EURASIAN JOURNAL OF EMERGENCY MEDICINE
Original Article
DOI: 10.4274/eajem.galenos.2024.59320
Eurasian J Emerg Med.

Role of Cardiac Biomarkers and Tomographic Right Ventricular Dysfunction Findings in the Treatment of Pulmonary Thromboembolism

Maşide Arı[1], Zeycan Kübra Cevval[2], Eren Usul[3], Emrah Arı[4], Uğur Kahveci[5]

[1]Atatürk Sanatorium Training and Research Hospital, Clinic of Pulmonology, Ankara, Turkey
[2]Kastamonu Training and Research Hospital, Clinic of Radiology, Kastamonu, Turkey
[3]Etlik City Hospital, Clinic of Emergency Medicine, Ankara, Turkey
[4]Mamak Public Hospital, Clinic of Emergency Medicine, Ankara, Turkey
[5]Eskişehir City Hospital, Clinic of Emergency Medicine, Eskişehir, Turkey

Abstract

Aim: Deaths from acute pulmonary thromboembolism are caused by right ventricular dysfunction (RVD) and often occur within the first hour. Diagnostic computed tomography-pulmonary angiography (CTPA) is a useful tool for the early and rapid evaluation of RVD. We aimed to evaluate the effect of RVD findings on risk classification and treatment.

Materials and Methods: This retrospective study included patients who applied to the emergency department on specified dates and were diagnosed with pulmonary thromboembolism. The right ventricle (RV) and left ventricle (LV) diameters (mm), ratio of these diameters RV/LV, pulmonary artery and aortic diameter (mm), troponin, and BNP were evaluated.

Results: A total of 119 patients were studied. The average age of the participants was 63.3 years. The mortality rate was 12.6%. Reperfusion therapy was applied to 25 (21%) patients. RV/LV was superior for predicting thrombolytic therapy. N-terminal proBNP (NT-proBNP) was more significant than troponin. When both parameters were evaluated together, the result was superior in predicting reperfusion therapy in patients with RVD.

Conclusion: CTPA can be used safely to determine the risk group and for treatment with its high sensitivity. NT-proBNP is an important biomarker for determining thrombolytic treatment, and its diagnostic specificity increases when evaluated together with RV/LV.

Keywords: BNP, pulmonary embolism, reperfusion therapy, RV/LV, pulmonary artery diameter, troponin

Introduction

Pulmonary thromboembolism (PTE), which develops as a result of varying degrees of occlusion of the pulmonary arteries caused by any material originating from another body part, is a cardiovascular emergency that can be fatal. Despite treatment optimization, all-cause mortality in the first 30 days is between 3-12%. Early mortality in high-risk PTE can reach 50% (1). Right ventricular dysfunction (RVD) is the most important cause of adverse clinical outcomes in PTE (2). Therefore, early detection of RVD in patients who may require more aggressive treatment, such as systemic reperfusion, is the primary prognostic step. Echocardiography is frequently used to evaluate RVD in acute pulmonary thromboembolism (APTE) (3). However, the role of parameters obtained from computerized tomography-pulmonary angiography (CTPA) in predicting adverse outcomes and early mortality in patients with APTE has recently been evaluated (4). One of the most frequently evaluated parameters, the ratio of right ventricle to left ventricle (RV/LV), has been reported to correlate with the severity of the disease (5). An RV/LV >1 has been shown to be associated with increased in-hospital mortality and intensive care admission rates (6). In a recent study, it was

Corresponding Author: Maşide Arı MD, Atatürk Sanatorium Training and Research Hospital, Clinic of Pulmonology, Ankara, Turkey
Phone: +90 534 542 21 73 **E-mail:** masidetuten@icloud.com **ORCID ID:** orcid.org/0000-0002-5078-3176

Cite this article as: Arı M, Cevval ZK, Usul E, Arı E, Kahveci U. Role of Cardiac Biomarkers and Tomographic Right Ventricular Dysfunction Findings in the Treatment of Pulmonary Thromboembolism. Eurasian J Emerg Med. .

Received: 26.05.2024
Accepted: 18.09.2024

reported that the ratio of the pulmonary artery diameter to aortic diameter (PAD/AOD) is a useful tool for identifying high-risk patients and can be used for risk classification (7).

