrated by other imaging techniques such as CT [9].

Pulmonary CTA in patients with CTEPH and CTED shows direct vascular features such as laminated thrombi with obtuse angles, vessel narrowing or complete retraction, intimal irregularities, "webs and bands" and poststenotic dilatation, and indirect vascular features such as dilatation of the pulmonary artery or dilatation of bronchial collateral vessels [3,10]. Indirect cardiac features such as right ventricular hypertrophy and parenchymal features such as mosaic perfusion or parenchymal bands are also suggestive of CTEPH [10].

While there have been studies comparing the sensitivity and specificity of CT findings with VQ scintigraphy in the diagnosis of CTEPH and CTED and investigating the frequency of radiologic abnormalities, the correspondence of images in both modalities has never been studied. In our study, we aimed to determine which pattern radiologic findings lead to on V/Q scintigraphy, thereby making V/Q scintigraphy more specific in the diagnosis of CTEPH and investigating its role in the differentiation of acute/chronic thrombus.

Subjects and Methods

For this retrospective study, the files of 23 patients diagnosed with CTEPH and CTED in our institution between January 2020 and January 2024 were reviewed. Two patients did not have V/Q scintigraphy and 3 patients did not have CTA, and these patients were not included in the study. Demographic data, previous history of pulmonary embolism/deep venous thrombosis (DVT), comorbidities, and echocardiography (ECHO) findings of 18 patients were recorded. CTA and V/Q scintigraphies were re-evaluated by 1 radiologist and 1 nuclear medicine specialist and reported in detail (both doctors evaluated the images independently).

The diagnosis of CTEPH was made by CTA and V/Q scintigraphy in patients with PH on ECHO after at least 3 months of anticoagulant treatment. For the diagnosis of PH, a systolic pulmonary artery pressure (sPAP) ≥40mmHg measured by ECHO was accepted as the threshold value [11]. Patients whose CTA and V/Q scintigraphy were compatible with CTEPH but whose sPAP was <40mmHg were also classified as 'CTED'.

Lung perfusion-ventilation planar and SPECT imaging protocol

Lung perfusion and ventilation imaging were performed on two separate days. Perfusion imaging was performed on the first day. In lung perfusion imaging, the standard 5mCi (185MBq) technetium-99m (^{99m}Tc-)macro aggregate albumin (MAA) was given to the patient in the supine position by slow infusion intravenously (IV). Planar and single photon emission computed tomography (SPECT) images were acquired on two separate dual-headed gamma cameras (Siemens Ecam - Germany and GE Infinia - USA) at an energy of 140keV and a 20% window using a low-energy, high-resolution, parallel hall collimator. First, planar perfusion images were taken in 8 different projections with anterior, posterior, lateral, right, and left anterior oblique and posterior oblique viewing angles. It was performed at 128x128 pixels by collecting 300-400 thousand counts per image. Single photon emission computed tomographyimaging was performed after planar imaging. In SPECT imaging, the gamma camera was at 360 degrees 12 seconds of images were taken for each image, and the imaging was done in a 64x64 matrix. Ventilation imaging was performed on the day following perfusion imaging. In ventilation, imaging, 12-18mCi (444-666MBq) ^{99m}Tc-Technegas (Australia) was inhaled into the patient and then images were taken for 15 seconds per image. Ventilation imaging was performed with the same method and viewing angles as perfusion images.

A segmental or subsegmental perfusion defect detected in perfusion and returning to normal in ventilation was defined as a 'mismatch defect'. If the perfusion defect detected in perfusion did not return to normal on ventilation and remained constant, it was interpreted as a 'match defect'. The defect was termed 'segmental' if it involved more than 75% of a segment and 'subsegmental' if it did not [12]. According to the European Association of Nuclear Medicine (EANM) guidelines, CTEPH was considered positive if there were at least one segmental or two subsegmental mismatch perfusion defects [13].Normal lung perfusion and ventilation, reverse mismatch defects, or match defects were considered negative PE. Perfusion-ventilation match defects due to lung parenchymal diseases were interpreted as nondiagnostic for PE. In our study,the location (segmental, subsegmental, lobar), number, and appearance (wedge or patchy) of mismatch perfusion defects were recorded.This study was approved by Abant Izzet Baysal University Ethics Committee (approval number:2024/05, date:06.02.2024) and informed consent was obtained from all subjects.

