

## Original Article

# Tips for Computed Tomography Angiographic Imaging of Pulmonary Embolism

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**Background:** To measure parameters suggesting right heart failure on computed tomography angiography (CTA) taken in pulmonary embolism (PE) and to evaluate their possible contribution to the diagnosis. To investigate the changes in the parameters of PE cases at the 6th month-1 year and to evaluate the importance of these values in prognosis. PE is a disease which may be difficult to diagnose because of its different symptoms and can be fatal. The evaluation of right heart failure findings with CTA is very important in diagnosis and follow-up.

**Methods:** The mean pulmonary artery (PA) diameter, the ratio of the right ventricle to the left ventricle diameter (RV/LV), contrast material reflux to vena cava inferior and the elapsed time (ET), which was the time required to reach the targeted contrast threshold of 95 patients were measured at the first visit and under treatment.

**Results:** RV/LV, ET and contrast medium reflux at PE group were significantly higher than those without embolism ( $P=0.009$ ,  $P=0.001$ ,  $P=0.014$ ). In the first CTAs of the PE group, these parameters were significantly reduced in the control CTAs ( $P=0.005$ ,  $P=0.013$ ,  $P=0.016$ ).

**Conclusion:** It can be said that the values we measured are important in terms of prognosis of PE by assisting in diagnosis and in evaluating post-treatment recovery.

**Keywords:** Angiography, Pulmonary embolism, Tomography

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**Introduction**

Pulmonary embolism (PE) is a disease with a broad spectrum of clinical outcomes, which may be fatal.<sup>1,2</sup> In untreated cases, mortality is approximately 30%, but with correct diagnosis and early anticoagulant therapy, this rate is reduced to 3%.<sup>3</sup> Because early treatment is vital, rapid and accurate diagnosis is very important.<sup>4</sup>

Computed tomography angiography (CTA) is an easily accessible and reliable imaging method that allows for differential diagnoses and is the first imaging modality in cases suspected of acute PE.<sup>4,5</sup> CTA is a high-accuracy examination with high interobserver agreement, which bears lower risk than conventional angiography and ventilation/perfusion scintigraphy and allows direct blood clot imaging.<sup>6</sup> Embolism in the vascular lumen is observed as an intravascular filling defect.<sup>5</sup> In addition, small emboli in subsegmentary arteries can be shown via fine X-ray collimation.<sup>7</sup> CTA examination can provide detailed information, but may be also affected by artifacts such as breathing movements and beam hardening, which can make it impossible to evaluate the images.<sup>8</sup>

In routine practice, the severity of PE and treatment recommendations are usually determined using clinical findings. However, it can be sometimes difficult to

detect thromboembolic patients only on the basis of clinical findings.<sup>9,10</sup> Obstruction of pulmonary vascular structures may lead to an increase in right ventricular (RV) afterload, which may result in RV dilatation or ischemia. RV dilatation and dysfunction cause the interventricular septum to ridge to the left. Left ventricular compression and decreased cardiac output due to right heart failure constitute the most common cause of mortality in massive PE.<sup>10</sup> The size of cardiac chambers and the position of the septum can be evaluated by CTA. Various CTA indices have been proposed to assess the severity of PE. The degree of arterial obstruction can be assessed by specific CTA indices. There are studies showing the relationship between CTA obstruction scores and severity of PE and clinical value of CTA in detecting RV dysfunction.<sup>4,12-14</sup> Findings such as the ratio of RV diameter to left ventricle (RV/LV) and the reflux of intravenous contrast medium to hepatic veins can be detected with CTA. The increase in RV/LV ratio correlates with RV dysfunction.<sup>15,16</sup> In RV dysfunction diagnosed by echocardiography (ECHO), the sensitivity of RV/LV ratio has been reported<sup>17</sup> to be 91% while the specificity has been reported at 79%. The American Heart Association and the European Society of Cardiology guidelines recommend that ECHO or CTA

should be used for risk classification in PE.<sup>18,19</sup>

CTA techniques used today are equipped with automatic monitoring systems in order to ensure adequate filling of the pulmonary artery (PA) with contrast medium and to maintain synchronous image acquisition. The distribution of contrast medium from peripheral veins to PAs is a dynamic process that mainly reflects the blood flow of the right heart.<sup>20</sup> Therefore, with increased right heart load and/or RV dysfunction, the time required for the contrast medium to reach the pulmonary trunk should be longer.<sup>20-22</sup>

