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Agreement Between Transthoracic Echocardiography and Computed Tomography Pulmonary Angiography for Detection of Right Ventricular Dysfunction in Pulmonary Embolism

ABSTRACT

Background: Right ventricular dysfunction (RVD) is the main determinant of mortality in patients with pulmonary embolism (PE). Thus, guidelines recommend the assessment of RVD with transthoracic echocardiography (TTE) or computed tomography pulmonary angiography (CTPA) among these patients. In this study, we investigated the agreement between TTE and CTPA for the detection of RVD.

Methods: This single-center retrospective study included patients who were diagnosed with CTPA and underwent TTE within the first 24 hours following the diagnosis.

Results: Two hundred fifty-eight patients met the inclusion criteria. In 71.3% (184) of them, CTPA and TTE agreed on both the presence and absence of RVD. There was a moderate agreement between the 2 tests (Cohen's kappa = 0.404, $P < .001$). The agreement between right ventricle dysfunction on TTE and the increased right ventricle/left ventricle (RV/LV) on CTPA was fair (Cohen's kappa = 0.388, $P < .001$). Three patients died due to PE, and another 5 patients required urgent reperfusion therapy. Overall, adverse outcomes occurred in 4% (8) of patients. The sensitivity of modalities in the detection of adverse outcomes was 100%. Transthoracic echocardiography was more specific compared to CTPA (43% vs. 28%). Statistically, flattening/bulging of the interventricular septum on TTE was significantly associated with adverse outcomes. No individual CTPA parameter was related to adverse outcomes.

Conclusion: Both CTPA and TTE are reliable imaging modalities in the detection of RVD. However, TTE is more specific, and this may help in the identification and appropriate management of patients at higher risk of decompensation. A combination of CTPA parameters rather than individual RV/LV ratios increases the sensitivity of CTPA.

Keywords: Pulmonary embolism, risk stratification, prognosis, transthoracic echocardiography, computed tomography

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INTRODUCTION

Right ventricular dysfunction (RVD) is the main determinant of mortality in pulmonary embolism (PE).[1] Patients considered to be at low risk may have RVD, and early discharge of PE patients may cause increased mortality.[2-4] Thus, current guidelines[1] recommend assessment of the right ventricle (RV) to avoid erroneous discharge of patients with RVD and catastrophic consequences like post-discharge mortality.

Transthoracic echocardiography (TTE) is the standard method in the assessment of RV, which shows more parameters and real-time images of RV and enables the detection of intracardiac thrombus and/or RV hypokinesia.[5-8] However, it is operator-dependent and not always available, especially during night shifts and emergencies.

Computed tomographic pulmonary angiography (CTPA) enables both diagnosis and risk stratification. Also, the extent of thrombi can be visualized with CTPA. It is widely available and can be reviewed by different clinicians, even from outside the hospital. However, CTPA gives static information about the RV. Intracardiac thrombus and/or RV hypokinesia cannot be recognized by CTPA.

Right ventricle assessment is crucial for safe discharge. And if the assessment is done with CTPA, it must be at least as accurate and reliable as TTE. Though studies revealed the accuracy of CTPA in risk stratification of PE,[9-11] we hypothesized that inferiorities of CTPA, such as the inability to detect RV hypokinesia or RV thrombus, may cause misclassification of patients who need longer medical attention. Thus, we aimed to investigate the accuracy of CTPA in the identification of RVD and compare it with TTE.

METHODS

In this single-center retrospective study, we reviewed the electronic medical files of patients who were diagnosed with PE between 2013 and 2022. Patients who were diagnosed with CTPA and underwent TTE within the first 24 hours following the diagnosis were enrolled.

Exclusion Criteria

- Transthoracic echocardiography after 24 hours of diagnosis or after thrombolytic therapy
- Patients known to have pulmonary hypertension or RV failure before PE
- Patients with recurrent PE (pulmonary embolism is developed after completion of anticoagulation) or breakthrough PE (pulmonary embolism developing while under anticoagulation)
- Patients diagnosed with CTPA acquisition phase incompatibility and movement artifacts, and/or those in whom measurement of heart chambers, evaluation of inferior vena cava (IVC) reflux, and interventricular septum (IVS) morphology was not possible.