Most PTE mortality prediction models require RVD measurement and/or myocardial biomarkers. Troponin and natriuretic peptides are used for this purpose. Increased cardiac biomarkers are adverse prognostic factors (8,9).

In acute PTE, deaths often occur within the first hour, and RVD caused by thrombi is the main cause of mortality. Therefore, patients with dysfunction should be identified early. This study was designed to evaluate the role of cardiac biomarkers in treatment management with RVD findings measured using CTPA, which is considered the gold standard for diagnosis, as well as all these advantages, such as obtaining easily accessible, rapid results in risk classification, and not relying on the experience of the practicing physician.

Materials and Methods

This Study

This retrospective, single-center study included patients who applied to Dışkapı Yıldırım Beyazıt Training and Research Hospital emergency department and were diagnosed with PTE.

Ankara Etlik City Hospital Clinical Research Ethics Committee (decision number: AESH-EK1-2023-441, date: 31.08.2023), and it was conducted following the ethical principles determined by the Declaration of Helsinki.

Patients were classified into low, intermediate-low, intermediate-high, and high risk groups in terms of early death according to the European Society of Cardiology (ESC) guidelines. The demographic characteristics, comorbidities, vital signs, chest radiography, computed tomography (CT) angiography, laboratory values and medical treatments of the patients were studied.

Patients with APTE were included in the study. Patients under the age of 18 years, pregnant women, those with decompensated congestive heart failure, those with contraindications to thrombolytic therapy, those with previous pulmonary hypertension, those with advanced chronic obstructive pulmonary disease, those with advanced interstitial lung disease, those with chronic thrombi, and those with missing data were excluded from the study.

Radiological Measurements

All images in this study were obtained using a 128-segment multi-detector CT device with the standard CTPA protocol created for the diagnosis of pulmonary embolism (detector width 40 mm, slice thickness 0.625 mm, rotation time 0.4 seconds, 120 kVp and 380 mAs). During BTPA recording, 100 mL of contrast material was administered at a rate of 5 mL/s. In CTPA, parameters such as RV and LV diameters (mm), the ratio of these diameters to each other (RV/LV), main PAD (mm), and ascending AOD were measured. RV and LV diameter measurements were made in axial sections from the distances between the septum endocardium and ventricle lateral wall endocardium, just below the atrioventricular valve, and were rated to each other (Figure 1). As a result of the ROC analysis, the cutoff value for RV/LV was 1.01, and a value >1.01 was defined as dysfunction. Pulmonary artery measurements were obtained from the axial section in the mediastinal window immediately before pulmonary bifurcation, and the diameters of the ascending aorta at the same level were measured obliquely in millimeters and rated to each other (Figure 2). As a result of the ROC analysis, the cutoff value for the PAD was determined to be 28.05 mm, and a value above this value was defined as an increase in pulmonary vascular resistance (PVR).

Statistical Analysis

The statistical analysis of the data obtained was performed using the IBM SPSS 27.0 Statistical Package program. The suitability of the variables for normal distribution was examined using visual analytical methods (Shapiro-Wilk test). Descriptive statistics were expressed as mean and standard deviation in normally distributed numerical data, median and minimum-maximum range in non-normally distributed data, and number and percentage in nominal data. We analyzed normally distributed numerical variables using the "t-test in independent groups" for two groups and 'ANOVA' for three groups. Numerical variables that did not show normal

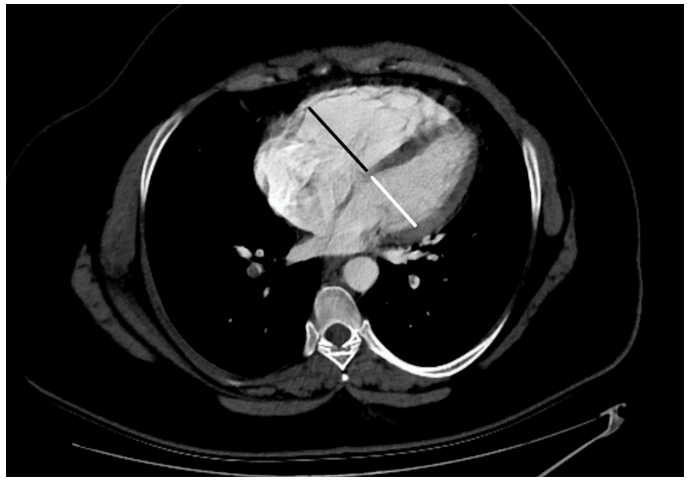

Figure 1. In computed tomography-pulmonary angiography, right ventricular diameter (black line) and left ventricular diameter (white line) are measured in the axial section in the mediastinal window, and it is noteworthy that the right ventricular diameter has increased significantly and the interventricular septum has flattened

