Pulmonary Artery Diameter Measurement and Semiquantitative Visual Scoring with Q-SPECT-CT in Acute Pulmonary Embolism

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ABSTRACT
Objective: To investigate whether pulmonary artery diameters obtained from lung perfusion single-photon emission computed tomography-computed tomography (SPECT-CT) images and semiquantitative visual scoring (SVS) could serve as predictors of chronic pulmonary thromboembolic disease (CPTED) in acute pulmonary embolism patients (APE).

Study Design: Observational study.

Place and Duration of the Study: Department of Nuclear Medicine, Samsun Provincial Health Directorate, Gazi State Hospital, Samsun, Turkey, from January 2016 to March 2021.

Methodology: A total of 142 patients undergoing lung perfusion SPECT-CT were included in this study. Patients were classified as APE (+) (n=42) and APE (-) (n=100) based on laboratory and radiological findings, clinical diagnosis, and treatment protocol. Non-contrast CT images were used to determine the diameters (mm) of the main (MPA), right (RPA), and left (LPA) pulmonary arteries and the main pulmonary artery/aorta (PA/AO) ratio. All perfusion defects were scored using SVS for the PE (+) group. Seventeen patients with a diagnosis of CPTED were followed up. The scores and arterial diameters of recovered APE and follow-up patients were compared.

Results: The mean diameters (mm) of MPA, RPA, and LPA and PA/AO ratio were 29.74±5.51, 21.73±4.11, 22.74±4.16, and 0.83±0.16 in the APE (+) group and 26.18±4.99, 19.35±3.84, 19.49±4.15, and 0.77±0.15 in the APE (-) group, respectively (p<0.001). Mean MPA diameter (mm), total defect (TD), right visual defect (RVD), and PA/AO ratio were 31.67±15.65, 17.65±10.51, 0.91±0.18 in the CPTED group and 28.06±4.59, 18.92±13.30, 10.4±7.41, and 0.78±0.15 in the recovered APE group, respectively (p<0.05).

Conclusion: Assessment of pulmonary artery diameter and PA/AO ratio may indicate APE, but TD and RVD scores may be predictive factors for CPTED when included in the assessment along with MPA dilatation and PA/AO ratio.

Key Words: Acute pulmonary embolism, Pulmonary artery diameter, Lung SPECT-CT, Chronic pulmonary thromboembolic disease, Semiquantitative visual scoring.


INTRODUCTION
Acute pulmonary embolism (APE) is a life-threatening and potentially fatal disease. The mortality rate of APE can be as high as 30% in untreated patients.¹ Chronic thromboembolic pulmonary hypertension (CTEPH) is the major concern of chronic pulmonary thromboembolic disease (CPTED) with high rates of morbidity and mortality.²,³ Patients with a previous APE and persistent clots in arterial vasculature and/or mismatch perfusion defects, pulmonary artery pressure increase, accompanying symptoms and signs of pulmonary hypertension, after completing three months of anticoagulant therapy are candidates for CTEPH with the diagnosis of CPTED.⁴

Computed tomography pulmonary angiography (CTPA), seeking defects of contrast media as a sign of vessel clots, is commonly used in the workup of suspected APE due to its readily available and rapid acquisition time.⁵

Lung ventilation/perfusion (V/Q) scintigraphy or perfusion single-photon emission computed tomography/computed tomography (Q-SPECT-CT) are frequently employed diagnostic techniques known for their high sensitivity and specificity. There have been different approaches used to interpret lung V/Q scintigraphy, with the primary objectives to minimise non-diagnostic interpretations, enhance the diagnostic precision of radionuclide imaging, and streamline the interpretation process.⁶,⁷ According to the 2019 ECR guidelines, further confirmatory testing is unnecessary if V/Q scintigraphy is normal or shows a high probability of PE.⁸ In the field of nuclear medicine, advances in hybrid technology have provided a new approach for the diagnosis of APE. This approach involves the utilisation of SPECT imaging in combination with co-registered low-dose non-contrast CT.⁹ Studies comparing CTPA and pulmonary artery pressure measurements in APE have reported that pulmonary artery cross-sectional diameter increase in proportion to pulmonary artery pressure.¹⁰,¹¹
The literature review revealed a gap in the existing studies regarding the investigation of pulmonary artery diameter changes in individuals with APE who underwent V/Q SPECT-CT. There was also a lack of research on V/Q SPECT-CT studies that examined the pulmonary artery diameter, perfusion defect scores, and their relationship with CPTED. Therefore, the objective of this study was to assess the additional value of pulmonary artery diameters and perfusion defect scores obtained through Q-SPECT/CT in predicting the potential of candidates for CPTED in patients with APE.

