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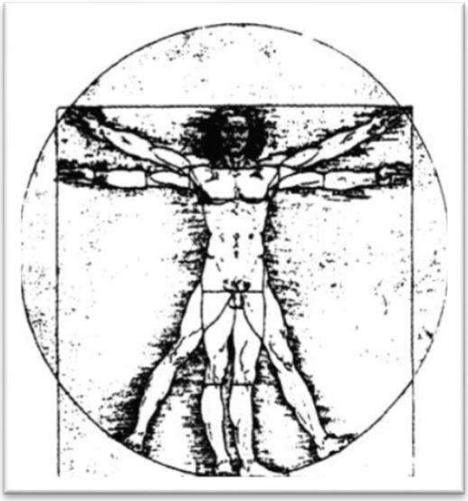

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ORIGINAL ARTICLE

EVALUATION OF THE RELATIONSHIP BETWEEN PULMONARY ARTERIAL OBSTRUCTION INDEX AND SEVERAL CT MARKERS OF RIGHT VENTRICULAR DYSFUNCTION IN PATIENTS WITH ACUTE PULMONARY EMBOLISM

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ABSTRACT

Introduction: Pulmonary thromboembolism (PTE) ranks third in mortality among the most common cardiovascular diseases. Usual cause of death in acute pulmonary embolism (APE) patients is development of right ventricular dysfunction (RVD).

Aim: The study aimed to evaluate the relationship between pulmonary arterial obstruction index (PAOI) and several computed tomographic (CT) markers of right ventricular dysfunction (RVD), using computed tomographic pulmonary angiography (CTPA) in patients with acute pulmonary embolism (APE).

Material and methods: We evaluated the initial and follow-up CTPAs of 22 patients with acute pulmonary embolism (APE) from January 2017 to January 2018, who had previous echocardiographic examination. We calculated the pulmonary arterial obstruction index (PAOI) and several CT markers of right ventricular dysfunction (RVD), then made a comparison with the echocardiographic findings in order to detect patients with acute pulmonary hypertension (PAH) and right ventricular dysfunction (RVD). All patients underwent CTPA according to appropriate diagnostic protocol for acute pulmonary embolism (APE) on a 64-slice Somatom Definition AS + computed tomography (Siemens Healthineers, USA).

Results: There was a strong and statistically significant positive correlation between the pulmonary arterial obstruction index and the right ventricular diameter as well as the PAOI and the right and left ventricular diameter ratio, on the first and follow-up measurements (r=0 .5306, p=0.011 and r=0.5359, p=0.010; r=0.5568, p=0.007 and r=0.6077, p=0.003).

Conclusion: The semi-quantitative measurements of pulmonary arterial obstruction index (PAOI) acquired on CTPA not only enable thrombi quantification, but also risk stratification for undesirable outcomes. Such and similar studies can aid the selection of appropriate CT protocols for acute pulmonary embolism (APE) diagnosis and appropriate therapy selection, as well as the avoidance of additional and unnecessary diagnostic examinations.

Keywords: pulmonary arterial obstruction index (PAOI), right ventricular dysfunction (RVD), computed tomography pulmonary angiography (CTPA), acute pulmonary embolism (APE), pulmonary arterial hypertension (PAH)

INTRODUCTION

Pulmonary thromboembolism (PTE) is a cardiovascular disease with a high rate of mortality. The most common cause of death in patients with acute pulmonary embolism (APE) is right ventricular dysfunction (RVD) [1, 2, 3]. Pathophysiologically speaking, RVD is the

result of a sudden increase of the right ventricular filling due to mechanical pulmonary artery obstruction and pulmonary vasoconstriction, all driven by neurohumoral factors.

Although the first diagnostic line of RVD is presented by echocardiography [3], computed tomographic pulmonary angiography (CTPA) is the preferred imaging modality for the diagnosis of PTE in stable patients, due to its accuracy and 24-hour availability in many institutions [4].

Several studies have evaluated various CT signs in order to determine the risk of developing RVD and predicting the patient's outcome, such as right atrial diameter, right ventricular diameter, right-to-left ventricular diameter ratio, pulmonary artery diameter, pulmonary artery and aortic diameter ratio, the superior vena cava diameter, the azygos vein diameter, contrast reflux into the inferior vena cava and hepatic veins, and the right to left interventricular septal shift [6, 7, 8, 9].