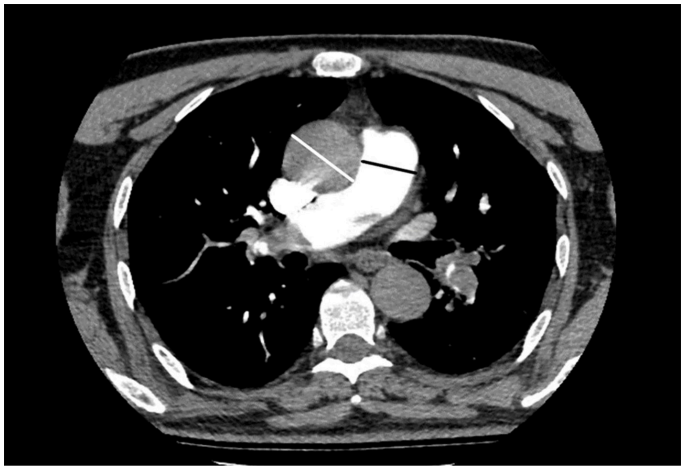

Figure 2. Computed tomography-pulmonary angiography axial section shows ascending aorta diameter (white line) and pulmonary artery diameter (black line) measurements in the mediastinal window. Embolism is observed in the right pulmonary artery and left lobar arteries

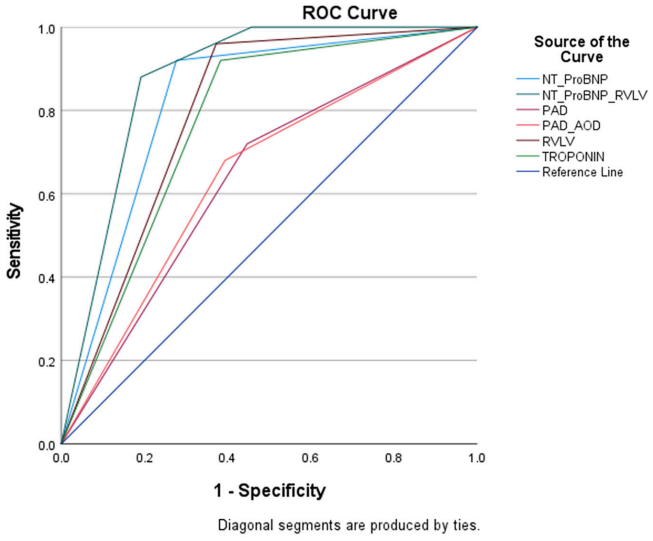

Figure 3. ROC curve in reperfusion therapy prediction

ROC: Receiver operating characteristic, NT-proBNP: N-terminal proBNP, RVLV: Right ventricle/Left ventricle, PAD: Pulmonary artery diameter, AOD: Aortic diameter

distribution were analyzed using the "Mann Whitney U test" between two groups and the "Kruskal Walls test" between three groups. Intra-group analyses were evaluated using the "paired t-test" for those with normal distribution. Nominal data were evaluated between the two groups using the "Pearson chi-square test" or "Fisher's exact test". To determine the factors affecting the prediction of reperfusion treatment, the area under the curve (AUC) was evaluated in the ROC curve analysis, and the data were expressed with a 95% confidence interval (CI). The correlation of normally distributed numerical variables was analyzed with the "Pearson's correlation test", and non-normally distributed numerical variables were analyzed with the "Spearman's correlation test". Comparisons with a p-value 0.05 were considered statistically significant.

Results

One hundred and nineteen patients were included in the study. The average age of the patients was 63. Sixty-five (54.4%), and the patients included in the study were women. When the thrombus burden of the patients included in the study was evaluated radiologically, 64.7% of the patients had non-massive PTE and 35.3% had massive PTE.

