ARTICLE ORIGINAL



Prognostic value of the echocardiographic ratio tricuspid annular plane systolic excursion/ Pulmonary arterial systolic pressure in acute pulmonary embolism

Valeur pronostique du rapport échocardiographique excursion systolique du plan de l'anneau tricuspide/ Pression artérielle pulmonaire systolique dans l'embolie pulmonaire aigue

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Abstract

Background: The occurrence of death from acute pulmonary embolism (PE) is often linked to right ventricular (RV) failure, arising from an imbalance between RV systolic function and heightened RV afterload. In our study, we posited that an echocardiographic ratio derived from this disparity [RV systolic function assessed by tricuspid annular plane systolic excursion (TAPSE) divided by pulmonary arterial systolic pressure (PASP)] could offer superior predictive value for adverse outcomes compared to individual measurements of TAPSE and PASP alone.

Methods: We conducted a retrospective analysis using data from a University Hospital Centre spanning from 2017 to 2023. All individuals with confirmed PE and a formal transthoracic echocardiogram within 7 days of diagnosis were included. The primary endpoint was a composite outcome of death, hemodynamic deterioration needing introduction of inotropes or thrombolysis within 30 days. Secondary endpoints included 6 months all-cause mortality and onset of right-sided heart failure.

Results: Thirty-eight patients were included. Mean age was 58 ±15 years old. A male predominance was noted: 23 male patients (60.5%) and 15 female patients (39.5%). Eight patients met the primary composite endpoint while nine patients met the secondary composite endpoint.

In multivariate analysis, the TAPSE/PASP ratio was independently associated with the primary outcome (OR=2.77, 95% CI 1.101–10.23, P=0.042). A TAPSE/PASP ratio <0.3 was independently associated with the secondary outcome (OR=3.07, 95% CI 1.185–10.18, P=0.034).

Conclusion: This study suggests that a combined echocardiographic ratio of RV function to afterload is effective in predicting adverse outcomes in acute PE.

Key words: Acute pulmonary embolism, echocardiography, right ventricular afterload, right ventricular function, outcome.

Résumé

Introduction: La survenue d'un décès par embolie pulmonaire (EP) aigue est souvent liée à une insuffisance ventriculaire droite, résultant d'un déséquilibre entre la fonction systolique du ventricule droit (VD) et une élévation de la postcharge du VD. Dans notre étude, nous avons postulé qu'un rapport échocardiographique dérivé de cette disparité [fonction systolique du VD évaluée par l'excursion systolique du plan de l'anneau tricuspide (TAPSE) divisée par la pression artérielle systolique pulmonaire (PAPS)] pourrait offrir une valeur prédictive supérieure pour l'issue défavorable par rapport aux mesures individuelles de TAPSE et PAPS seules.

Méthodes: Nous avons mené une étude rétrospective colligeant les données d'un centre hospitalier universitaire s'étendant de 2017 à 2023. Tous les patients présentant une EP confirmée et une échocardiographie transthoracique dans les 7 jours suivant le diagnostic ont été inclus. Le critère de jugement principal était un résultat composite de décès, de détérioration hémodynamique nécessitant l'introduction d'inotropes ou de thrombolyse dans les 30 jours. Les critères de jugement secondaire comprenaient une mortalité toutes causes confondues à 6 mois et l'apparition d'une insuffisance cardiaque droite.

Résultats: Trente-huit patients ont été inclus. L'âge moyen était de 58 ± 15 ans. Une prédominance masculine a été notée : 23 patients de sexe masculin (60.5 %) et 15 patientes de sexe féminin (39.5 %). Huit patients ont atteint le critère de jugement principal tandis que neuf patients ont atteint le critère de jugement secondaire.

En analyse multivariée, le rapport TAPSE/PAPS était associé de manière indépendante au critère de jugement principal (OR=2.77, IC à 95 % 1.101-10.23, P=0.042). Un rapport TAPSE/PAPS <0,3 était indépendamment associé au critère de jugement secondaire (OR=3.07, IC à 95 % 1.185-10.18, P=0.034).