BTA protocol

The patients underwent a CTA examination with a 64-slice CT device (General Electric Revolution EVO, 64-slices). The scan parameters were as follows: 0.6mm collimation, 1.5mm slice thickness, 1.4mm increment, 100kV, 135mAs, a pitch of 0.9, and a gantry rotation time of 0.33s. Thrombus location, vessel narrowing or complete retraction, abnormal vessel tapering and abrupt vessel interruption, intimal irregularities, intraluminal webs-bands, post stenotic dilatation, mean pulmonary artery (PA) diameter, dilatation of bronchial collateral vessels, right ventricle to left ventricle (RV/LV) ratio, ventricular septal flattening, mosaic perfusion, parenchymal bands, pulmonary scar or infarction, proximal bronchial dilatation, presence of diameter differences in segmental vessels were recorded in CTA. The relationship between the findings of the two imaging methods was evaluated.

Statistics

The analysis of the data obtained as a result of the research was made in the SPSS 20 statistical package program. Descriptive statistical methods (frequency, arithmetic mean, standard deviation, median, minimum, maximum, and crosstabs) were used. Compliance with normal distribution

was examined with Shapiro-Wilk and Kolmogorov-Smirnov. Independent Sample t-test was used for two independent groups by comparing the arithmetic means of the normally distributed groups. The Mann-Whitney U test was used to compare two independent groups by comparing the medians of the groups that did not show normal distribution. Chi-square, Fisher exact test was used to examine the correlation between categorical variables. The correlation between continuous variables was analyzed with Pearson's or Spearman's correlation coefficient, depending on the suitability of the data. The statistical significance level was accepted as $P<0.05$.

Results

The average age of a total of 18 patients: was 63.3±11.7, in the CTED group: 61.6±10.1, in the CTEPH group: 65.1±13.4 and there was no significant difference (P=0.535). Female predominance was evident overall and in both groups, and the majority of patients were non-smokers. Comorbidities; cardiovascular disease (CVD: Hypertension, atrial fibrillation, coronary artery disease, heart failure, atrial fibrillation, venous insufficiency) pulmonary (asthma, chronic obstructive pulmonary disease) other (Parkinson's, epilepsy, systemic lupus erythematosus, rheumatoid arthritis, hypothyroidism, laryngeal carcinoma, chronic renal failure), comorbidity was common in both groups, with CVD in the CTED group and pulmonary diseases in the CTEPH group. No significant emphysema and/or fibrosis was detected on CTA in patients with pulmonary disease.The previous history of PE was known in fifteen patients (Table 1). Of the three patients with unknown PE history, one had venous insufficiency, one had a history of being examined for polycythemia, and detailed information could not be obtained on the other.

Three patients had thrombophilia (PAI serpentine heterozygous and MTHFR heterozygous association, factor 5 Leiden heterozygous and MTHFR heterozygous association and polycythemia) but there was no significant difference between the groups (P=0.576, Table 1). Four of the 18 patients had undergone endarterectomy and two patients were using riociquat. Other patients were referred to specific centers for endarterectomy and were not followed-up.

The mean pulse oxygen saturation (pSO2) of the total patients was 94% (82-97) and the CTEPH group was significantly more hypoxemic (95% (85-97) in the CTED group; 92% (82-96) in the CTEPH group, P=0.039).There was no significant difference in the presence of DVT [1 (11.1%) in the CTED group; 2 (22.2%) in the CTEPH group, P=1.0, Table 1]. Information about the use of thrombolytics was available only in 1patient with CTEPH, regarding catheter and parenteral use.

Table 1. *Comparison of demographic and clinical data of patients with CTED and CTEPH.*