The APE diagnostic CT criteria are direct visualization of a non-occlusive or occlusive endoluminal thrombus in a blood vessel of normal or enlarged diameter. In addition to the signs of RV overload and dilatation, the APE outcome is determined by semi-quantitative CT measurement of the pulmonary arterial obstruction index (PAOI) which is a good predictor of RVD development. PAOI can distinguish between patients with or without RVD.

Given the fact that RVD indicates a high recurrence rate and a potentially fatal outcome of PTE, even after anticoagulation, it is of utter importance to analyze the relationship between pulmonary obstruction index (PAOI) and CT parameters of RVD. At the same time, PAOI is an important prognostic factor of right ventricular response to the APE.

OBJECTIVES

The aim of this study was to evaluate the relationship between the pulmonary artery obstruction index (PAOI) and several CT markers of RVD, using computed tomographic pulmonary angiography (CTPA) in patients with APE, as well as to determine the thrombus resolution rate and the variations that CT markers of RVD undergo on the follow-up CTPAs after therapy.

MATERIAL AND METHODS

Study population - This study included the initial and follow-up CTPAs of 22 patients with APE during January 2017 - January 2018. It had a retrospective approach and was performed in a single diagnostic center. All patients had previously undergone echocardiography. Data was retracted from the computer data archiving system of the Institute of Radiology and analyzed by a subspecialist in thoracic and cardiovascular radiology. All patients were aged 18 years and older. PAOIs and several CT markers of right ventricular failure were measured and compared with echocardiographic findings in order to detect patients with acute pulmonary hypertension and RVD. All patients had a follow-up CTPAs performed after appropriate anticoagulant therapy, and thrombus resolution rate. RVD regression was also evaluated.

CTPA Scan Protocol - CTPA was performed according to an appropriate diagnostic protocol for APE on a 64-slice Somatom Definition AS + computed tomography (Siemens Healthineers, USA). A bolus of 70-100 ml iodine contrast was injected with a concentration of 300 mg / ml in the left antecubital vein, with a flow rate of 3-5 ml per second, using an automated injection system. The CT scan was performed after the start of the contrast medium injection with a bolus-tracking technique. All examinations were performed with a single breath technique, in a supine position and cranio-caudal direction. The following parameters were used: cross-sectional thickness of 1 mm, cross-sectional interval of 0.5 mm, scan time of 2.76 ms with a delay of 3 seconds, average voltage of 120 kV and exposure of 108 ms. Axial CT scans were transferred to a workstation that enables post-processing with multiplanar reconstruction, and all were analyzed on a mediastinal and parenchymal window.

Calculating PAOI and signs of RVD - The CT examinations mentioned in the introduction analyzed a number of parameters for RVD including the RV/ LV diameters ratio > 1 that was limited in hemodynamically stable PTE patients. The right / left ventricle ratio was calculated through the short axes of the RV and LV in the axial plane, from the endocardial edge of the free wall to the interventricular septum (Figure 1A). The diameters of the pulmonary trunk were measured on the axial scans at the level of continuation with the right pulmonary artery, where we also calculated the diameter of the ascending aorta. The superior vena cava diameter was obtained from the axial scans at the inflow point of the azygos vein (Figure 1B). A significant contrast reflux in the inferior vena cava was considered in those exams where the contrast reached the intrahepatic segment of the vein (Figure 1C). A significant interventricular septum shift was considered in findings where we observed a straightened or convex D-septum on the left (Figure 1D).