**METHODOLOGY**

The regional ethics committee approved this retrospective study protocol (2021000214/8 April 2021). This single-centre study was based on lung V/Q-SPECT-CT data of patients with suspected APE that were collected from the database of the Department of Nuclear Medicine, Samsun Provincial Health Directorate, Gazi State Hospital, Samsun, Turkey. The imaging data and archive files of patients admitted to the Department of Nuclear Medicine between January 2016 and March 2021 for V/Q SPECT-CT imaging for APE were reviewed. The clinical likelihood of APE was assessed according to the recommendations of the current guidelines. The diagnosis of APE was made using a composite reference standard including ECG, lower limb ultrasound, D-dimer levels, CTPA (when available), V/Q SPECT-CT imaging, and clinical follow-up for at least 3 months. After reviewing the database, the patients with insufficient data, no clinical follow-up, a history of heart disease, CPTED, chronic obstructive pulmonary disease, pulmonary hypertension (PH), and those who had received anticoagulant therapy were excluded from the study. Finally, 142 patients' data were eligible for this study.

The CPTED diagnostic criteria was the presence of PH despite adequate antiocoagulation for at least 3 months, mismatched defects in lung V/Q scan or visualisation of chronic thrombus in pulmonary arteries in CTPA, and exclusion of other aetiology of PH than PE.

Lung V/Q SPECT-CT imaging was performed using 3.5-4 mCi Tc-99m macroaggregated albumin (MAA). In cases with perfusion abnormalities, a ventilation study was performed. Following a dose of 1-1.5 mCi Tc-99m Technegas inhalation, lung V-SPECT-CT was obtained. In the centre, the standard routine test for the evaluation of APE is combined Tc-99m MAA/Tc-99m Technegas lung V/Q imaging with SPECT/CT system (InterViewTM Fusion software, version 3.08.008.0000, Anyscan-SC, Mediso Ltd., Budapest, Hungary). The CT was performed as a low-dose CT scan without contrast enhancement during free breathing (120 kVp, 80 mAs/slice, collimation 20 x 1.25 mm, rotation time 0.66s, pitch 1, matrix 512 x 512) immediately after the lung V/Q-SPECT scan.

The interpretation of the Q-SPECT-CT scans was conducted by two nuclear medicine specialists. PE was defined by the presence of a wedge-shaped perfusion defect seen in all orthogonal planes, with a size corresponding to that of the lobar, segmental, or subsegmental regions of the lung, without CT image abnormality in the related field, as previously described.

Each lung was divided into ten segmental regions (three for the upper lobe, two for the middle lobe and lingula, and five for the lower lobe). The perfusion defects were counted with a semiquantitative visual scoring (SVS) between 1-4: 1 point defect = one-quarter of the segment; 2 point defect = half of the segment; 3 point defect = more than half of the segment; and 4-point defect = entire segment. The total perfusion defect score ranged from 0 to 40 for each lung.

MPA, RPA, LPA, and AO diameters were measured using electronic calipers at the level of the PA bifurcation. Measurements were conducted using mediastinal windows with a width of 400 and a window centre of 40. Since the images were not contrast-enhanced, the measurement of pulmonary artery (PA) diameter included the vessel wall. The diameters of the RPA and LPA were measured at their widest points after the bifurcation. The CT and SVS variables obtained from the Q-SPECT-CT scans of patients undergoing CPTED follow-up and recovering from APE were analysed.