Conclusion: Cette étude suggère qu'un rapport échocardiographique combiné de la fonction du VD à la postcharge est efficace pour prédire l'issue défavorable de l'EP aigue.

Mots clés: Embolie pulmonaire aigue, échocardiographie, postcharge ventriculaire droite, fonction ventriculaire droite, issue.

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INTRODUCTION

Pulmonary embolism (PE) ranks as the third leading cause of cardiovascular mortality, with fatalities primarily attributed to right ventricular (RV) dysfunction and failure [1,2]. The rapid escalation in RV afterload, resulting from a combination of mechanical obstruction in the pulmonary arteries and vasoconstriction, can often exceed the ventricle's compensatory capacity [3–6].

As about 5% of PE patients present with sustained hypotension, obstructive shock, or cardiac arrest, primary emphasis in management should be put on prompt reperfusion therapies [7,8]. However, in normotensive PE cases, risk stratification is crucial for identifying individuals at an increased risk of hemodynamic collapse or a heightened risk of significant bleeding.

This risk stratification includes assessment of physiological parameters, right heart dysfunction, and identification of comorbidities. Validated tools such as European Society of Cardiology guidelines [2] and Bova score [9]can identify normotensive patients with PE and an elevated risk of subsequent hemodynamic collapse.

Biomarkers, electrocardiography, computed tomography, and especially transthoracic echocardiography (TTE) are used to predict adverse outcomes in patients with acute PE. In this context, Several TTE parameters were studied such as TAPSE[10], RV dilatation, interventricular septal geometry and PASP. Nevertheless, the sensitivity and specificity of these existing tools in predicting adverse outcomes related to PE are limited, typically ranging from 40% to 80% [11–13].

Therefore, we decided to study the TAPSE/PASP ratio to better stratify the risk of pulmonary embolism.

Methods

Patients and study design

This was a retrospective single center cross-sectional study, conducted from January 2017 to March 2023 in the Internal Security Forces Hospital of Marsa Tunisia.

We included adult patients with confirmed PE who underwent a formal TTE within 7 days of follow up.

Patients were excluded if PE was not confirmed, TTE was not performed within 7 days or thrombus-reducing intervention occurred before TTE.

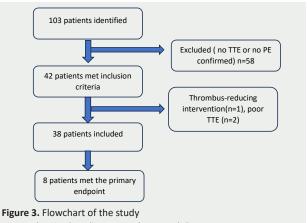
Patient demographic and anthropometric data, cardiovascular risk factors, comorbidities and risk factors for PE were collected. Initial symptoms such as dyspnea, cough, hemoptysis, chest pain, palpitations, lower limb edema and lower limb pain leading to diagnosis were noted.

Clinical signs such as tachycardia, hypotension, hypoxia and tachypnea were also noted at the time of diagnosis.

All patients underwent usual biology tests including troponin levels. Some patients performed N terminal pro brain natriuretic peptide (NT-Pro BNP) levels examination. Biomarker positivity was defined if either troponin or NT-Pro BNP was elevated.

All patients underwent CT pulmonary angiogram or lung

ventilation perfusion scan to confirm the PE. Duplex ultrasound assessment was performed.



TTE: transthoracic echocardiogram, PE: pulmonary embolism

Outcomes

The primary endpoint was a 30-day composite outcome, including all-cause mortality and PE-related clinical deterioration (systemic systolic hypotension <90 mmHg with need for inotropes or vasopressor, systemic thrombolysis). Secondary endpoints were 6 months allcause mortality and onset of right-sided heart failure.

Echocardiography

All patients underwent an ultrasound examination at rest using a Philips EPIQ 7C echocardiography and q-VIVID 7 with simultaneous and continuous electrocardiographic tracing. All measurements were performed according to

the recommendations of the American Society of Echocardiography and the European Association of Cardiovascular Imaging (ASE/EACVI) [14].