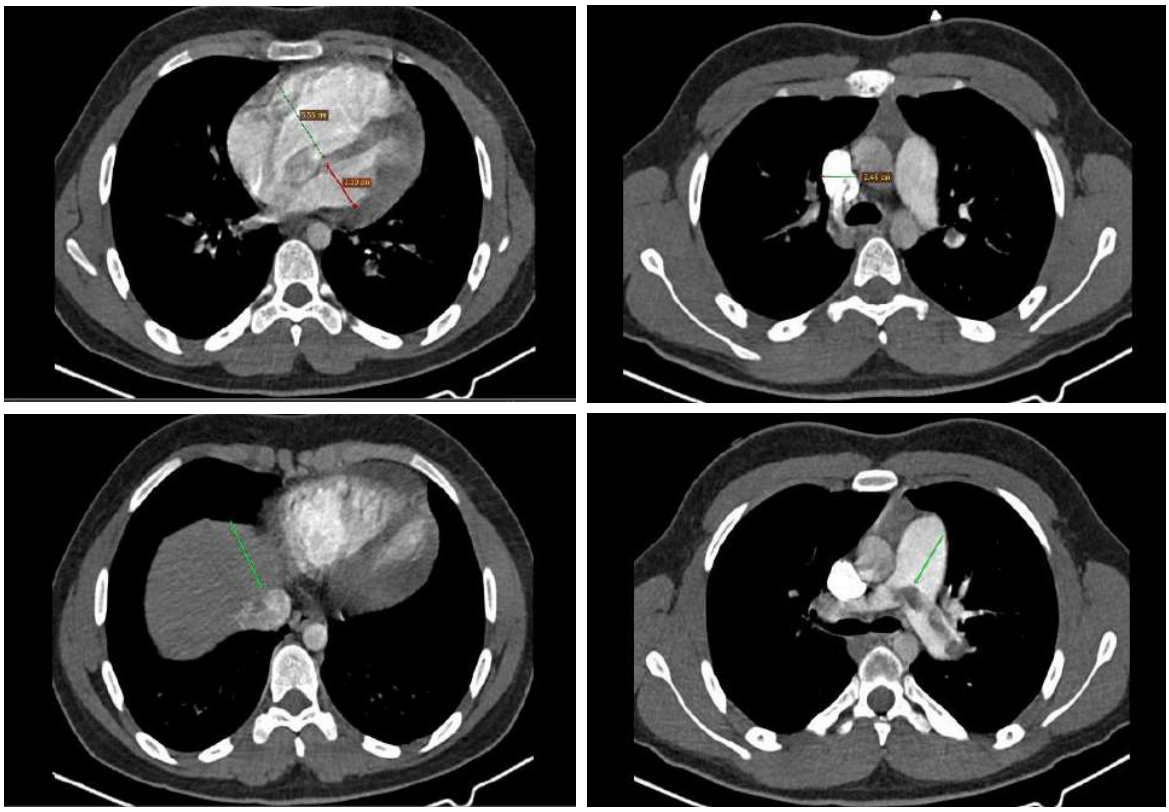


Fig. 1. A: Measurements of the right and left ventricular diameters on axial scans. B: Measuring the superior vena cava diameter at the inflow level of v. azygous. C: Assessment of contrast reflux into the inferior vena cava. D: Detection and quantification of thrombi in the pulmonary arterial system using PAOI.

In the study of Qanadli *et al*. [10], which was the foundation for defining the pulmonary obstruction index, the arterial trunk of each lung contained 10 segmental branches (3 for the upper lobes, 2 for the middle lobe and lingula, and 5 for the lower lobes). The presence of a thrombus in a segmental artery was given a value of 1 point. If a proximal arterial trunk was affected, the value given was the total number of non-visualized segmental arteries arising from the trunk. Regarding whether there was a complete or partial occlusion of the blood vessel lumen, values from 0-2 were given (0 - no, 1 - partial occlusion, 2 - complete occlusion). Therefore, the maximum CT obstruction index was 40. We calculated the percentage value according to the formula {(n x d) / 40} x 100, where n is the number of segmental arteries

affected (minimum 1, maximum 20), and d is the degree of obstruction of the affected blood vessel (minimum 1, maximum 2) (Figure 1G). Obstruction index of 40-60% in patients without hypotension is associated with PTE with intermediate, i. e. high risk [11, 12].

Echocardiography findings - We collected and analyzed the echocardiography findings of all patients in the first 48 hours of admission. RVD on echocardiography was defined as right ventricular hypokinesia and one or more of the following findings present: right ventricular dilatation (end-diastolic diameter> 30 mm); right and left ventricular end-diastolic diameters ratio > 1; paradoxical septal movement and pulmonary hypertension.

RESULTS

A total of 22 patients with radiologically confirmed APE on initial CTPAs, as well as a control group of the same patients who underwent follow-up CTPA after appropriate therapy, in order to exclude possible residues or disease complications were included in the study. According to a previously performed echocardiogram, patients were divided into two groups - those with and those without pulmonary arterial hypertension. The first group consisted of 9 patients (5 men and 4 women), while the second group of 13 patients (7 men and 6 women) (Figure 2).