	CTED (n:9)	CTEPH (n:9)	Total (n:18)	p-value
Age	61.6±10.1	65.1±13.4	63.3±11.7	0.535
Gender (F/M)	6(66.7%)/3 (33.3%)	6(66.7%)/3 (33.3%)	12(66.7%)/6 (33.3%)	1.0
Smoking Non-smoker Ex-smoker Smoker	6(75%) 1(12.5%) 1(12.5%)	6 (66.7%) 2(22.2%) 1(11.1%)	12(70.6%) 3(17.6%) 2(11.8%)	0.871
Additional diseases (n:17) CVD Pulmonary Thrombophilia Other	6(75%) 4(50%) 2(25%) 2(25%) 3(37.5%)	7(77.8%) 3(33.3%) 5(55.6%) 1(11.1%) 5(55.6%)	13(76.5%) 7(41.2%) 7(41.2%) 3(17.5%) 8(47.1%)	1.0 0.637 0.335 0.576 0.637
Previous acute PE	7(87.5%)	8(88.9%)	15(88.2%)	1.0
pSO_2 (%)	95(85-97)	92(82-96)	94(82-97)	0.039
Presence of DVT	1(11.1%)	2(22.2%)	3(16.7%)	1.0
Use of thrombolytics	0	1(11.1%)	1(5.9%)	1.0
sPAP (mmHg)	27.9±9.1	69.9±17.5	48.9±25.5	0.000

F: female, M: male, CVD: cardiovascular disease, PE: pulmonary embolism, pSO2: pulse oxygen saturation, DVT: deep venous thrombosis, sPAP: systolic pulmonary artery pressure

Mismatch defect was detected in all patients, and the location and number of the defect did not differ between the two groups. The number of Macht defects accompanying Mismacht defects was similar between the groups. The shape of mismatch defects was mostly wedge-shaped, but there were no significant differences between groups. Although parenchymal bands and mosaic perfusion patterns were more frequent in the CTEPH group, no significant difference was detected. PA diameter (mean PA diameter: 33.9± 9.1mm) and RV/LV ratio ≥1 were also similar between the groups (Table 2).

Table 2. *Comparison of CT angiography and V/Q scintigraphy findings of patients with CTED and CTEPH.*

	CTED (n:9)	CTEPH (n:9)	Total (n:18)	P-value
V/Q scintigraphy Match defect	2 (22.2%)	1 (11.1%)	3 (16.7%)	1.0
Number of mismatch defects Subsegmental Segmental Lobar	3.11±2.4 0(0-2) 1(0-9) 0(0-3)	4.56±1.9 1 (0-5) 2 (0-8) 0 (0-2)	3.83±2.2 5 (0-5) 1.5(0-9) 0(0-3)	0.176 0.367 0.753 0.936
Mismatch defect shape Wedge Patchy	8 (88.9%) 3 (33.3%)	8 (88.9%) 5 (55.6%)	16(88.9%) 8 (44.4%)	1.0 0.637
Vessel Narrowing Partial Full No	3(33.3%) 4(44.4%) 2(22.2%)	4(44.4%) 2(22.2%) 3(33.3%)	7(38.9%) 6(33.3%) 5(27.8%)	0,604
Abrupt vessel interruption	7 (77.8%)	6(66.7%)	13(72.2%)	1.0
Intraluminal meshes and bands	2 (22.2%)	4 (44.4%)	6 (33.3%)	0.620
Poststenotic dilatation	0	0	0	0
Diameter differences in segmental vessels	5(55.6%)	4(44.4%)	9(50%)	1.0
Bronchial collateral dilatation	3(33.3%)	2 (22.2%)	5(27.8%)	1.0
Bronchial dilation	2(22.2%)	1(11.1%)	3(16.7%)	1.0
Parenchymal bands	4(44.4%)	7(77.8%)	11(61.1%)	0.335
Mosaic perfusion	1(11.1%)	5(55.6%)	6(33.3%)	0.131
Pulmonary scar/infarction	1(11.1%)	1(11.1)	2(11.1%)	1.0
PA diameter (mm)	35.7±11.7	32.2±5.9	33.9±9.1	0.440
RV/LV ratio ≥1 RV/LV<1	5(55.6%) 4(44.4%)	5(55.6%) 4(44.4%)	10 (55.6%) 8(44.4%)	1.0
Ventricular septal deviation	0	1(11.1%)	1(5.6%)	1.0

PA: pulmonary artery diameter, RV/LV: right ventricle/left ventricle

The most common CTA abnormalities were: sudden venipuncture (77.8%), chronic thrombus (72.2%) parenchymal bands (61.1%), RV/LV ratio ≥1 (55.6%), diameter differences in segmental vessels (50%), vessel narrowing (partial 38.9%, complete 33.3%), mosaic perfusion (33.3%), intraluminal webs and bands (33.3%), dilatation of bronchial collaterals (27.8%), bronchial dilatation (16.7%), pulmonary scar/infarction (11.1%), ventricular septal deviation (5.6%) (Table 2).