Values were averaged on at least three cardiac cycles, or more in the case of an irregular rhythm.

TAPSE, RV diameter, maximal tricuspid regurgitation velocity (TRV), and PASP were measured. The TAPSE/ PASP ratio was derived.

TAPSE was measured on M-mode images, calculating the difference in RV basal motion from peak systole to end-diastole (Fig.1).

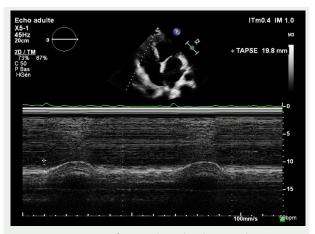


Figure 1. Measurement of tricuspid annular plane systolic excursion (TAPSE) by calculating the difference in right ventricular basal motion from peak systole to end-diastole

RV diameters were measured in end-diastole at the level of the tip of the atrioventricular valve.

The maximal TRV via continuous-wave Doppler was used to derive the right atrial (RA)–RV pressure gradient using the simplified Bernoulli equation.

PASP was calculated as the sum of RAP and RA–RV pressure gradients, given that no patient had pulmonic valve stenosis (Fig.3). The TAPSE/PASP ratio was derived.

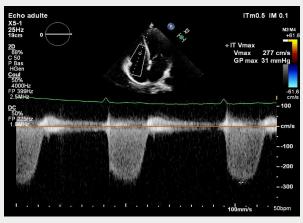


Figure 2. Measurement of Pulmonary artery systolic pressure (PASP).

Statistics

Data were analyzed using IBM SPSS Statistics 23 software. Values were expressed as mean ±SD. Categorical variables were expressed as single and relative frequencies.

Differences between groups were sought by using Student's T test for continuous variables and chi-square or Fisher test for discontinuous variables.

The determination of the cut-off values of the studied parameters was made by analyzing their receiver operating characteristic (ROC) curves. Multinomial logistic regression analysis was performed for the multivariate study in which we enrolled parameters with p value < 0.05 after univariate analysis.

In all statistical tests, the significance level was set at 0.05.

RESULTS

General characteristics

A total of 38 patients were eligible for the study (Figure 3). Patient's characteristics are summarized in Table 1. Mean age was 58 \pm 15 years old. A male predominance was noted: 23 male patients (60.5%) and 15 female patients (39.5%). Tobacco, Diabetes and hypertension were the most common cardiovascular risk factors, being found in 39.5% (n=15), 36.8% (n=14) and 31.5% (n=12) of patients, respectively.

Six had active neoplasia (15.8%) and four had an history of prior thrombo-embolism (10.5%)

Ten patients had high biomarkers levels (26.3%).

Table 1. General population characteristics

	General population		
Age (years)	58±15		
Sex (Male %/Female %)	23 (60.5)/15 (39.5)		
Hypertension (n, %)	12 (36.8)		
Diabetes (n, %)	14 (36.8)		
Dyslipidemia (n, %)	5 (13.2)		
Chronic kidney disease (n, %)	1 (2.6)		
Tobacco (n, %)	15 (39.5)		
Coronary artery disease (n, %)	2 (5.3)		
Heart failure(n, %)	4 (10.5)		
Asthma (n, %)	2 (5.3)		
COPD (n, %)	2 (5.3)		
Cancer (n, %)	6 (15.8)		
History TEVD (n, %)	4 (10.5)		
Hight trop/ProBNP (n, %)	10 (26.3)		
TAPSE (mm)	19.7±4.1		
TRV max (cm/s)	2.8±0.9		
PASP (mmHg)	49±20		
TAPSE/PASP	0.50±0.2		
IVS paradox (n, %)	2 (5.3)		
RV basal diameter (mm)	40±10		
LVEF (%)	54±17		

COPD: Chronic obstructive pulmonary disease; TEVD: Thromboembolic veinous disease; TAPSE: Tricuspid annular plane systolic excursion; TRV: tricuspid regurgitation velocity; PASP: Pulmonary artery systolic pressure; IVS: interventricular septum; RV: Right ventricle; LVEF: Left ventricle ejection fraction.