For statistical analysis, SPSS 22.0 software was utilised. The data were presented as means±standard deviation, overall percentages and frequencies. Given the normal distribution of the data, a t-test was employed for comparing independent groups. Receiver operating characteristic (ROC) curve analysis was conducted to determine the optimal cut-off values. A p-value of less than 0.05 was considered statistically significant.

**RESULTS**

The study group consisted of 42 APE (+) and 100 APE (-) patients. The mean age of the patients was 63.33 ± 16.56 (range 20-94) years. There were 51 (36%) males and 91 (64%) females. Ventilation scintigraphy was performed on 54 patients. Embolisms were bilateral in 28 patients, whereas 12 patients had only right and 2 patients had only left-sided embolisms. Three patients had more than a score of 20 in each lung. An aperfused right lung with a score of 40 was observed in one. Eleven patients had right lung perfusion defects with SVS>20. Twenty-eight patients had right lung perfusion defects with SVS<20. Seven patients had left lung perfusion defects with SVS≥20. Twenty-three patients had left lung perfusion defects with SVS<20. The mean D-dimer (mg/L) was 2.70±3.06 in the APE (+) group and 1.12 ± 1.32 in the APE (-) group (p<0.001).

The results for the APE (+) and APE (-) cases are summarised in Table I. The mean MPA, RPA, and LPA diameters (mm) determined by Q-SPECT/CT were 29.74 ± 5.51, 21.73 ± 4.11, and 22.74 ± 4.16 in APE (+) patients and 26.18 ± 4.99, 19.35 ± 3.84, and 19.49 ± 4.15 in APE (-) patients, respectively, and the differences between APE (+) and APE (-) patients were statistically significant (p<0.001). AO diameters (mm) and PA/AO ratios were 36.03 ± 4.42 and 0.83 ± 0.16 in APE (+) patients and 33.95 ± 5.43 and 0.77 ± 0.15 in APE (-) patients, respectively, and the differences between APE (+) and APE (-) patients were statistically significant (p<0.05). There was no statistically significant difference in age (years) between APE (+) and APE (-) patients (p>0.05, Table I).
Table I: CT and laboratory findings of APE (+) and APE (-) patients.

<table>
<thead>
<tr>
<th></th>
<th>APE (+) (n=42)</th>
<th>APE (-) (n=100)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age/years (mean±SD)</td>
<td>64.71±16.42</td>
<td>62.65±16.62</td>
<td>0.49</td>
</tr>
<tr>
<td>D-Dimer (mg/L) (mean±SD)</td>
<td>2.70±3.06</td>
<td>1.12±1.32</td>
<td>0.002</td>
</tr>
<tr>
<td>Pulmonary artery diameter</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MPA (mm) (mean±SD)</td>
<td>29.74±5.51</td>
<td>26.18±4.99</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>RPA (mm) (mean±SD)</td>
<td>21.73±4.11</td>
<td>19.35±3.84</td>
<td>0.001</td>
</tr>
<tr>
<td>LPA (mm) (mean±SD)</td>
<td>22.74±4.16</td>
<td>19.49±4.15</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AO (mm) (mean±SD)</td>
<td>36.03±4.42</td>
<td>33.95±5.43</td>
<td>0.035</td>
</tr>
<tr>
<td>PA/AO (mean±SD)</td>
<td>0.83±0.16</td>
<td>0.77±0.15</td>
<td>0.047</td>
</tr>
</tbody>
</table>

Significant at 0.05 level according to the t-test. APE: Acute pulmonary embolism, MPA: Main pulmonary artery, RPA: Right pulmonary artery, LPA: Left pulmonary artery, AO: Aorta, PA/AO: Pulmonary artery/aorta.

Table II: Cut-off values, sensitivity, and specificity of the variables in the prediction of the APE and CPTED.