The time required to reach a targeted contrast threshold at a specified region of interest value is defined as elapsed time (ET) in this study. ET value may vary in each patient. It is said to be associated with pulmonary hypertension and RV dysfunction.<sup>22</sup>

There are several parameters with prognostic value in PE. However, there is no consensus on which CTA parameter is the most predictive.<sup>4,13,22-25</sup> The classical parameter is the dilatation of the short axis of the RV or the ratio of this parameter to the short axis of the left ventricle.<sup>26</sup> Recently, it has been suggested that<sup>27</sup> monitoring of contrast medium reflux in inferior vena cava inferior (IVC) and hepatic veins is a better prognostic marker. Another study showed that<sup>28</sup> a time-density curve obtained from CTA performed with a test bolus technique correlated with mortality. Therefore, ET is associated with circulatory status and may have prognostic value in patients with PE. In this study, which is conducted on patients with pulmonary CTA, the differences in CTA parameters (RV/LV ratio, main PA diameter, contrast medium reflux to IVC and ET value) in patients with and without PE were evaluated and the diagnostic capabilities of these parameters were explored. Also in this study, the effect of these parameters on PE moment and 6-month/1-year post-control control CTA was compared and their importance for the healing process and hence the prognosis was examined.

## Patients and Methods

### Study Design

After obtaining approval from the relevant ethics committee, we retrospectively evaluated all pulmonary CTA examinations performed with the preliminary diagnosis of PE between January 2017 and July 2018 using the recorded archive images.

Patients who had no PE on their CTA examination performed within the specified dates were included as the control group. In the control group and in patients with PE, we measured the predetermined parameters – main PA diameter, RV/LV ratio, contrast material reflux to IVC and ET. Differences between the two groups were evaluated. Also, the same parameters were measured in the 6th month or one year control CTA of the patients with PE. In each patient, the measurements taken at the PE and the control CTAs were compared. In addition, the

CT severity index was calculated to evaluate the severity of embolism in PE cases.

Cases with breathing and motion artifacts preventing measurement during examination and cases with CTA without standard protocols were excluded from the study. In addition, PE cases without control examination were excluded from the study. We also excluded patients with other causes of right ventricular overload such as cardiac disease and connective tissue disorder.

### CT Protocols

The subjects were examined with their arms extended above their heads, in supine position. We used a computed tomography device with 128-multidetector system (Optima CT660, General Electric Healthcare Systems, Milwaukee, USA) in our research.

Our standard imaging parameters were: 120 kVp, 150–300 mAs, slice thickness 1 mm, a pitch of 0.6–1.4 (depending on body size).

We injected the contrast medium with a bolus tracking system (“SmartPrep” protocol, GE Healthcare). SmartPrep is a feature that allows real-time monitoring of intravenous contrast enhancement in one particular section of anatomy that is in the area of interest. The contrast flow is monitored by Low-Dose scans until the contrast enhancement reaches the preferred point and the operator initiates the scan prescription. The SmartPrep protocol entailed acquiring non-incremental scans at the level of the pulmonary trunk and/or left and right main pulmonary arteries while contrast medium was being injected. Once the initial “blush” of contrast medium was observed in the pulmonary vessels, image acquisition was initiated, commencing after a 3 sec delay, during which time the patient was instructed to breathe in and hold their breath. PA enhancement measures were visualized in a graphic (time intensity curve) which were uploadable with CTA images. In our examinations, 50–60 mL iodinated intravenous medium was injected at a speed of 4.0 mL/s and the contrast medium was injected with an 18 or 20 gauge cannula catheter in antecubital veins. All examinations were executed with a single-chamber power injector.