Outcomes

Within 30 days, eight (21%) patients met the primary endpoint, which included 2 deaths, 3 instances of systemic thrombolysis, and 7 requiring vasopressors due to systemic hypotension; it's noteworthy that a patient could have experienced more than one endpoint. They exhibited significantly lower TAPSE (15.3+/-2 Vs 21 +/-1.6; p=0.001), and a significantly lower TAPSE/PASP ratio of 0.27+/-0.8 vs 0.56+/-0.29; p=0.009) compared to those who did not meet the primary endpoint (table 2).

Additionally, those patients exhibited higher TRV and higher PASP. with no statistically significant difference.

At 6 months, night (23.7%) patients met the secondary endpoint, 7 had died and 2 had a new onset of right-sided heart failure. They had significantly lower TAPSE (17+/-3 vs 21+/-3; P=0.017), higher PASP (63+/-19 vs 44+/-20; P=0.021), and lower TAPSE/PASP ratio (0.30+/-0.15 vs 0.58+/-0.29 P=0.011) compared to those who did not meet the secondary endpoint (table3).

Association with Adverse Outcome

In univariate analysis, the TAPSE/PASP ratio demonstrated a significant association with the primary endpoint. TAPSE individually was also associated with the primary outcome (Table 2). In ROC analysis, the TAPSE/PASP ratio exhibited an area under the curve (AUC) of 0.815 for predicting the primary endpoint.
 Table 2. Parameters correlated to primary endpoint in univariate analysis

	Primary endpoint +	Primary endpoint -	P value
Age (years)	55±10	58±16	0.569
Sex (Male %/Female %)	2 (25)/6 (75)	21 (70)/9 (30)	0.021
Hypertension (n, %)	3 (37.5)	11 (36.7)	0.965
Diabetes (n, %)	3 (37.5)	11 (36.7)	0.965
Dyslipidemia (n, %)	2 (25)	3 (10)	0.265
Chronic kidney disease (n, %)	0	1 (3.3)	0.601
Tabacco (n, %)	2 (25)	13 (43.3)	0.346
Coronary artery disease (n, %)	0	2 (6.7)	0.453
Heart failure (n, %)	1 (12.5)	3 (10)	0.838
Asthma (n, %)	1 (12.5)	1 (3.3)	0.302
COPD (n, %)	0	2 (6.7)	0.453
Cancer (n, %)	1 (12.5)	5 (16.7)	0.774
History TEVD (n, %)	1 (12.5)	3 (10)	0.838
Hight trop/BNP (n, %)	3 (37.5)	7 (23.3)	0.419
TAPSE (mm)	15.3±2	21±16	0.001
TRV max (cm/s)	3.1±0.5	2.7±0.9	0.375
PASP (mmHg)	59±12	46±21	0.137
TAPSE/PASP	0.27±0.08	0.56±0.29	0.009
IVS paradox (n, %)	1 (12.5)	1 (3.3)	0.302
RV basal diameter (mm)	41±10	40±10	0.758
LVEF (%)	49±23	55±15	0.336

COPD: Chronic obstructive pulmonary disease; TEVD: Thromboembolic veinous disease; TAPSE: Tricuspid annular plane systolic excursion; TRV: tricuspid regurgitation velocity; PASP: Pulmonary artery systolic pressure; IVS: interventricular septum; RV: Right ventricle; LVEF: Left ventricle ejection fraction.

Table 3. Multivariate	e analysis to	predict the	primary e	ndpoint
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	Р	Odds Ratio	95% IC	
			IB	SB
TAPSE	0.101	1.310	0.949	1.810
Female	0.236	0.279	0.034	2.304
TAPSE/PASP <0.30	0.042	2.77	1.101	10.23

TAPSE: Tricuspid annular plane systolic excursion; PASP: Pulmonary artery systolic pressure

The optimal value for predicting the outcome in PE based on the ROC was identified as a TAPSE/PASP ratio of 0.3 (95% Cl :1.6- 60, p=0.006).