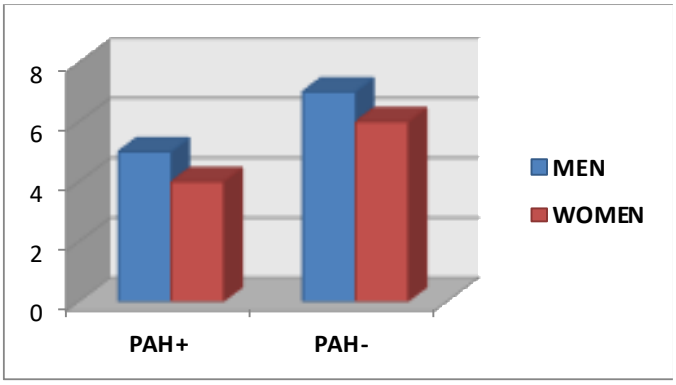


Fig. 2. Gender distribution in both groups of patients

Of the 22 patients, 10 were women (45.45%) and 12 men (54.55%). The patients age varied from 18 to 89 years, with an average of 55.18 ± 20.08. The average body weight was 78.82 ± 12.03 kg, with variations from 47 to 95 kg. Of the 22 patients, 7 (31.82%) were smokers, the rest were non-smokers. Systolic blood pressure average was 136.59 ± 20,84, diastolic 83.18 ± 10.18, and the pulse average was 95 ± 15.94. Six were diagnosed with deep vein thrombosis (DVT) (27.27%), while the remaining 16 did not have DVT. Table 1 depicts the mean values and standard deviations of PAOI and cardiological CT markers of RVD after the first measurement, as well as their minimum and maximum values. The average value of PAOI after the first measurement was 48.86 ± 28.42 with a minimum value of 15%, a maximum of 100% and the average value of the RV / LV diameters ratio was 1.17 ± 0.27 after the first measurement, with a minimum value of 0.9 and a maximum of 2.0. The remaining values are shown in Table 1.

Table 1. The average values of PAOI and CT markers of RVD on the initial CTPAs

CT markers	mean value	median±SD (min-max)
$PAOI_1$ (%)	48.86	38.75±28.42 (15-100)
RV_1 (mm)	46.86	46±6.94 (36-64)
LV_1 (mm)	40.45	40±4.16 (32-49)
RV/LV_1	1.17	1.1±0.27 (0.9-2)
PA_1 (mm)	29.59	29±4.22 (20-38)
AO_1 (mm)	32.23	33±4.49 (24-40)
PA/AO_1	0.92	0.9±0.14 (0.7-1.3)
SVC_1 (mm)	20.82	20.5±3.45 (12-27)

(PAOI-pulmonary obstruction index, RV-right ventricle, LV-left ventricle, PA-pulmonary artery, AO-aorta, SCV- superior vena cava)

The other measurements as part of the radiological evaluation of RVD exhibited a significant contrast reflux in the inferior vena cava to the middle segment of the hepatic veins in 9 patients (40.91%) and a significant interventricular right to left septal shift in 4 patients (18.18%). Peripheral triangular zones of consolidation, i. e. pulmonary infarction were detected in 14 patients (63.64%), atelectasis in 7 (31.82%), and pleural effusion in 8 patients (36.36%). We can conclude that there was a statistically significant difference for the initial PAOI measurements in both groups for $p < .05$ (Table 2). A statistically significant difference of $p < .05$ was also seen for the RV diameter and RV/ LV diameter ratio in both groups. The other parameters in both groups showed a statistically insignificant difference.