Computed Tomographic Pulmonary Angiography Imaging Analysis and Determinants of Right Ventricle Dysfunction

All examinations were performed on 64-detector row (Toshiba Aquilion, Otawara, Japan) and 16-detector row (General Electric's Healthcare Bright Speed Delight, Milwaukee, USA; Siemens Somatom Sensation, Forchheim, Germany) computed tomography (CT) scanners. Computed tomographic pulmonary angiography evaluation of patients was performed by 2 radiologists (M.K. and A.G.Ç), each with more than 6 years of experience. Right ventricular and left ventricular measurements were done by evaluating the ventricle diameters in the standard axial view, measuring the maximal distance between the ventricular endocardium and the IVS, perpendicular to the long axis of the heart, and using the maximum dimensions for both ventricles which may be found at different levels. Measuring RV/LV ratio ≥ 1 was considered as RV dysfunction. Interventricular septum morphology was defined as normal (convex to the RV), flattened, or bent [convex to the left ventricle (LV)]. When contrast material was detected in the intrahepatic part of the IVC, contrast media reflux was recorded.

If at least one of the RV/LV ratios is ≥1, IVS flattening/bulging, or IVC contrast media reflux is present, it is considered as RVD.

Determinants of Right Ventricle Dysfunction on Transthoracic Echocardiography

Transthoracic echocardiography findings were defined as the enlarged RV, flattened IVS, RV hypo/akinesia, pulmonary arterial systolic pressure ≥40 mm Hg, or right heart thrombus.

Troponin T ≥ 0.3 ng/mL and/or brain natriuretic peptide >150 pg/mL are considered high cardiac biomarkers.

Right ventricular function and dilatation were assessed according to the recommendations of the American Society of Echocardiography.[12,13] The recommended echocardiographic views for the evaluation of the right ventricular size and systolic function were the standard apical 4-chamber view and the apical 4-chamber view with a focus on the RV view. For interpreting the RV dilatation, loading measures reflect the systolic function. The cavity size of RV relative to LV and the shape of the IVS suggest RV dilatation. For evaluating the contractility of RV, such as hypokinetic, we use the measurement of change in the area of the cavity.

Patent foramen ovale (PFO) was assessed by subcostal view and parasternal short-axis view by Doppler echocardiogram.

Final risk stratification of patients was done according to the current European Society of Cardiology (ESC) guidelines.[1] Echocardiography findings were used for risk stratification. Some patients didn't have cardiac enzymes. Thus, patients are classified as intermediate if there was RVD on echocardiography. If echo findings were normal, patients were classified as not applicable (NA).

Definition of Adverse Events

An adverse event was defined as death due to PE or the requirement of urgent reperfusion therapy. PE-related death is defined according to International Society on Thrombosisnand Haemostasis (ISTH) recommendations.[14]

Statistical Analysis

Data were analyzed using SPSS 22.0 software (Chicago, Ill, USA). Demographic and clinical data are expressed as means with standard deviations for continuous variables and as frequencies with percentages for categorical variables. Sensitivity, specificity, and positive and negative predictive values for predicting adverse outcomes were assessed for CTPA or TTE-derived adverse outcomes. Inter-rater agreement between CTPA and TTE was determined using Cohen's kappa coefficient statistic. The relationships between age, gender, having any comorbid disease, and findings of CTPA and TTE were assessed with binary logistic regression analyses. For the multiple analysis, the

HIGHLIGHTS

- Both transthoracic echocardiography and computed tomography pulmonary angiography are reliable methods in risk stratification of pulmonary embolism.
- Transthoracic echocardiography has a higher specificity. This may help to identify patients at high risk of decompensation.

possible factors identified with univariant analysis were further entered into the logistic regression analyses. Hosmer–Lemeshow goodness of fit statistics was used to assess model fit. The statistical significance level was expressed as $P < .001$ for all tests.

Informed consent was obtained from all individual participants included in the study. This study was performed in line with the principles of the Declaration of Helsinki. The study was approved by Local Ethics Committee number: 2023000589-1 (2023/589).