Apart from the areas where chronic thrombus was localized on CTA, VQ scintigraphy revealed more widespread mismatch defects (Table 3). One of our cases is presented as an example in Figure 1. When CTA findings were compared with patchy and wedge appearance of mismatch defect, the presence of mosaic perfusion was observed in 62.5% of patients with patchy defect appearance and was statistically significant (P=0.043). No significant relationship was found between other CTA findings and the appearance of the defect (Table 4).

Table 3. *Comparison of chronic thrombus location on CTA and mismatch defect locations on V/Q scintigraphy.*

	Chronic thrombus location on CTA	Mismatch defect localization in V/Q
Patient 1	Left lower lobar-segmental branches	Right apex, left lower lobe posterobasal
Patient 2	Not observed	Right lower lobe laterobasal, right upper lobe posterior
Patient 3	Right middle-lower lobar and segmental branches	Right lower lobe anterobasal, right lower lobe superior
Patient 4	Left lower segmental branches	Left lower lobe anterobasal, mediobasal, laterobasal, posterobasal
Patient 5	Right lower lobe segmental	Right lower lobe superior, right upper lobe anterior
Patient 6	Right lower lobe segmental	Right lower lobe anterobasal, right middle lobe medial-lateral, left inferolingular, left lower lobe anteromediobasal
Patient 7	Left lower lobar-segmental branches	Right upper lobe, right middle lobe, left lower lobe
Patient 8	Not observed	Left inferolingular, left superior-lingular, right upper lobe anterior, right middle lobe medial-lateral
Patient 9	Not observed	Left lower lobe superior
Patient 10	Bilateral lower lobar-segmental branches	Left superior-lingular, left lower lobe anteromediobasal, left lower lobe laterobasal, left lower lobe posterobasal, right lower lobe posterobasal,
Patient 11	Bilateral lower lobar-left upper lobe	Right upper lobe posterior, right upper lobe anterior, left upper lingual
Patient 12	Left lower segmental branches	Left upper lobe apicoposterior, left upper lobe anterior, left superior-lingular, left infeolingular, right upper lobe apical
Patient 13	Not observed	Right upper lobe apical, right upper lobe anterior, left upper lobe anterior
Patient 14	Right lower lobe segmental	Left lower lobe superior, left lower lobe basals
Patient 15	Left upper-lower lobar-segmental branches	All segments in the left lung
Patient 16	Bilateral main PA, lower lobar and segmental, right middle lobar segmental	Right upper lobe apical, left superior-lingular, left lower lobe anterobasal, left upper lobe anterior

(Continued)

Patient 17	Right upper and lower lobar-segmental	Left upper lobe apicoposterior
Patient 18	Right main PA, middle-lower lobar-segmental	Right upper lobe anterior, right lower lobe anterobasal, left lower lobe anteromediobasal, left superior-lingular