Table 2. Overview of the initial CTPA average parameter values in relation to positive or negative PAH and t-test

CT markers	PAH Positive (N=9) median±SD	PAH Negative (N=13) median±SD	p-value
$PAOI_1$ (%)	63.89± 29.58	38.46± 23.31	0.02
RV_1 (mm)	50.22± 8.54	44.54± 4.61	0.03
LV_1 (mm)	39.44± 6.00	41.15± 2.23	0.18
RV/ LV_1	1.3± 0.36	1.08± 0.14	0.03
PA_1 (mm)	31± 3.54	28.62± 4.50	0.10
$AO1_1$ (mm)	34± 4.58	31± 4.16	0.06
PA/ AO_1 (mm)	0.9± 0.19	0.9±0.11	0.43
SVC_1 (mm)	21.44± 2.65	20.38± 3.95	0.25

(PAOI-pulmonary obstruction index, RV-right ventricle, LV-left ventricle, PA-pulmonary artery, AO-aorta, SCV- superior vena cava)

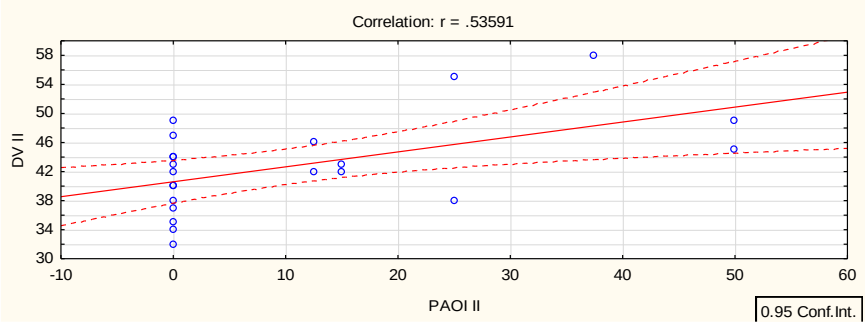
A correlation was made between PAOIs from the initial measurements with the other markers of RVD, using the Pearson's correlation. After the first measurements, there was a medium strong statistically significant positive correlation between PAOIs and RV diameter ($r=0.531$, $p=0.011069$), as well as a moderately strong statistically significant positive correlation between PAOI and RV / LV diameters ratio ($r=0.557$, $p =0.007112$). The remaining parameters showed a weak and statistically insignificant positive and negative correlation with PAOI.

The difference between average values of PAOI, RV, RV / LV, PA and PA / AO in the first and second measurements was statistically significant for p <0.05. The difference between average values of SVC diameter in the first and second measurement was statistically insignificant for p> 0.05. The correlation of PAOI and RV diameter and the RV/ LV diameters ratio in the first and second measurements depicted a strong and statistically significant positive correlation (r=0.5306, p=0.011 and r=0.5359, p=0.010; r=0.5568, p=0.007 and r=0.6077, p=0.003). The correlation of PAOI and the pulmonary artery and PA/ AO diameters ratio in the first and second measurements exhibited a weak, statistically insignificant correlation (r=0.0079, p=0.972 and r=0.0566, p=0.1844, p=0.411 and r=0.0726, p =0.748) (Table 3, Figure 2).

Table 3. Overview of the correlation of PAOI and other examined parameters during first and second measurements

FIRST MEASUREMENT	CORRELATION	SECOND MEASUREMENT	CORRELATION
PAOI	RV 0. 5306 p= 0. 011	PAOI	RV 0. 5359 p=0. 010
PAOI	RV/ LV 0. 5568 p= 0. 007	PAOI	RV/ LV 0. 6077 p=0. 003
PAOI	PA 0. 0079 P= 0. 972	PAOI	PA 0. 0566 p=0. 803
PAOI	PA/ AO -1. 844 p= 0. 411	PAOI	PA/ AO 0. 0726 p=0. 748
PAOI	SVC 0. 3808 p=0. 080	PAOI	SVC 0. 4685 p=0. 028

A



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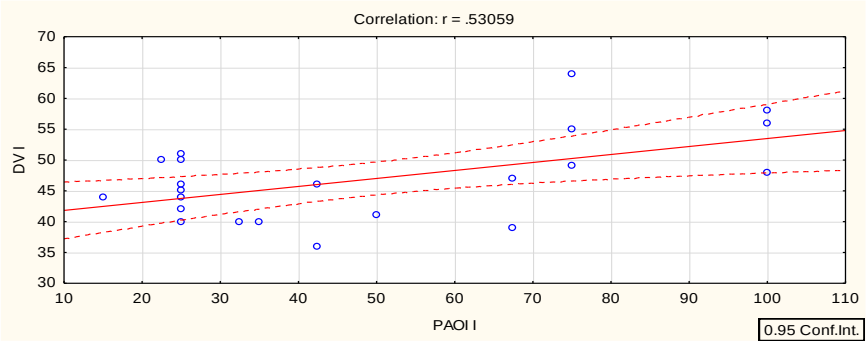