In multivariate analysis, the TAPSE/PASP ratio remained independently associated with the primary endpoint, with an OR of 2.77 per unit change (95% CI 1.101–10.23, P=0.042). Whereas TAPSE did not maintain independent associations with the primary endpoint (Table 3).

For the secondary endpoints of all-cause mortality and onset of right-sided heart failure at 06 months, univariate analysis reveals that patients who exhibited this endpoint had significatively lower TAPSE, higher PASP and lower TAPSE/PASP ratio of 0.30 (0.15-0.45) compared to those who did not meet the secondary endpoint (0.58 (0.29-0.87), P=0.011) (table 4).

In ROC analysis, the TAPSE/PASP ratio exhibited an area under the curve (AUC) of 0.802 for predicting the secondary endpoint. The optimal value for predicting the outcome at 6 months in PE based on the ROC was identified as a TAPSE/PASP ratio of 0.3 (95% CI :1.4-4.3, p=0.010) (figure 4).

In multivariate analysis, the TAPSE/PASP ratio <0.3 remained independently associated with the primary endpoint, with an OR of 3.07 per unit change (95% CI

1.185–10.18, P=0.034). Whereas TAPSE and PASP did not maintain independent associations with the secondary endpoints (Table 5).

Table 4. Parameters correlated to secondary endpoint.

	Secondary endpoint +	Secondary endpoint -	P value
Age (years)	56±11	56±16	0.940
Sex (Male %/Female %)	5 (55.6)/4 (44.4)	16 (64)/9 (36)	0.655
Hypertension (n, %)	3 (33.3)	9 (36)	0.886
Diabetes (n, %)	3 (33.3)	10 (40)	0.724
Dyslipidemia (n, %)	1 (11.1)	4 (16)	0.723
Chronic kidney disease (n, %)	0	1 (4)	0.543
Tabacco (n, %)	5 (55.6)	8 (32)	0.212
Coronary artery disease (n, %)	0	2 (6.7)	0.382
Heart failure(n, %)	1 (4)	3 (33.3)	0.019
Asthma (n, %)	0	2 (8)	0.382
COPD (n, %)	1 (11.1)	0	0.091
Tumer (n, %)	2 (8)	3 (33.3)	0.066
History TEVD (n, %)	1 (11.1)	3 (12)	0.943
Hight trop/BNP (n, %)	3 (33.3)	6 (24)	0.586
TAPSE (mm)	17±3	21±3	0.017
TRV max (cm/s)	3±0.7	2.7±1	0.527
PASP (mmHg)	63±19	44±20	0.021
TAPSE/PASP	0.30±0.15	0.58±0.29	0.011
IVS paradox (n, %)	1 (11.1)	0	0.091
RV basal diameter (mm)	45±10	39±10	0.091
LVEF (%)	49±23	55±15	0.004

systolic excursion; TRV: tricuspid regurgitation velocity; PASP: Pulmonary artery systolic pressure; IVS: interventricular septum; RV: Right ventricle; IVEF: Left ventricle ejection fraction. COPD: Chronic obstructive pulmonary disease; TEVD: Thromboembolic veinous disease; TAPSE: Tricuspid annular plane

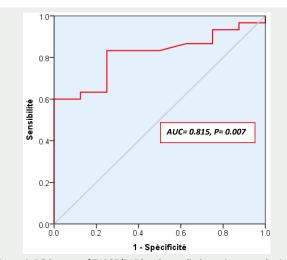


Figure 4. ROC curve of TAPSE/PAPS ratio predicting primary endpoint AUC: Area under the ROC Curve, TAPSE: Tricuspid annular plane systolic excursion; PASP: Pulmonary artery systolic pressure;