RESULTS

There were 299 patients. Among them, 41 were excluded (15 due to a previous history of PE, 13 due to the possibility of previous pulmonary hypertension, and 13 due to poor CTPA technique). Of the study population, 258 patients (52.3% female) with a mean age of 62.5 ± 16.3 met the inclusion criteria. All patients were hospitalized in the first few days of treatment.

Among the 258 patients, there were 70 (27.1%) low risk, 13 (5%) intermediate risk, 78 (30.2%) intermediate low risk, 72 (27.9%) intermediate high risk, and 8 (3.1%) high risk. In 17 (6.6%) patients, risk stratification was not applicable because eco findings were normal but patients didn't have cardiac enzyme results.

Right ventricular dysfunction was demonstrated in 65.9% (170) of CTPA and 55.8% (144) of TTE ($P < .001$). The main findings of CTPA and TTE are presented in Table 1. In 71.3% (n = 184) of patients, CTPA and TTE agreed on the presence or absence of RVD. Among the remaining 74 patients, 24 (9.3%) had normal CTPA but RVD on TTE, and 50 (19.3%) had normal TTE but CTPA demonstrated RVD (Table 2). There was a weak agreement between the 2 tests (Cohen's kappa = 0.404, $P < .001$).

As the RV/LV ratio is mostly used CT signs of right heart dysfunction in PE, we compared the TTE findings with the RV/LV ratio on CTPA. The agreement between RV dysfunction on TTE and increased RV/LV on CTPA was minimal (Cohen's kappa = 0.388, $P < .001$). In 40 patients, TTE showed RVD, but the RV/LV ratio was below 1.0 on CTPA (Table 3).

Overall, 8 patients had high-risk PE at presentation; both TTE and CTPA showed RVD in these patients.

There were 31 patients with RV hypokinesia on TTE. Among them, 27 had RVD on CTPA. There were 4 patients with intracardiac thrombus on TTE, and all of them had RVD on CTPA.

There were 96 (37.2%) patients with reflux in the IVC, and among them, 68 (70.8%) had RVD on TTE. Among the 96 patients with reflux in the IVC, 45 (54.2%) had increased cardiac biomarkers.

There were 10 patients with PFO, and all of them had increased estimated systolic pulmonary artery pressure. Thus, PFO might be due to increased pressure. Among these 10 patients, CTPA detected RVD in 8.

A total of 17 patients died. Among them, 3 died due to PE. The first patient was at high risk at presentation. The second presented with intermediate–high-risk PE but progressed to high risk and died during catheter-directed treatment. The last patient was admitted with intermediate–low-risk PE but died due to sudden cardiac arrest. Both TTE and CTPA revealed RVD in these 3 patients. Another 5 patients initially at intermediate risk required urgent reperfusion therapy. Both TTE and CTPA revealed RVD in these 5 patients. As a result, in 8 (4%) patients, adverse outcomes occurred.

To determine the effect of TTE and CTPA parameters on adverse outcomes, logistic regression analysis was performed and showed a significant association between the flattening/bulging of IVS on TTE and adverse outcomes (Table 4). Both modalities had high negative predictive values. However, TTE was more specific than CTPA (Table 5).

Table 1. Transthoracic Echocardiography and Computed Tomographic Pulmonary Angiography Findings

Transthoracic Echocardiography	**n (%)**
RV dilatation	75 (29.1)
Flattening/bulging of IVS	7 (2.7)
Hypokinesia	31 (12.0)
Intracardiac thrombus	4 (1.6)
PFO	10 (3.9)
Increased sPAP	136 (52.7)
Computed Tomography Pulmonary Angiography	**n (%)**
RV/LV ≥ 1	142 (55)
Flattening/bulging of IVS	120 (46.5)
IVC reflux	96 (37.2)

IVC, inferior vena cava; IVS, interventricular septum; PFO, patent foramen ovale; RV, right ventricle; sPAP, systolic pulmonary arterial pressure.

Table 2. Agreement Between Transthoracic Echocardiography and Computed Tomographic Pulmonary Angiography to Detect Right Ventricle Dysfunction

		RV Dysfunction on CTPA			Kappa Coefficient and *P*
		No	Yes	Agreement	
RV dysfunction on TTE	No	64	50	52.6%	κ = 0.404, <.001
	Yes	24	120	83.3%	

CTPA, computed tomography pulmonary angiography; RV, right ventricle; TTE, transthoracic echocardiography.