PA: pulmonary artery

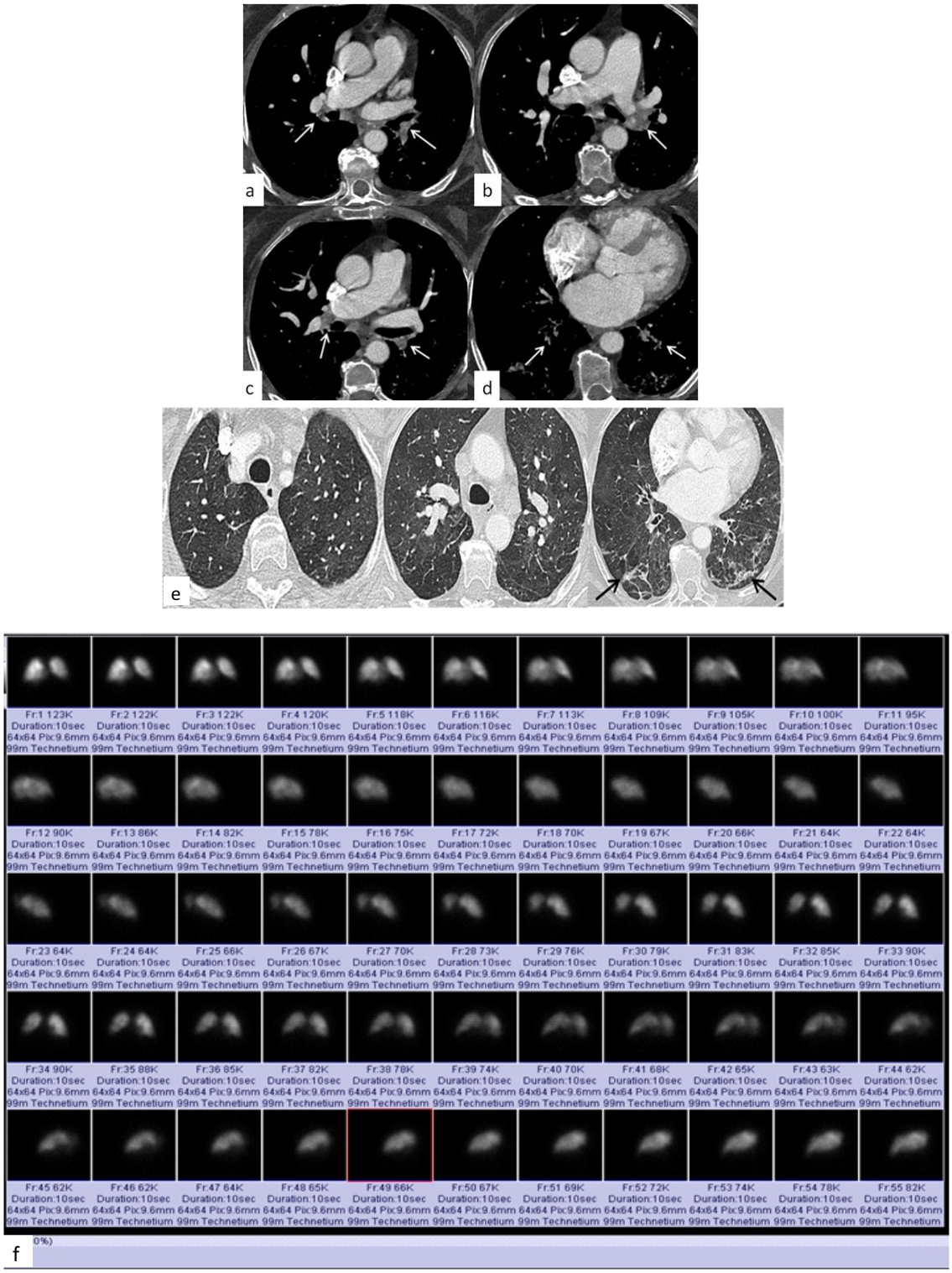

Figure 1. Comparison of CTA and V/Q scintigraphy of Patient 10. a: On axial plane examination of pulmonary angiography in the mediastinal window; Interruptions in the localization of the lower lobe basal segmental branches in both main pulmonary arteries secondary to chronic thromboembolism (a,b,c, arrows), hypodensity at this localization, decreased caliber and filling defect in distal segmental branches of the lower lobe (d, arrow). e: Sections in the parenchymal window at the axial plane of the same patient; Mosaic perfusion pattern in bilateral lung parenchyma and fibroatelectatic parenchymal changes (arrow) in the peripheral parenchyma of the lower lobe basal segments. f: V/Q scintigraphy showed mismatched defects in the right upper lobe apical, left superior-lingular, left lower lobe anterobasal, left upper lobe anterior.

Mean pulse oxygen saturation was negatively correlated with the number of mismatch subsegmental defects (r: -0.651, P=0.005). Systolic pulmonary artery pressure was positively correlated with the number of mismatch defects (segmental+subsegmental) (r: 0.523, P=0.026) (Table 5).

Discussion

The distribution of mismatch defects in V/Q was more widespread than in the area where the thrombus was located on CTA. Soler et al.(2012) also found that SPECT perfusion scintigraphy was more sensitive than CTA to identify occluded segments in CTEPH patients (62%±4.1% vs. 47.8%± 2.9%; P=0.03) [14]. This can be explained by the inability to fully evaluate the arteries at the subsegmental level in CTA. The location (segmental, subsegmental, lobar) and the number of defects did not differ in the CTED and CTEPH groups.