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>AUC (95%)</th>
<th>Cut-off</th>
<th>p</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MPA</td>
<td>0.681 (0.581-0.781)</td>
<td>28.07</td>
<td>0.000</td>
<td>65</td>
<td>67</td>
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<tr>
<td>RPA</td>
<td>0.673 (0.572-0.774)</td>
<td>20.87</td>
<td>0.001</td>
<td>65</td>
<td>68</td>
</tr>
<tr>
<td>LPA</td>
<td>0.721 (0.626-0.816)</td>
<td>21.05</td>
<td>0.000</td>
<td>65</td>
<td>71</td>
</tr>
<tr>
<td>PA/AO</td>
<td>0.624 (0.517-0.732)</td>
<td>0.79</td>
<td>0.047</td>
<td>59</td>
<td>57</td>
</tr>
<tr>
<td>TD</td>
<td>0.718 (0.559-0.876)</td>
<td>22.5</td>
<td>0.019</td>
<td>64</td>
<td>68</td>
</tr>
<tr>
<td>PA/AO</td>
<td>0.723 (0.552-0.893)</td>
<td>0.85</td>
<td>0.020</td>
<td>75</td>
<td>69</td>
</tr>
<tr>
<td>RVD</td>
<td>0.700 (0.530-0.870)</td>
<td>11</td>
<td>0.012</td>
<td>76</td>
<td>68</td>
</tr>
<tr>
<td>MPA</td>
<td>0.695 (0.511-0.879)</td>
<td>30</td>
<td>0.031</td>
<td>68</td>
<td>76</td>
</tr>
</tbody>
</table>

The ROC curve analysis was used to predict APE. Area under the curve (AUC), cut-off, p-value, sensitivity, and specificity were calculated for MPA, RPA, LPA and PA/AO (Table II).

Pulmonary artery diameters (mm), total (TD), right (RVD), and left (LVD) defect scores, and PA/AO ratio in patients with subsequent diagnosis of CPTED (n=17) and recovered APE (n=25) are compared in Table III. The mean MPA diameter (mm), TD, RVD, and PA/AO ratio determined by Q-SPECT-CT were 31.67 ± 0.65, 29.88 ± 15.59, 23.54 ± 4.20, and 23.18 ± 3.72 in the CPTED group and 28.06 ± 4.59, 21.00 ± 4.08, 21.05 ± 4.11, and 21.47 ± 4.28 in the recovered APE group, respectively, and the differences between CPTED and recovered APE cases were statistically significant (p<0.05, Table III).

The ROC curve analysis was used to predict CPTED. Area under the curve (AUC), cut-off, p-value, sensitivity, and specificity were calculated for TD, PA/AO, RVD and MPA (Table II).

DISCUSSION

APE attack and embolic vascular occlusion of a significant portion of the pulmonary circulation (usually more than 30%) leads to pulmonary vascular resistance and consequent acute pulmonary arterial hypertension.13

Residual blood clots and microscopic vascular abnormalities that persist after the onset of APE are recognised as contributing factors to the development of CPTED and PH. In this study, 17 out of 42 embolic cases (40%) were monitored and diagnosed with CPTED during the follow-up period. Significant differences in pulmonary artery diameter and SVS scores were observed between patients who recovered from APE and those who developed CPTED. The early identification of candidates for CPTED may lead to more favourable outcomes. It is well known that APE patients with PH have a poor prognosis and a higher risk of mortality, while patients with initially low pulmonary arterial systolic
pressure have a better prognosis as their pulmonary arterial pressure decreases in response to appropriate therapy.21

"Bonum diagnosis, bonum curatio" defines the worldwide effort for early diagnosis and appropriate treatment strategies for the complicated outcome of APE cases. For the screening of CPTED in patients with acute PE, V/Q scintigraphy is currently considered the technique of choice,6,14,15 which is higher sensitivity than that of CTPA.