### Measurements

Axial 1 mm-thick source images were employed for quantitative analysis. All distances were measured by two researchers twice, and the average of all measurements were used for the final analysis. Measurements were recorded to the nearest tenth of a millimeter.

The transversal diameter of the main PA was measured at the level of PA bifurcation. The upper limit of the normal diameter for the PA is 29 mm, as defined by Kuriyama et al.<sup>29</sup>

The maximum (diastolic) short axis of the RV and the maximum (diastolic) short axis of the left ventricle were

measured in the axial images and the RV/LV ratio was calculated. An example of the measurements is shown in Figure 1.

Retrograde opacification or contrast medium reflux to the IVC was considered present when the attenuation of the lumen of the IVC was visibly greater than that of a more caudal segment.<sup>30</sup> The reflux to the level of IVC was noted to be minimal, and reflux to the hepatic vein level was noted to be significant (Figure 2).

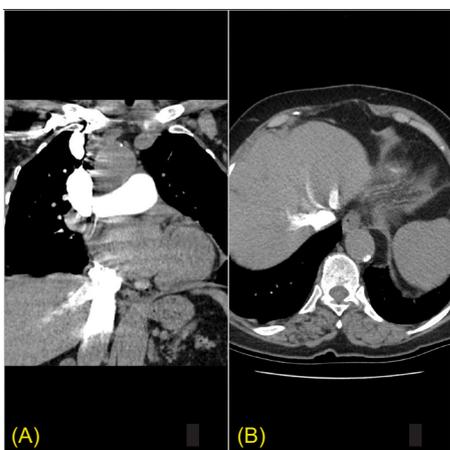
The CTA obstruction scores were evaluated using the index developed by Qanadli et al.<sup>12</sup> The CTA obstruction score can be expressed as  $\Sigma(n \cdot d)/40 \times 100$ , where  $n$  is the value of the proximal thrombus in the pulmonary arterial tree equal to the number of segmental branches arising distally (minimum, 1; maximum, 20) and  $d$  is the degree of vascular obstruction (no obstruction, 0; partial obstruction, 1; complete obstruction, 2).

### Statistical Analysis

For statistical analysis, the NCSS (Number Cruncher Statistical System) 2007 (Kaysville, Utah, USA) program



**Figure 1.** Measurement of Main Pulmonary Artery (A), Right and Left Ventricle (B) Diameter on Axial Image.



**Figure 2.** Contrast Medium Reflux to Inferior Vena Cava and Hepatic Veins on Coronal (A) and Axial Images (B).

was used. Data were reported using mean, standard deviation, median, frequency, minimum, and maximum. During the assessment of study data, Student  $t$  test was used to compare quantitative data showing normal distribution. Pearson's chi-square test was used to compare the qualitative data. Pearson correlation analysis was used to evaluate the relationships between variables. Paired sample  $t$  test was used to compare the paired measurements of the normally distributed parameters and Wilcoxon signed-rank test was used to compare the paired measurements of parameters that did not show normal distribution. Diagnostic scanning tests (sensitivity, specificity, PPV, NPV) and ROC analysis were used to determine cut-off values for parameters. Logistic regression analysis was used to evaluate multivariate risk factors on PE. Significance was evaluated with at least  $P < 0.05$ .

Based on Cohen's effect size coefficients, it was decided that there should be at least 26 people in the groups according to the calculation made by assuming that the evaluations to be made between the two independent groups will have a large effect size ( $d = 0.80$ ).

In multivariate analyses, we used parameters which were significant in univariate evaluations.

### Results

All CTAs between the specified dates were evaluated ( $n = 742$ ). A total of 126 cases were excluded from the study due to artefacts. Moreover, 150 cases were excluded due to cardiac pathologies and systemic diseases that increased right ventricular load. Also, 371 patients who were diagnosed with PE but did not have control CTA while under treatment were excluded from the study. All remaining cases were included in the study ( $n = 95$ ).