When the demographic characteristics and clinical findings of the patients included in the study were evaluated according to the ventricular diameter ratio, RVD was observed more frequently in elderly patients (p=0.011). Acquired risk factors and comorbid diseases were observed to be more common in patients with RVD findings (p=0.037; p=0.01). It was observed that patients with RVD presented with syncope more often (p=0.006).

When the vital signs of the patients included in the study were evaluated according to the ratio of their ventricular diameters, systolic and diastolic blood pressures were found to be significantly lower in patients with an RV/LV of 1.01 and above. The respiratory rate was significantly higher in patients with a higher RV/LV (p=0.006). Saturation was significantly lower in this patient group (p<0.001) (Table 1).

Twenty-eight (23.5%) patients were in the high-risk group, 17 (14.3%) were in the intermediate-high-risk group, 36 (30.3%) were in the intermediate-low-risk group, and 38 (31.9%) were in the low-risk group.

The PAD and AOD of the patients included in the study were rated, and the average was 0.86. Patients were divided into two groups: above and below the median. Among the risk groups, no significant difference was observed between the groups (p=0.312) (Table 2).

Twenty-five (21%) patients included in the study required thrombolytic treatment. When these patients were grouped according to their ventricular diameter, RV/LV was >1.01 (p<0.001) in 96% of the patients who received thrombolytic therapy (Table 3). When the pulmonary artery diameters were compared, a significant difference was found between the groups (p=0.004) (Table 3). Additionally, when evaluated according to the ratio of pulmonary artery to AOD, a significant difference was observed between the groups (p=0.01) (Table 3).

Table 1. Evaluation of patient admission vitals				
Vital signs	**All patients (n=119) Mean ± SD**	**RV/LV<1.01 (n=58) Mean ± SD**	**RV/LV>1.01 (n=61) Mean ± SD**	**p value**
Systolic blood pressure (mm/Hg)	114±21	122±19	106±21	**<0.001**
Diastolic blood pressure (mm/Hg)	69±12	72±10	65±15	**0.010**
Pulse (beats/min)	98±19	94±15	102±21	0.058
Respiratory rate	21±7	20±9	22±4	**0.006**
Saturation	87±7	90±7	84±7	**<0.001**
SD: Standard deviation, RV: Right ventricle, LV: Left ventricle				

Table 2. Distribution of patients in risk groups according to RV/LV and PAD/AOD ratios					
Early mortality risk classification	**Low risk (n=38)**	**Intermediate-low risk (n=36)**	**Intermediate-high risk (n=17)**	**High risk (n=28)**	**p value***
RV/LV>1.01 (n=61)	5 (13.2%)	15 (41.7%)	14 (82.4%)	27 (96.4%)	**<0.001**
PAD/AOD>0.86 (n=54)	17 (44.7%)	12 (33.3%)	10 (58.8%)	15 (53.6%)	0.312
*The test was evaluated using the Kruskal-Wallis test, RV: Right ventricle, LV: Left ventricle, AOD: Aortic diameter, PAD: Pulmonary artery diameter					

Table 3. Evaluation of CTPA findings and cardiac biomarkers according to reperfusion status			
	Patients who require reperfusion therapy	**Patients who do not need reperfusion therapy**	**p value**
RV/LV>1.01	24 (96%)	1 (4%)	**<0.001**
PAD/AOD>0.86	17 (68%)	8 (32%)	**0.01**
Pulmonary arter diameter (mm)	31.42±4.24	28.39±4.38	**0.004**
Troponin elevation	23 (92%)	2 (8%)	**<0.001**
Nt-proBNP	3429± 2730	997±780	**<0.001**
CTPA: Computed tomography-pulmonary angiography, RV: Right ventricle, LV: Left ventricle, PAD: Pulmonary artery diameter, AOD: Aortic diameter, Nt-proBNP: N-terminal proBNP			

Among the CTPA findings, RV/LV, PAD, and PAD/AOD were identified as determinants of the need for thrombolytic treatment (Table 4).

When the reperfusion therapy status of the patients included in the study was evaluated according to cardiac biomarkers, troponin and N-terminal proBNP (NT-proBNP) were found to be determinative (Table 4).

When NT-proBNP and RV/LV were evaluated together, they were found to be predictive of the need for thrombolytic treatment with 88% sensitivity and 80.9% specificity (AUC: 0.877, 95% CI 0.815-0.939, p<0.00) (Figure 3). In determining thrombolytic treatment, combining these parameters was superior to separately evaluating them.