The link between dilatation of the MPA and PH is widely recognised, and such dilatation has been observed in patients across various PH aetiologies.16,17 Numerous studies have focused on enrolling CPTED patients and assessing their pulmonary artery diameters and pressures through CT imaging to aid in the management of this condition. While several radionuclide studies have been published in relation to CPTED, they do not offer additional anatomical information regarding pulmonary artery diameters.18

In this study, the measurements of the MPA and its branches in the APE (-) group were consistent with the previous findings in cases where PE was not detected.19 During the hypothesis phase of the study, it was aimed to identify an increase in the diameter of the main arteries and their branches, particularly in the region with the most impaired perfusion. The size of the perfusion defects observed in Q-SPECT was scored using a semi-quantitative approach. In the PE (+) patient group, the defect scores were assessed by creating a SVS to determine which defect scores correlated with an increase in MPA diameter and the PA/AO ratio, and to assess the lung in which these defects were present. In the APE (+) group, enlarged pulmonary artery diameters and a higher PA/AO ratio were found compared to the APE (-) group. The optimal cut-off for predicting PE was 28.07 for MPA, with a sensitivity of 65% and specificity of 67%.

The PA/AO diameter ratio was significantly greater in patients with PH compared with controls.20 In the present study, the cut-off value for the PA/AO ratio was 0.79 for acute embolism and 0.85 for chronic one (Table II). At the defined cut-offs, RVD sensitivity was higher than TD sensitivity and their specificities were found to be equal for predicting CPTED. While PA/AO ratio and RVD score were more sensitive in predicting CPTED, MPA was more specific (Table II).

In clinical studies, a positive correlation was found between MPA diameter and the development of PH. The magnitude of MPA diameter expansion was influenced by the mechanical effects of high blood volume and pulmonary fibrosis of the adjacent vessels, both of which led to passive expansion of the pulmonary vessels.21 Previous studies have established a value of 29.0 mm as the maximum normal MPA diameter and suggested this value as a cut-off for the detection of PH.22,23 An MPA diameter of 29 mm or greater was found to have a PPV of 97%, a sensitivity of 87%, and a specificity of 89% for the presence of PH.24 However, another study suggested that 31.6 mm may be a more statistically robust cut-off in patients without interstitial lung disease (specificity 93%) and that a diameter of <29 mm does not necessarily exclude PH.25 In this study, the MPA cut-off was 28.07 mm with a specificity of 68% for the diagnosis of acute PE and the MPA cut-off was 30 mm with a specificity of 76% for the diagnosis of CPTED.

As a non-invasive diagnostic approach, low-dose and non-contrast SPECT/CT not only assisted in the diagnosis of APE but also served as a starting point for determining the development of CPTED. The statistically significant differences in pulmonary artery diameters and defect scores between the patients who developed CPTED during follow-up and the patients who recovered were surprising. Measurement of MPA diameter, PA/AO ratio, and SVS can be used as indicators of CPTED. These factors as determined by SPECT/CT, may assist in the development of therapies targeting lung perfusion by providing assessments of the extent of perfusion defect, identifying the presence of therapeutic targets, and monitoring the effectiveness of interventions. This study was the first radionuclide study to define pulmonary artery diameter and SVS in the APE and that relationship to the potential for CPTED. The limitations of this single-centre and retrospective study are the lack of pulmonary artery pressure measurement and the relatively small number of APE patients. The preliminary findings should be checked in larger series.

**CONCLUSION**

SPECT/CT is an imaging technique used for the diagnosis of APE. It offers the advantage of simultaneous measurement of vessel diameter and visual quantification of perfusion defects. The non-contrast CT allows for vessel diameter measurements, while SPECT enables the visual assessment of perfusion defects. This combined approach provides valuable information regarding potential CPTED and PH, serving as early indicators without the need for additional screening.

**ETHICAL APPROVAL:**
This study was approved by the Ondokuz Mayis University Clinical Research Ethics Committee (Approval no: 2021000214/ 8 April 2021).

**PATIENTS’ CONSENT:**
Data for this retrospective study were obtained from the medical records of the hospital and patient consent was waived by the approval of the Institutional Review Board.
COMPETING INTEREST:
The authors declared no competing interest.

AUTHORS’ CONTRIBUTION:
GS: Design of the work, collection, and interpretation of the data, statistical analysis, data curation, writing of the original draft, reviews and editing.
AA: Design of the work, writing original draft, review and editing.
All authors approved the final version of the manuscript to be published.

REFERENCES


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