Table 4. *Comparison of CTA and V/Q scintigraphy findings.*

	Patchy defect (n:8)	P-value	Wedge defect (n:16)	P-value
Mosaic perfusion	5(62.5%)	0.043	5(31.2%)	0.596
Bronchial collateral dilatation	2(25%)	0.814	4(25%)	0.457
Vessel Narrowing Partial Full	3(37.5%) 3(37.5%)	0.941	7(43.8%) 4(25%)	0.105
Diameter differences in segmental vessels	4(50%)	1.0	7(43.8%)	0.134
Vascular networks, bands	3(37.5%)	0.737	6 (37.5%)	0.289
Parenchymal bands	6(75%)	0.280	10(62.5%)	0.732
Bronchial dilation	2(25%)	0.396	2(12.5%)	0.180
Abrupt vessel interruption	6(75%)	0.814	11(68.8%)	0.352
RV/LV≥1	5(62.5%)	0.596	9 (56.2%)	0.867
PA diameter (mm)	33.1± 9.6	0.745	33.7±8.3	0.807

PA: pulmonary artery diameter, RV/LV: right ventricle/left ventricle

Table 5. *Correlation table of CTA findings, pSO_2, and sPAP with the number of mismatch defects.*

	Number of mismatch subsegmental defects		Number of mismatch defects (segmental+subsegmental)	
	r	P	r	P
pSO_2(%)	-0.651	0.005	-0.107	0.683
sPAP (mmHg)	0.369	0.132	0.523	**0.026**
Bronchial collateral dilatation	-0.131	0.560	0.157	0.553
PA diameter (mm)	0.213	0.397	0.228	0.363

pSO_2: pulse oxygen saturation, sPAP: systolic pulmonary artery pressure, PA: pulmonary artery

An average of 3.83±2.2 total mismatch defects was detected in the total patient group. Le Pennec et al. (2022) also found more than 4 segmental mismatch defects in 95% of patients with CTEPH [15]. In our study, the shape of mismatch defects was mostly wedge-shaped, but there was no significant difference between groups. The presence of mosaic perfusion was detected in 62.5% of those with mismatch patchy defects (P=0.043). A high agreement between mosaic perfusion and scintigraphic perfusion abnormalities has also been shown in previous studies [16]. Our patients included in the study also had pulmonary disease. However, these patients did not have significant emphysema or fibrosis. Additionally, matching defects in V/Q scintigraphy are expected in patients with pulmonary disease. There is a need for studies with larger patient groups regarding the relationship of mismatch patchy appearance with chronic thromboembolic diseases.

Mosaic perfusion is characterized by sharply demarcated zones of hypoattenuation produced by hypoperfusion in lung regions distal to occluded vessels or small vessel arteriopathy in non-occluded lung regions [17]. Hyperattenuation is; are the sequelae of a compensatory increase in blood flow to occluded pulmonary vessels [18]. Bergin et al. (1996) reported that disparity in the size of segmental vessels and mosaic perfusion on HRCT can differentiate CTEPH patients from patients with nonthrombotic PAH and other pulmonary abnormalities [19]. Although the mosaic perfusion pattern was observed with a frequency of 33.3% in our study and was more common in the CTEPH group, no statistically significant difference was detected.

Ventilation/perfusionscintigraphy will show a complete defect in perfusion if complete obstruction occurs in acute embolism, whereas a partial perfusion defect with partial recanalization may be detected in chronic thromboembolism. Although hemodynamic abnormalities progress in CTEPH, the prominence of perfusion defects may decrease over time [20]. In conclusion, the size of perfusion defects may not correlate with pulmonary vascular resistance or mean PAP [21]. However, in our study, the number of mismatch perfusion defects was correlated with sPAP. Hypoxemia was also correlated with the number of mismatch subsegmental defects. The high number of mismatch perfusion defects can predict the severity of CTEPH, but studies need to be conducted to determine threshold values.

Renard et al. (2011) reported a higher frequency of mesh, band, focal stenosis, and occlusion and more extensive ipsilateral systemic collaterals in segments with perfusion defects by dual-energy CTA [22]. We analyzed the shape of the defects to diagnose CTEPH based on perfusion defects. Wedge-shaped perfusion defects are a typical sign of vascular occlusion in both CTEPH and acute PE [23, 24]. In our study, the shape of the mismatch defects was mostly wedge-shaped, but there was no significant difference between the groups. Patchy mismatch defects can be interpreted as secondary to the vasculopathy that develops in CTEPH as well as mosaic perfusion. It is known that arteriopathic changes and vascular remodeling occur in unoccluded arteries and distal segments of occluded arteries in CTEP [25].