In total, 62.1% ( $n = 59$ ) of the cases were female and 37.9% ( $n = 36$ ) were male. While 28.4% ( $n = 27$ ) of the cases had no PE (control group), 71.6% ( $n = 68$ ) had PE. The subjects were aged between 24 and 91 years and the mean age was  $63.3 \pm 2$  years.

There was a statistically significant difference between the subjects' age according to the presence of PE ( $P = 0.045$ ); the age of the group with embolism was lower than that of the non-embolic group. According to the presence of PE, the gender distribution of the cases did not differ significantly ( $P = 0.564$ ).

A statistically significant difference was found between RV/LV measurements of the control group and the first arrival CTA measurements of PE ( $P = 0.009$ ); RV/LV measurements at the first visit were higher in the group with embolism compared to those without embolism. PA diameter measurements did not show a statistically significant difference between the two groups ( $P = 0.829$ ). There was a statistically significant difference between the incidence of contrast material reflux to IVC ( $P = 0.014$ ); the rate of embolism was higher in cases with reflux than those without reflux. Table 1 shows the evaluation of RV/

LV, PA, and ET measurements according to the presence of emboli.

When the two groups were compared, a statistically significant difference was found between the ET measurements of the cases ( $P = 0.001$ ); ET measurements at the first visit were higher in the group with embolism compared to the control group without embolism. Based on this significance, it was considered to calculate the cut-off point for ET. According to the presence of emboli, ROC analysis and diagnostic screening tests were used to determine the cut-off point. The cut-off point was 11 and above for ET measurement according to the groups (Table 2). For an ET cut-off value 11, we found 82.4% sensitivity, 70.4% specificity, 87.5% positive predictive value, 61.3% negative predictive value and 79% accuracy. The area under the ROC curve was 0.857 (95% CI: 0.78–0.94) (Figure 3). There was a statistically significant relationship between the presence of emboli and the cut-off value of 11 for ET level ( $P = 0.001$ ). The risk of embolism was 11.1 times higher in patients with ET level 11 and above. The odds ratio for ET measurement was 11.1 (95% CI: 3.937–31.199). The relationship between emboli and ET cut-off value of 11 is shown in Figure 4.

We evaluated the effect of age, RV/LV ratio, ET and contrast medium reflux to IVC variables on PE using logistic regression analysis for univariate risk factors. In this

model, it was found that an ET value above 11 increased the odds value 12.2 times (95% CI: 3.88–34.41), age under 65 years increased the odds value 3.5 times (95% CI: 1.08–11.54), reflux increased the odds value 3.9 times (95% CI: 0.99–15.42) and the effect on PE was significant ( $P \leq 0.001$ ;  $P = 0.037$ ;  $P = 0.050$ , respectively). ET, age and contrast medium reflux to IVC may be considered as independent risk factors for PE. Although RV/LV ratio was significant in univariate analysis, its effect was not significant in multivariate analysis ( $P = 0.304$ ).

The Qanadli scores of cases with PE ranged from 5 to 90, with a mean of  $33.7 \pm 25.8$  and a median of 25.

There was a significant decrease in those parameters in the control CTAs of patients with high RV/LV, high PA diameter and high ET values in the first CTA and the difference was statistically significant ( $P = 0.005$ ,  $P = 0.041$ ,  $P = 0.013$ ). In addition, in emboli cases, the decrease in the rate of reflux in the last measurement compared to the first measurement was statistically significant ( $P = 0.016$ ). Evaluation of RV/LV, PA diameter, ET levels and reflux to IVC rates of cases with embolism are summarized in Table 3.