Discussion

PTE encompasses a wide spectrum, ranging from asymptomatic to life-threatening shock (10). In acute PTE, deaths frequently occur within the first hour, with RVD caused by the thrombus being the primary cause of mortality. Therefore, early identification of patients with dysfunction is crucial. CTPA has become an effective tool not only for diagnosing acute PTE but also for developing therapeutic strategies and risk classification (11). In our study, CTPA, which provides rapid diagnostic results, was a significant tool in determining the risk of PTE.

In the evaluation of RVD in acute PTE, echocardiography or CTPA can be performed. Particularly in patients with obesity or chronic lung disease, visualizing the RV free wall via echocardiography may be challenging. Additionally, rapid access to echocardiography may not always be feasible. For this reason, the ratio of RV/LV measured on CTPA has become a parameter used to assess RVD (12). The RV/LV ratio can also be used in therapeutic strategies and risk classification (13). A study by Ammari et al. (14) demonstrated a strong correlation between RVD measured on CTPA and echocardiographic parameters, with similar specificity in predicting 30-day mortality risk. In our study, the RV/LV ratio was an important tool in determining mortality risk.

APTE can present as a clinical spectrum ranging from asymptomatic to hemodynamic instability and sudden death (15). Therefore, the greatest challenge in managing APTE is the rapid and accurate classification of prognosis. Since 2014, the risk classification of APTE has been based on the patient's hemodynamic status (1). Hemodynamically unstable patients are

Table 4. Evaluation of parameters for predicting patients' needs for reperfusion therapy

	AUC	95% Confidence interval	Sensitivity	Specificity	PPV	NPV	LR+	LR-	p value
Troponin positivity	0.769	0.676-0.861	92	61.7	39	96.7	2.40	0.24	<0.001
NT-proBNP>665 pg/ml	0.822	0.737-0.907	93	72.3	46.9	97.1	3.35	0.25	<0.001
RV/LV and NT-proBNP	0.877	0.815-0.939	88	80.9	55	97.4	4.60	0.14	<0.001
PAD>28.05mm	0.637	0.517-0.756	72	55.3	30	88	1.61	0.50	0.016
PAD/AOD>0.86	0.643	0.522-0.764	68	63.8	31.5	87.7	1.87	0.50	<0.001

AUC: Area under the curve, PPV: Positive predictive value, NPV: Negative predictive value, R+: Likelihood ratio +, LR-: Likelihood ratio -, NT-proBNP: N-terminal-proBNP, RV: Right ventricle, LV: Left ventricle, PAD: Pulmonary artery diameter, AOD: Aortic diameter

immediately classified into the high-risk group, and reperfusion therapy is recommended regardless of other risk markers. Our study showed that patients with a higher RV/LV ratio had a lower mean arterial pressure. Among patients who received systemic reperfusion therapy, 96% had an RV/LV ratio >1.01. This suggests that the RV/LV ratio is also an important parameter for determining the appropriate treatment approach.

In patients with PTE who do not present with hypotension or shock, further risk assessment should be performed after diagnosis. This risk assessment combines the pulmonary embolism severity index (PESI) or simplified pulmonary embolism severity index (sPESI) scores with RVD cardiac biomarkers (1). In our study, patients were grouped based on their early mortality risk according to the ESC guidelines, and when comparing their RV/LV ratios, 96% of high-risk patients had an RV/LV ratio >1.01. A significant difference was observed between the risk groups. The RV/LV ratio, which can be easily calculated using a single parameter, can also be used as an indicator for determining patient risk.

In acute PTE, direct mechanical obstruction caused by clot burden leads to increased. Additionally, an increase in vasoactive mediators (such as thromboxane A2) elevates PVR (16). On CTPA, PVR is a well-defined and straightforward measurement used to detect pulmonary hypertension (17). A study by O'Corragain et al. (18) demonstrated that the PAD correlates with echocardiographic parameters and can be used to assess RVD. In our study, an increase in PVR was defined as a PAD of 28.05 mm or greater. In the intermediate-high and high-risk groups, PAD was higher than that in the other groups. Additionally, PAD was higher in patients who received reperfusion therapy. PAD is a key parameter that can be used in the assessment of RVD and in guiding treatment management.