Fig. 3. Correlation of PAOI and RV diameter in the initial and follow- up measurements, A and B

The ROC analysis indicated that PAOI contributed to the diagnosis of right heart failure with 72.73% (p = 0.000) (good predictor), closer to the ideal value of 1.0 and above the worst value of 0.5 (Figure 3). Cut-off indicated the value of the variable, the range that predicted a positive state and according to the coordinates on the ROC curve, sensitivity was 85% whereas the specificity was 60.5%, which corresponded to the value - 41% (cut-off) (Figure 2).

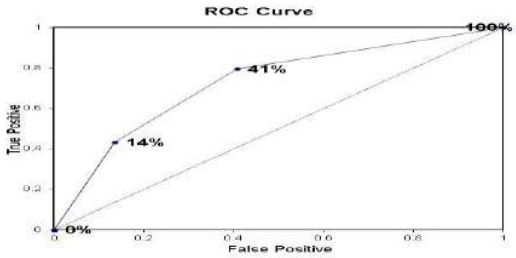

Fig. 4. ROC curve for PAOI

The ROC analysis indicated that the right and left ventricular diameters ratio contributed to the diagnosis of right heart failure with 90.91% (p = 0.000) (excellent predictor), closer to the ideal value of 1.0 and above the worst value of 0.5 (Figure 5). According to the coordinates on the ROC curve the sensitivity was 100%, whereas the specificity was 81.8%, which corresponded to the value - 0.9 (cut-off) (Figure 4).

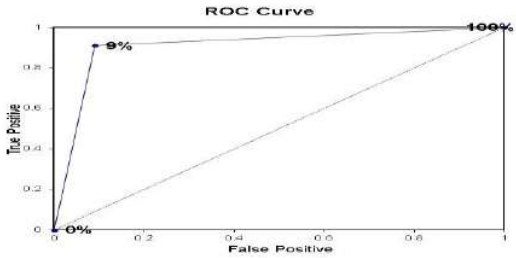

Fig. 5. ROC curve for RV/ LV diameter ratio

The number of patients without pulmonary arterial hypertension (PAH) in the follow-up measurements increased from 13 to 17. According to the dynamic index, an increase rate of 30.8% and a decrease rate of 44.4% were registered (Table 4).

Table 4. Decrease rate of PAH in follow-up measurements.

PAH/ MEASURE	I		II	
	N.	%	N.	%
POSITIVE	13	59.1	17	77.3
NEGATIVE	9	40.9	5	22.7
TOTAL	22	100.0	22	100.0

DISCUSSION

Semi-quantitative measurements of PAOI made on CTPA enable APE severity quantification, as well as risk stratification of undesirable outcomes. In our study, PAOI exhibited a positive and statistically significant correlation with echocardiographic findings of RVD and with certain CT markers of RVD, such as the RV diameter and the RV/ LV diameter ratio. PAOI manifested a close relationship with the RV diameter in patients with APE and thus it can be used as a prognostic marker for its outcome. In as many as 55% of patients, there was a complete resolution of thrombi during the follow-up CTPA (30 to 180 days).

ROC analysis of selected parameters demonstrated that the RV/ LV diameter ratio had the greatest influence in predicting right heart failure and contributed to the diagnosis with 90.91%, with a cut-off value of 0.9, whereas the PAOI participated in the diagnosis with 72.73% and the cut-off value was 41%.

Our goal was to show that values of PAOI and CT markers of RVD decreased on the follow-up CTPAs. We found a statistically significant correlation between the resolution degree of PAOI and the reduction in RV diameter, as well as reduction in RV / LV diameter ratio on the follow-up CTPAs.

CONCLUSION

The disadvantages of this study include the retrospective design, as well as the small population size, echocardiographic findings based on a written result, CTPA examinations performed without ECG-gating and different time interval of the follow-up CTPAs.

The semi-quantitative measurements of PAOI acquired on CTPA not only enable thrombi quantification, but also risk stratification for undesirable outcomes. Such and similar studies can aid the selection of appropriate CT protocols for APE diagnosis and appropriate therapy selection, as well as the avoidance of additional and unnecessary diagnostic examinations.

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