## Discussion

Due to the non-specific nature of PE symptoms, there may be difficulties in diagnosing and CTA may be required even

**Table 1.** Evaluation of RV/LV, PA, ET Measurements According to the Presence of Pulmonary Embolism

		Total (n = 95)	PE (-) (n = 27)	PE (+) (n = 68)	P	Effect Size (95% CI)
RV/LV	Min-Max (Median)	0.6–1.7 (1)	0.6–1.3 (1)	0.7–1.7 (1.1)		
	Mean $\pm$ SD	1.1 $\pm$ 0.2	1.0 $\pm$ 0.2	1.1 $\pm$ 0.2	<sup>a</sup> 0.009**	0.610 (0.16–1.06)
RV/LV	Normal ( $\leq 0.9$ )	23 (24.2)	9 (33.3)	14 (20.6)		
	High ( $> 0.9$ )	72 (75.8)	18 (66.7)	54 (79.4)	<sup>b</sup> 0.191	1.929 (0.72–5.20)
PA diameter	Min-Max (Median)	20–45 (29)	20–39 (31)	23–45 (29)		
	Mean $\pm$ SD	29.6 $\pm$ 4.9	29.8 $\pm$ 5.3	29.6 $\pm$ 4.7	<sup>a</sup> 0.829	0.049 (-0.50–0.40)
PA diameter	Normal ( $< 30$ )	51 (53.7)	12 (44.4)	39 (57.4)		
	High ( $\geq 30$ )	44 (46.3)	15 (55.6)	29 (42.6)	<sup>b</sup> 0.255	0.595 (0.24–1.46)
Contrast medium reflux to inferior vena cava; n (%)	(-)	63 (66.3)	23 (36.5)	40 (63.5)		
	(+)	32 (33.7)	4 (12.5)	28 (87.5)	<sup>b</sup> 0.014*	
	None	63 (66.3)	23 (36.5)	40 (63.5)		
	Minimal	21 (22.1)	4 (19)	17 (81)		
	Significant	11 (11.6)	0 (0)	11 (100)		
ET	Min-Max (Median)	6–22 (13)	7–16 (9)	6–22 (14)		
	Mean $\pm$ SD	13.0 $\pm$ 3.7	9.9 $\pm$ 1.8	14.2 $\pm$ 3.6	<sup>a</sup> 0.001**	1.367 (0.91–1.82)

Abbreviations: PE, pulmonary embolism; RV/LV, ratio of the right ventricle to the left ventricle diameter; PA, pulmonary artery; ET, elapsed time.

<sup>a</sup> Student *t* test; <sup>b</sup> Pearson's chi-square test; \* $P < 0.05$ ; \*\* $P < 0.01$ .

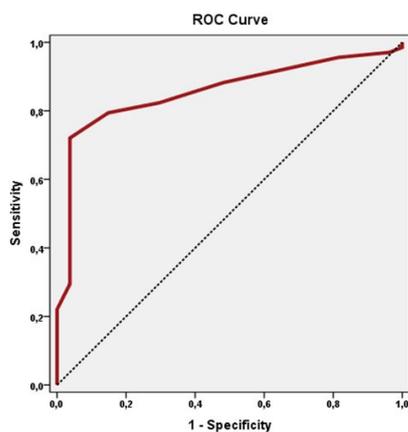
Effect sizes of numerical data were calculated by (Difference of means) / (Pooled standard deviation). Effect sizes of categorical data were reported as odds ratios.

**Table 2.** Relationship Between Presence of Pulmonary Embolism and Elapsed Time (Cutting Value 11) Measurement

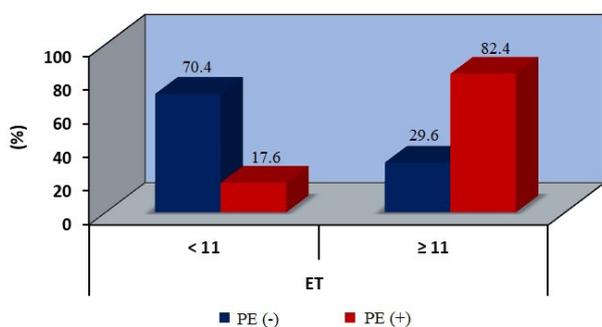
		Elapsed Time (s)				P <sup>b</sup>	Effect Size (95% CI)
		< 11		$\geq 11$			
		No.	%	No.	%		
Pulmonary Embolism	(-)	19	7.4	8	29.6	0.001**	11.083 (3.94–31.19)
	(+)	12	17.6	56	82.4		

<sup>b</sup> Pearson's chi-square test; \*\* $P < 0.01$ .