After PA occlusion, systemic blood flow to the lung has been shown to increase by up to 30% relative to the original blood flow [26]. This systemic collateral circulation is significantly increased in chronic PE compared with acute PE [26, 27] and may be the cause of the different pulmonary perfusion patterns observed in patients diagnosed with chronic PE. Centrally located thrombi induce more severe systemic collateral formation than peripherally located thrombi [28]. In two-phase dual-energy CT studies, the delayed phase parenchymal enhancement of lung segments with perfusion defects in chronic PE is explained by increased systemic collateral circulation and this delayed phase enhancement is not seen in acute PE [29]. In our study, dilatation of bronchial collaterals was observed in 27.8%, but it was not correlated with the number of mismatch defects and the presence of patchy mismatch defects.

Patients with CTEPH have significantly increased RV mass. Increasing regurgitation on the tricuspid valve eventually leads to an enlarged right atrium. Chronic RV pressure overload can cause flattening of the interventricular septum [30]. Gertz et al. (2023) reported that CTEPH patients had a higher RV/LV ratio than acute PE (acute PE, 1.09±0.36; CTEPH, 1.26±0.43; P=0.02), and flattened interventricular septum and right ventricular hypertrophy were also more frequently observed [10]. In our study, although the RV/LV ratio was ≥1 in 55.6% of the total patients, there was no difference between the groups. The ventricular septal deviation was observed in only one patient.

Gertz et al. (2023) found that patients with CTEPH had a larger mean PA diameter than patients with acute PE (acute PE, 28.8±4.5; CTEPH, 34.0±5.5; P<0.001) [10]. In our study, the mean PA diameter measured on CT was above normal values in both groups, but the difference between the groups was not significant. Pulmonary artery diameter was not correlated with the number of mismatch defects.

In a study on airway abnormalities in chronic and acute PE, it was reported that ipsilateral proximal bronchial dilatation was more common in chronic PE [31]. In our study, although the frequency was 16.7%, there was no significant difference between CTED and CTEPH.

In CTEPH, the gender ratio was reported to be equal in European data [32], whereas 75% of CTEPH patients in Japan were female [33]. There was also female dominance in our study. It is not clear whether sex hormones or gender differences are a risk factor for CTEPH. Tobacco use has been reported to be significantly lower in CTEPH than in PAH. This difference may also be due to the higher prevalence of female patients with CTEPH [34]. The majority of our patients were non-smokers.

The initial diagnosis of CTEPH based on V/Q scanning should then be hemodynamically confirmed using right heart catheterization (RHC). Right heart catheterizationshould ideally be combined with conventional pulmonary angiography, which is the gold standard technique for assessing the location and extent of thromboembolism and therefore whether the patient is suitable for PEA. Computed tomography angiographyis also routinely used to evaluate the diagnosis and operability of CTEPH [35]. Our limitation is that we did not have RHC findings, although our patients were CTEPH or CTED compatible with clinical, CTA, and V/Q scintigraphy findings, and a history of previous embolism. Although it is a single-center and small patient series, it suggests that patchy mismatch defects may be a sign of chronic thrombus and the

number of mismatch defects may be correlated with the severity of the disease. There is a need for studies with larger series of patients in this regard.

In conclusion, since well-endothelialized or subsegmental thrombi may be missed on CTA, V/Q scintigraphy is superior in the diagnosis of CTEPH/CTED. However, it needs more definitive features to distinguish acute and chronic embolism. In patients with appropriate clinical, ECHO, and CTA findings, the presence of mismatch patchy defects on V/Q scintigraphy and the total number of mismatch defects may guide the diagnosis and management of CTEPH/CTED. Cut-off values can be determined by examining large patient series in multicenter studies.

Ethical approval

This study was approved by Abant Izzet Baysal University Ethics Committee (approval number: 2024/05, date: 06.02. 2024) The study was performed in accordance with the declaration of Helsinki.

The authors declare that they have no conflicts of interest.

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