In a study conducted by Schneider et al. (19), the ratio of PAD/AOD was identified as a marker that can be used in the diagnosis of pulmonary hypertension, emphasizing that it should be assessed in all patients suspected of having pulmonary hypertension. In a study by Gašparović et al. (20), PAD/AOD was evaluated in patients with advanced COPD, and it was noted that this ratio had high specificity and was an independent predictor of pulmonary hypertension. Cheng et al. (21) found that an increase in the PAD was associated with treatment failure in patients hospitalized for COPD exacerbations. A recent study indicated that an elevated PAD/AOD ratio is associated with PTE and may be linked to the development of chronic thromboembolic pulmonary hypertension (22). In a study assessing risk factors associated with mortality in acute PTE, increased PVR was found to be correlated with adverse outcomes (23). Another recent study suggested that the PAD/AOD ratio is a useful tool for identifying high-risk patients and could be employed for risk classification (7). In our study, when patients were evaluated according to their risk groups, no significant difference was observed in the PAD/AOD ratio. However, both the PAD and the PAD/AOD ratio were shown to be predictive parameters for systemic reperfusion therapy.

In PTE, a rapid increase in RV afterload leads to an increase in wall tension. The reduction in lung perfusion results in decreased oxygen delivery, but the oxygen demand in the ventricular muscle rises, leading to ischemia and ultimately causing troponin release (24). High cardiac troponin levels are observed in 30-60% of patients with acute PTE. An increase in troponin levels is an adverse prognostic factor of acute PTE (25). In patients without hypotension, elevated troponin levels are associated with an early mortality (26). It has been shown that combining troponin levels with clinical scores (PESI or sPESI) improves the prognostic classification of patients with PTE (27). In our study, 96% of patients who underwent reperfusion therapy had elevated troponin levels. The increase in troponin levels was found to be a predictive factor for thrombolytic therapy requirement.

An increase in RV afterload in APTE induces RV dilation, leading to the release of brain natriuretic peptide and its precursor, NT-proBNP. In 2003, the first study was published showing that elevated NT-proBNP levels are associated with an increased risk of PTE-specific mortality or adverse outcomes (28). In a study by Chen et al. (29), NT-proBNP was found to be a highly sensitive

marker for detecting RV dysfunction and predicting mortality, with significantly lower mortality observed when NT-proBNP levels were low. In our study, NT-proBNP levels were higher in patients who received reperfusion therapy and were determined to be a key predictor of thrombolytic therapy. Compared with the other parameters, NT-proBNP level and the RV/LV ratio showed high sensitivity and negative predictive value in determining the need for reperfusion therapy.

Most mortality prediction models for PTE require assessment of RVD and/or measurement of myocardial biomarkers. The combination of RVD and biomarkers is recommended for predicting early mortality (1). In a study by Santos et al. (30) evaluating treatment management in PTE, the cumulative presence of cardiac biomarkers and imaging findings of should be considered. Particularly in normotensive patients, the combined assessment of NT-proBNP, troponin, and CT parameters can improve diagnostic accuracy and prevent delayed treatment (31). In our study, the combined use of NT-proBNP and the RV/LV ratio was superior to that of other markers or their individual use. It is recommended that both parameters be used together to identify patients with acute PTE who may require more aggressive treatment.

Study Limitations

There are some limitations in our study. Due to changes in the hospital information management system, not all radiological images could be accessed. Therefore, the number of patients in the study was limited. Another limitation is that this study was conducted in a single center; supporting it with multicenter studies will increase the value of our study.

Conclusion

In APTE, a significant cause of cardiovascular mortality, CTPA is a readily accessible imaging method that is unaffected by patient compliance or the clinician's experience. With these advantages, CTPA can be reliably used for risk classification and treatment management. NT-proBNP is an important biomarker for determining the need for thrombolytic therapy, and when evaluated together with the RV/LV ratio, its specificity increases. Therefore, it should be used together in the identification and treatment management of patients who may be mortal due to RVD.

Footnote

Ethical Committee Approval: Ankara Etlik City Hospital Clinical Research Ethics Committee (decision number: AESH-EK1-2023-441, date: 31.08.2023), and it was conducted following the ethical principles determined by the Declaration of Helsinki.

Informed Consent: Retrospective study.