Table 3. Agreement Between Right Ventricle Dysfunction on Transthoracic Echocardiography and Right Ventricle/Left Ventricle > 1 on Computed Tomography Pulmonary Angiography

		RV/LV > 1 on CTPA			Kappa Coefficient and *P*
		No	Yes	Agreement	
RV Dysfunction on TTE	No	76	38	66.7%	κ = 0.388, <0.001
	Yes	40	104	72.2%	

RV, right ventricle; TTE, transthoracic echocardiography; CTPA, computed tomography pulmonary angiography

Table 4. Binary Logistic Regression Analyses Between Composite Outcome and Findings Related to Right Ventricle Dysfunction

	Univariate Analysis		Multiple Analysis	
	OR (95% CI)	*P*	OR (95% CI)	*P*
Age	0.994 (0.953-1.037)	.798		
Gender (male)	1.864 (0.436-7.970)	.401		
Increased cardiac biomarker	1.104 (0.713-1.869)	.507		
RV dilatation on TTE	7.87 (1.551-39.931)	.013	1.683 (0.083-34.135)	.734
Flattening/bulging of IVS (TTE)	36.9 (6.482-210.06)	<.001	60.651 (3.038-1210.717)	.007
Hypokinesia	14.359 (3.243-63.575)	<.001	6.923 (0.880-54.479)	.066
Intracardiac thrombus	11.762 (1.084-127.671)	.043	0.137 (0.001-14.406)	.403
sPAP (mm Hg)	1.068 (1.023-1.115)	.003	1.070 (0.980-1.169)	.131
Flattening/bulging of IVS (CTPA)	3.579 (0.709-18.076)	.123	0.992 (0.140-7.025)	.994
IVC reflux	1.808 (0.358-9.140)	.474	4.842 (0.541-43.348)	.158

CTPA, computed tomography pulmonary angiography; IVC, inferior vena cava; IVS, interventricular septum; OR, odds ratio; RV, right ventricle; sPAP, systolic pulmonary arterial pressure; TTE, transthoracic echocardiography.

Table 5. Performance of Computed Tomography Pulmonary Angiography and Transthoracic Echocardiography on Prediction of Adverse Outcomes

	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
RV dysfunction on TTE	100%	43%	93%	100%
RV dysfunction on CTPA	100%	28%	94%	100%

CTPA, computed tomography pulmonary angiography; TTE, transthoracic echocardiography.

DISCUSSION

In this study, we aimed to compare the accuracy of CTPA with TTE in the identification of RVD. We found that CTPA was more sensitive and less specific compared to TTE in the identification of RVD and adverse outcomes.

There are a few studies that compare the correlation between CTPA and TTE. In the prospective study by Dudzinski et al,[15] CT findings of RV strain were defined as RV/LV ≥0.9 or interventricular bowing. Two modalities agreed in 59% of patients (κ = 0.24). Computed tomography was more sensitive but less specific compared to TTE. Park et al[16] compared the hypokinesia on TTE with RV/LV ≥1, septal bowing, and embolus location on CTPA. The combination of CTPA parameters increased the specificity and sensitivity of CTPA. Wake et al[17] found a moderate correlation between CTPA-derived RV/LV ratio and RV size determined with TTE. The sensitivity of CTPA was higher. Right ventricle was enlarged in 39% of TTE, and 48.6% of patients had RV/LV >1 on CTPA. Contrary to these studies, Ammari et al[18] found similar proportions of patients with RV/LV >1 and a statistically significant correlation between TTE and CTPA. Also, in our study, CTPA was more sensitive compared to TTE. Right ventricular dysfunction was detected in 65.9% (170) of CTPA and 55.8% (144) of TTE ($P < .001$). Also, in patients with increased cardiac biomarkers, CTPA detected more RVD compared to TTE (93.3% vs. 81.3%). The higher sensitivity of CTPA might be due to the timing of TTE. Patients received anticoagulation and oxygen supplementation, if necessary, before TTE, and during this time, cardiac functions might have been normalized.