Effect size was reported as odds ratio.



**Figure 3.** ROC Curve for Elapsed Time Level According to the Presence of Pulmonary Embolism. ET; elapsed time.



**Figure 4.** Relationship between pulmonary embolism and elapsed time when cut-off value is 11. PE; pulmonary embolism, ET; elapsed time.

if there is low clinical probability.<sup>31</sup> Multislice CTA is the most commonly used imaging method for the diagnosis of acute PE.<sup>32,33</sup> In recent years, the severity of PE with CTA has been evaluated and scores for PA occlusion have been developed in several studies.<sup>12,13,34</sup> Some studies have found a significant relationship between pulmonary artery score and mortality<sup>35,36</sup> but some studies have failed

to find any relationship.<sup>12,23,32</sup> This situation shows that the clinical outcome in patients with acute PE indicates is not only determined by the pulmonary obstruction score, but also later RV dysfunction.<sup>34</sup> In our study, the Qanadli scoring system was used to determine the severity of PE. The Qanadli scores of the cases with PE ranged from 5 to 90. Since there was no mortality in follow-up, the relationship between embolism scores and mortality was not evaluated. Since some of the patients included in the study were referred to centers outside our hospital, no comparison was made between hospitalization time and morbidity.

For appropriate treatment of PE, it is important to know the severity of embolism and whether right heart dysfunction develops.<sup>4</sup> The prognosis of PE is associated with the presence of pre-existing cardiovascular disease, the degree of pulmonary hypertension and vascular occlusion, and in particular with RV dysfunction.<sup>37</sup> Plugging of more than 30% of pulmonary vessels leads to acute pulmonary hypertension and a sudden increase in RV afterload. This may lead to RV dilatation, hypokinesia and RV insufficiency.<sup>38</sup> The main cause of PE-related mortality is acute right heart failure. In previous studies with ECHO, RV dysfunction has been reported to have prognostic significance in PE patients.<sup>39</sup> Acute PE was defined by acute cor pulmonale findings including ECHO severity, RV dilatation, paradoxical movement of interventricular septum, hypokinesia of the free wall of RV and/or systolic pulmonary hypertension.<sup>13</sup> ECHO is required to identify RV dysfunction, but in routine practice, it is not possible to apply it to all PE patients.<sup>4</sup> The ratio of the short axes of the ventricles on CT is a morphological parameter of heart function. In conditions like PE and right heart stress, it can change quite quickly. Therefore, it is thought to be correlated with the current cardiac condition. A healthy person should have a rate of 0.9 or less.<sup>26,40</sup> Contractor et al<sup>25</sup> defined the situation where the RV/LV ratio is greater than 1 and the ridging of interventricular septum to the

**Table 3.** Evaluation of RV/LV, Pulmonary Artery Diameter, Elapsed Time Levels and Contrast Reflux to Inferior Vena Cava Inferior Rates in Patients with Pulmonary Embolism<sup>a</sup>

		Pulmonary Embolism (+) (n = 68)		P	Effect Size
		First Measurement	Second Measurement		
RV/LV	Normal (≤0.9)	14 (20.6)	25 (36.8)	0.005**	0.979
	High (>0.9)	54 (79.4)	43 (63.2)		
	Min-Max (Median)	0.7–1.7 (1.1)	1.6–0.7 (1)		
Pulmonary artery diameter	Normal (<30)	39 (57.4)	48 (70.6)	0.041*	0.978
	High (≥30)	29 (42.6)	20 (29.4)		
	Min-Max (Median)	23–45 (29)	21–45 (28)		
Elapsed time	Normal (<11)	12 (17.6)	28 (41.2)	0.013*	0.962
	High (≥11)	56 (82.4)	40 (58.8)		
	Min-Max (Median)	6–22 (14)	5–19 (11.5)		
Contrast reflux to vena cava inferior, No. (%)	(-)	40 (58.8)	51 (75)	0.016*	
	(+)	28 (41.2)	17 (25)		

Wilcoxon Signed-rank test, RV/LV; ratio of the right ventricle to the left ventricle diameter.