Authorship Contributions

Surgical and Medical Practices: M.A., Z.K.C., Concept: M.A., E.A., Design: M.A., E.A., Data Collection or Processing: Z.K.C., E.U., E.A., U.K., M.A., Analysis or Interpretation: E.A., U.K., Literature Search: E.U., E.A.,Writing: M.A., Z.K.C., E.U.

Conflict of Interest: The authors declare that they have no conflict of interest.

Financial Disclosure: There are no financial conflicts of interest to disclose.

References

1. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing GJ, Harjola VP, et al. 2019 ESC Guidelines for the diagnosis and management of acute pulmonary embolism developed in collaboration with the European Respiratory Society (ERS). Eur Heart J. 2020;41:543-603.
2. Prosperi-Porta G, Ronksley P, Kiamanesh O, Solverson K, Motazedian P, Weatherald J. Prognostic value of echocardiography-derived right ventricular dysfunction in haemodynamically stable pulmonary embolism: a systematic review and meta-analysis. Eur Respir Rev. 2022;31:220120.
3. Oh JK, Park JH. Role of echocardiography in acute pulmonary embolism. Korean J Intern Med. 2023;38:456-70.
4. Enea I. Usefulness of an imaging tool on CT pulmonary angiography in the prognostic stratification of patients with acute pulmonary embolism. Int J Cardiol. 2021;340:94-5.
5. Miyagawa M, Okumura Y, Fukamachi D, Fukuda I, Nakamura M, Yamada N, et al. Clinical Implication of the Right Ventricular/Left Ventricular Diameter Ratio in Patients with Pulmonary Thromboembolism. Int Heart J. 2022;63:255-63.
6. Cho SU, Cho YD, Choi SH, Yoon YH, Park JH, Park SJ, et al. Assessing the severity of pulmonary embolism among patients in the emergency department: Utility of RV/LV diameter ratio. PLoS One. 2020;15:e0242340.
7. Marginean A, Putnam A, Hirai T, Serritella A, Besser SA, Lee M, et al. Performance of the right ventricular outflow tract/aortic diameter as a novel predictor of risk in patients with acute pulmonary embolism. J Thromb Thrombolysis. 2020;50:165-73.
8. Elshahaat HA, Zayed NE, Ateya MA, Safwat M, El Hawary AT, Abozaid MN. Role of serum biomarkers in predicting management strategies for acute pulmonary embolism. Heliyon. 2023;9:e21068.
9. Klok FA, Mos IC, Huisman MV. Brain-type natriuretic peptide levels in the prediction of adverse outcome in patients with pulmonary embolism: a systematic review and meta-analysis. Am J Respir Crit Care Med. 2008;178:425-30.
10. Emektar E, Dağar S, Uzunosmanoğlu H, Çevik Y. Analysis of Patients with Pulmonary Thromboembolism Who Received Thrombolytic Therapy in The Emergency Department. Eurasian J Crit Care. 2021;3:87-91.
11. Zantonelli G, Cozzi D, Bindi A, Cavigli E, Moroni C, Luvarà S, et al. Acute Pulmonary Embolism: Prognostic Role of Computed Tomography Pulmonary Angiography (CTPA). Tomography. 2022;8:529-39.
12. Osman AM, Abdeldayem EH. Value of CT pulmonary angiography to predict short-term outcome in patient with pulmonary embolism. Int J Cardiovasc Imaging. 2018;34:975-83.
13. Cozzi D, Moroni C, Cavigli E, Bindi A, Caviglioli C, Nazerian P, et al. Prognostic value of CT pulmonary angiography parameters in acute pulmonary embolism. Radiol Med. 2021;126:1030-6.

14. Ammari Z, Hasnie AA, Ruzieh M, Dasa O, Al-Sarie M, Shastri P, et al. Prognostic Value of Computed Tomography Versus Echocardiography Derived Right to Left Ventricular Diameter Ratio in Acute Pulmonary Embolism. Am J Med Sci. 2021;361:445-50.

15. Attems J, Arbes S, Böhm G, Böhmer F, Lintner F. The clinical diagnostic accuracy rate regarding the immediate cause of death in a hospitalized geriatric population; an autopsy study of 1594 patients. Wien Med Wochenschr. 2004;154:159-62.