In the present study, there was a fair correlation between the RV/LV ratio on CTPA and TTE findings (Cohen's kappa = 0.388). In 40 patients, despite the RVD findings on TTE, the RV/LV ratio was below 1 on CTPA. But when the RV/LV ratio was combined with other CTPA parameters, flattening/bulging of IVS, Vena Cava Inferior (VCI) reflux agreement with TTE, and the sensitivity of CTPA increased. This was also reported by Park et al.[13] The authors found that the combination of RV/LV ratio with septal bowing and embolus location resulted in sensitivity and specificity. These results show the importance of the holistic assessment of CTPA findings. A combination of CTPA parameters increases the sensitivity and specificity compared to individual RV/LV ratios.

The main limitation of CTPA is its inability to detect intracardiac thrombus and RV hypokinesia. In our cohort, there was 1 patient with intracardiac thrombus on TTE, and even though CTPA did not recognize intracardiac thrombus, it detected RVD in all this patient. There were 25 patients with RV hypokinesia on TTE. Computed tomography pulmonary angiography showed RVD in 22 of these 25 (88%) patients. Although the remaining 3 patients with RV hypokinesia did not experience any adverse outcome, we think this is an important inferiority of CTPA in patients with a plan of early discharge.

In our study, adverse outcomes occurred in 8 (4%) patients. Despite the high number of RVD on TTE or CTPA, there was a relatively low rate of adverse outcomes. Also, in the previous studies, RVD was a common finding, but the rate of an adverse outcome was low.[8,15,18-20] There are some possible other explanations. First, this may be due to the compensatory mechanism of the heart. Second, it might be due to an improved detection and effective treatment of patients with RVD. As Barco et al[21] reported, pulmonary embolism-related mortality is decreasing in the European region, and one of the possible explanations is improved treatment. Third, as Hadad et al[22] stated, maybe the increased RV/LV ratio is due to the patient's baseline conditions rather than a cardiac response to PE. High rates of RVD on CTPA or TTE may cause the utilization of additional tests such as cardiac biomarkers and possibly longer hospitalization. On the other hand, these precautions might provide increased safety for patients and minimize the possibility of post-discharge mortality or early complications.

No individual CTPA parameter was related to adverse outcomes. Although univariate analysis showed a significant association between RV hypokinesia and adverse outcomes, in multiple analysis, this association lost its significance. Transthoracic echocardiography had a higher specificity compared to CTPA in our study. Statistically, TTE flattening/bulging of IVS on TTE was significantly associated with adverse outcomes. Some previous studies also showed higher specificity of TTE.[13,14,17] This means the ability of TTE to detect patients at imminent risk of hemodynamical decompensation is higher compared to CTPA. Thus, TTE might be more accurate in the selection of appropriate management, such as reperfusion therapy or intensive care unit admission, especially in intermediate high-risk pulmonary embolism.

Reflux in the IVC is a sign of right-sided heart disease[23,24] and has previously been shown as a predictor of mortality.[25-27] Thus, we thought that reflux in the IVC might be a more specific parameter for the determination of RVD with CTPA. However, there was no significant association between IVC reflux and adverse outcomes.

Study Limitations

There are several limitations of our study. First is the performance of TTE by different operators on duty. Second, some echocardiographic parameters such as tricuspid annular plane systolic excursion (TAPSE) were missing. Third, sPAP rather than the velocity of tricuspid regurgitation (TRV) was reported for assessment of RV pressure overload. Thus, we had to define a cutoff for sPAP. According to the Bernoulli equation ($4 \times TRV^2$ + right atrial pressure), 40 mm Hg sPAP corresponds approximately to the TRV 2.8 m/s as recommended by ESC pulmonary hypertension guidelines.[28] So, we accepted 40 mm Hg as a cutoff. However, we are aware that this cutoff is open to debate.

CONCLUSION

Both CTPA and TTE have high sensitivity in the detection of RVD. A combination of CTPA parameters rather than individual RV/LV ratios increases the reliability of CTPA. Transthoracic echocardiography is more specific, and this may help in the identification and appropriate management of patients at higher risk of decompensation.

Ethics Committee Approval: The study was approved by the Ankara University Ethics Committee No: 2023000589-1 (2023/589). This study was performed in line with the principles of the Declaration of Helsinki.

Informed Consent: Informed consent was obtained from all individual participants included in the study.

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