<sup>a</sup> Measurements made under first arrival and treatment; \*  $P < 0.05$ , \*\*  $P < 0.01$ .

Note: Effect sizes of numerical data were calculated by (Mean of difference) / (SD of difference) / Sqrt(1-r) where r is correlation between first and second measurement.

left in axial images as RV dysfunction. In their study, they reported RV dysfunction with 78% sensitivity and 100% specificity based on the findings of CTA compared with ECHO findings. Ghuysen et al<sup>26</sup> reported that most of the patients who died from PE had a RV/LV ratio (calculated from axial images) over 1.5 and this value could be taken as a threshold for survival. In our study, the RV/LV ratios were higher than that of the non-embolic group in the CTA measurements of PE patients on their first admission. The mean RV/LV ratio was  $1.1 \pm 0.2$  in patients with PE. In addition to the literature, in our study, the changes that occurred during treatment were evaluated by taking measurements from the control CTAs taken under treatment or in the 6th month/one year after treatment. There was a significant decrease in control tomography results of the cases who had a high ratio of RV/LV and high PA diameter in their first CTAs and the difference was statistically significant. This result shows that these parameters can also be used in follow-up and evaluation of response to therapy.

Reflux of contrast medium into the IVC and hepatic veins has been suggested to serve as a pathophysiologic marker of right heart dysfunction and PE.<sup>41</sup> In some case reports and small series, retrograde opacification of the IVC or hepatic veins in intravenous contrast-enhanced imaging has been associated with right-sided heart disease such as tricuspid regurgitation, pulmonary hypertension and RV systolic dysfunction.<sup>30,42</sup> In a study<sup>30</sup> where low injection rates were compared with high intravenous contrast injection rates, it was reported that contrast agent reflux detected heart disease with higher sensitivity and lower specificity. The retrograde flow of the contrast medium is initially independent of the injection rate. However, since high injection rate tests were performed with shorter screening delays than the low injection rate tests, in the high-injection ratio group (i.e., the group undergoing a shorter scan delay time during examination), the IVC could be visualized prior to antegrade blood flow, and the hepatic veins might have pushed the refluxed contrast medium back to RV. In addition, as intravenous contrast medium administration increases the intravascular volume, the volume of recirculated blood that pushes the refluxed contrast medium back into the heart may be larger in patients who are given contrast medium with larger bolus.<sup>43</sup> However, previous studies<sup>30</sup> show that the contrast injection rate itself contributes to the frequency of reflux, and that a faster injection rate acts as a volume loading that reveals a decreased right heart flow reserve. In another study, the amount of reflux to IVC was measured in millimeters and the reflux was associated with 30-day mortality (with 54% sensitivity, 83% specificity) with a craniocaudal length of 31 mm or more.<sup>27</sup> Bach et al<sup>40</sup> reported that pathologically increased reflux had a significant relationship with prolonged time to threshold during shots. In our study, there was also a statistically

significant difference in the incidence of contrast medium reflux to IVC when the control group was compared with the PE group. The rate of embolism was higher in patients with reflux than those without reflux. Moreover, unlike the studies in the literature, in our study, patients' CTA images at PE moment and the images under treatment were compared with each other and the decrease in the rate of reflux in the last measurements was statistically significant. This result indicates that similar to the RV/LV ratio, contrast agent reflux is a parameter that can be used in evaluating response to therapy.