16. Smulders YM. Pathophysiology and treatment of haemodynamic instability in acute pulmonary embolism: the pivotal role of pulmonary vasoconstriction. Cardiovasc Res. 2000;48:23-33.

17. Shen Y, Wan C, Tian P, Wu Y, Li X, Yang T, et al. CT- base pulmonary artery measurement in the detection of pulmonary hypertension: a meta-analysis and systematic review. Medicine (Baltimore). 2014;93:e256.

18. O'Corragain O, Alashram R, Millio G, Vanchiere C, Hwang JH, Kumaran M, et al. Pulmonary artery diameter correlates with echocardiographic parameters of right ventricular dysfunction in patients with acute pulmonary embolism. Lung India. 2023;40:306-11.

19. Schneider M, Ran H, Pistritto AM, Gerges C, Heidari H, Nitsche C, et al. Pulmonary artery to ascending aorta ratio by echocardiography: A strong predictor for presence and severity of pulmonary hypertension. PLoS One. 2020;15:e0235716.

20. Gašparović K, Pavliša G, Hrabak Paar M, Brestovac M, Lovrić Benčić M, Šeparović Hanževački J, et al. Diagnostic accuracy, sensitivity, and specificity of CT pulmonary artery to aorta diameter ratio in screening for pulmonary hypertension in end-stage COPD patients. Croat Med J. 2021;62:446-55.

21. Cheng Y, Li L, Tu X, Pei R. The Main Pulmonary Artery to the Ascending Aorta Diameter Ratio (PA/A) as a Predictor of Worse Outcomes in Hospitalized Patients with AECOPD. Int J Chron Obstruct Pulmon Dis. 2022;17:1157-65.

22. Silov G, Ayan A. Pulmonary Artery Diameter Measurement and Semiquantitative Visual Scoring with Q-SPECT-CT in Acute Pulmonary Embolism. J Coll Physicians Surg Pak. 2023;33:1229-34.

23. Lyhne MD, Schultz JG, MacMahon PJ, Haddad F, Kalra M, Tso DM, et al. Septal bowing and pulmonary artery diameter on computed tomography pulmonary angiography are associated with short-term outcomes in patients with acute pulmonary embolism. Emerg Radiol. 2019;26:623-30.

24. Meyer T, Binder L, Hruska N, Luthe H, Buchwald AB. Cardiac troponin I elevation in acute pulmonary embolism is associated with right ventricular dysfunction. J Am Coll Cardiol. 2000;36:1632-6.

25. Janisset L, Castan M, Poenou G, Lachand R, Mismetti P, Viallon A, et al. Cardiac Biomarkers in Patients with Acute Pulmonary Embolism. Medicina (Kaunas). 2022;58:541.

26. Weekes AJ, Johnson AK, Troha D, Thacker G, Chanler-Berat J, Runyon M. Prognostic Value of Right Ventricular Dysfunction Markers for Serious Adverse Events in Acute Normotensive Pulmonary Embolism. J Emerg Med. 2017;52:137-50.

27. Lankeit M, Jiménez D, Kostrubiec M, Dellas C, Hasenfuss G, Pruszczyk P, et al. Predictive value of the high-sensitivity troponin T assay and the simplified Pulmonary Embolism Severity Index in hemodynamically stable patients with acute pulmonary embolism: a prospective validation study. Circulation. 2011;124:2716-24.

28. Pruszczyk P, Kostrubiec M, Bochowicz A, Styczyński G, Szulc M, Kurzyna M, et al. N-terminal pro-brain natriuretic peptide in patients with acute pulmonary embolism. Eur Respir J. 2003;22:649-53.

29. Chen YL, Wright C, Pietropaoli AP, Elbadawi A, Delehanty J, Barrus B, et al. Right ventricular dysfunction is superior and sufficient for risk stratification by a pulmonary embolism response team. J Thromb Thrombolysis. 2020;49:34-41.

30. Santos AR, Freitas P, Ferreira J, Oliveira A, Gonçalves M, Faria D, et al. Risk stratification in normotensive acute pulmonary embolism patients: focus on the intermediate-high risk subgroup. Eur Heart J Acute Cardiovasc Care. 2020;9:279-85.

31. Gao Y, Chen L, Jia D. A predictive tool for the assessment of right ventricular dysfunction in non-high-risk patients with acute pulmonary embolism. BMC Pulm Med. 2021;21:42.