In recent years, with the development of computer and imaging technologies, new systems have gained increasing influence in clinical and research applications.<sup>44</sup> In modern CTA devices, automatic contrast monitoring systems have been developed to synchronize the adequate filling and image acquisition of PAs with contrast medium. This system captures the contrast intensity measured in Hounsfield Units in the pulmonary trunk and begins to acquire data when the contrast medium fills the PA.<sup>20</sup> Optimal arterial opacification is very important for imaging PAs with CTA. This reveals the difficulty of data acquisition from the pulmonary vascular structures with the same timing as the contrast medium transition.<sup>45</sup> The distribution of contrast medium from peripheral veins to PAs is a dynamic process and reflects the right heart blood flow.<sup>20</sup> Therefore, the time required for the contrast medium to reach the pulmonary trunk should be long, and if the right heart load is increased and/or in the case of right heart failure, the slope of the increasing intensity of contrast should be flatter.<sup>21,22</sup> This approach may contribute to the prognostic information provided by CTA in the PE cases. Factors that affect contrast enhancement are associated with the contrast delivery protocol (eg, iodine concentration, flow rate, injection time) and patient's physiology, such as the cardiac output.<sup>46,47</sup> All cases included in the study<sup>48</sup> were given the same amount of iodine, and the same automatic injector system was used for all cases. PA pressures affect the speed of contrast agent bolus spread. Therefore, increased PA pressure and associated low transpulmonary blood flow prolongs the time to the inflection point and the time to peak.<sup>20</sup> A retrospective study<sup>28</sup> suggested that the characteristics of contrast enhancement over time may be related to the risk of death. Bach et al<sup>40</sup> reported that the time to threshold value of CTA imaging parameter was associated with circulatory status parameters and 30-day mortality in PE cases. In this study, high time to threshold value was reported to be associated with poor prognosis.

In our study, comparing the group with PE and the control group, ET measurements at the first visit were higher in the group with embolism compared to the control group without embolism. Based on this significance, the cut-off point was found to be 11 and above for ET measurement, and the risk of embolism was 11.1 times higher in cases with ET level of 11 and above. Based on our results, it

can be said that the parameters of the time-intensity curve obtained in the CTA shots with bolus tracking method (ET was used in this study) are related to RV dysfunction evaluated from CTA images. There was also a statistically significant decrease in the value of ET after treatment compared to the first ET values measured in initial CTAs. When the first and second arrival values of each patient were compared with each other, the factors causing the difference from person to person were eliminated, and the change in the results showed directly the patient's own hemodynamic changes. The decrease in ET observed in follow-up exams indicates that this parameter can be used in the recovery process and follow-up of the disease.

In our study, we aimed to emphasize the importance of imaging findings, and since the measurements were made only on CTA images, no physical examination, laboratory findings (such as PO<sub>2</sub> pressure, d-dimer) and ECHO findings were recorded for the cases included in the study. Therefore, the diagnosis of right heart failure was not clinically confirmed in patients with RV dysfunction in CTA. In addition, hospitalization and morbidity results could not be achieved because some cases were referred to other centers for acute phase treatment. Our sample size is limited, because our study only included the cases with PE whose CT was taken in our follow-up CT center. The odds ratio for ET measurement was 11.1. The huge odds ratio estimate of more than 10 may suggest sparse data bias.<sup>49</sup>

In our study, findings suggesting RV dysfunction with CTA (RV/LV and contrast medium reflux to the IVC) were found to be significantly higher in patients with PE compared to the control group. In this respect, our results are consistent with most studies in the literature. In addition, the change in the parameters of the time-intensity curve obtained with the bolus tracking system (ET used for this study) suggests RV dysfunction secondary to PE. There is a very limited number of studies in the literature on this topic and our findings will contribute to the literature. Apart from these, in our study, in addition to the available literature, the results of CTA measurements of PE case changes were evaluated in treatment and recovery process and their importance in prognosis was shown. However, there are limitations in our study, and larger series are needed in which clinical findings, morbidity and mortality are evaluated together with CTA findings.

#### Authors' Contribution

Both authors participated in the study design, the practical work, data analysis and writing the manuscript.

#### Conflict of Interest Disclosures

The authors declared no potential conflicts of interest with respect to research, authorship and publication of this article.

#### Ethical Statement

The Ethics Committee of of clinical research of Diskapi Yildirim

Beyazit Research and Training Hospital, Ankara, Turkey approved the present study (Number: 47/12, 19.03.2018).

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