Table 5. Multivariate analysis to predict the secondary endpoint

	Р	Odds Ratio	95% IC	
			IB	SB
TAPSE	0.308	0.969	0.864	1.590
PASP	0.462	1.031	0.890	1.054
TAPSE/PASP <0.30	0.034	3.07	1.185	10.18
LVEF	0.951	0.888	0.020	39.17
Right-sided heart failure	0.308	5.267	0.215	128

TAPSE: Tricuspid annular plane systolic excursion; PASP: Pulmonary artery systolic pressure; LVEF: Left ventricle ejection fraction

DISCUSSION

The major findings of the present study were:

- TAPSE/PASP ratio was strongly correlated with adverse outcome at short and mid-term in PE.

- The cut-off value to predict adverse outcome was 0.3.

This study demonstrates that the echocardiographic index TAPSE/PASP, was independently associated with adverse outcomes in PE and emerged as a robust predictor for adverse PE-related outcomes.

The RV and the pulmonary arterial vasculature form a system characterized by low resistance and high capacitance [10]. In the context of a PE, there is a sudden surge in pulmonary vascular resistance and RV afterload. Even an obstruction of 25–30% of the pulmonary arteries is sufficient to elevate pulmonary pressures and reduce RV stroke volume by 30%. When the obstruction reaches 50–75% of the pulmonary vasculature, it can lead to outright RV failure[15]. This increased strain on the RV initially manifests as chamber dilation and a slight leftward bulging of the interventricular septum. These changes, coupled with a decline in RV stroke volume, impede preload to the left ventricle (LV). The reduction in LV stroke volume results in hypotension, diminished coronary perfusion, and ischemia.

This sequence of events sets off a detrimental progression where the compromised LV contractility further diminishes RV contractility. Remarkably, approximately 40% of the RV's contractile forces are derived from the LV [16]. Thus, the interplay between RV and LV dynamics contributes to a worsening spiral effect in the face of significant pulmonary vascular obstruction due to a PE.

The current study highlights the limitations of prior attempts at risk stratification, which often focused on isolated parameters such as the RV/LV ratio on computed tomography pulmonary angiography or TTE [12,17,18], as well as regional or global RV dysfunction on TTE.

Additionally, some studies focused solely on pulmonary circulation characteristics, such as early systolic notching in the pulmonary artery Doppler, a sign of pulmonary obstruction and vasoconstriction in PE, without directly assessing right ventricular function [19].

Our findings argues that the failure to consider the right ventricle and pulmonary artery (RV–PA) unit as a cohesive entity may explain why certain studies exploring potential imaging prognostic measures in PE did not yield robust predictions of patient outcomes.

The implication is that a more comprehensive approach, possibly involving the integration of parameters like the TAPSE/PASP ratio, could offer a more accurate and holistic assessment of risk in acute PE.

This study underscores the importance of considering RV function and the pulmonary circuit as a unified entity, as exemplified by the TAPSE/PASP ratio. The TAPSE/PASP ratio, which has normal values in the range of 0.8–1.8, is highlighted as a valuable metric for assessing RV function relative to afterload.

A high TAPSE/PASP ratio suggests effective RV function given the afterload, while a decrease in the ratio may indicate an increase in PASP or a decline in RV function estimated by TAPSE, or a combination of both.

Tello et al. research showed that echocardiographic TAPSE/PASP ratio is a clinically relevant and valid surrogate of invasively measured Ees/Ea to assess RV-arterial coupling in severe chronic pulmonary hypertension and provides information on RV diastolic stiffness but not RV contractility [20], as TAPSE lacks information on ventricular mass and does not consider time-related factors like acceleration. Despite these potential concerns, the TAPSE/PASP ratio has demonstrated its value in conditions such as pulmonary hypertension, tricuspid regurgitation, and left ventricular dysfunction. this analysis extends the application of the TAPSE/PASP ratio to the context of acute PE.

In the context of chronically progressive pulmonary hypertension, the TAPSE/PASP values were observed to be even lower than those reported in acute PE as patients with TAPSE/PASP <0.31 mm/mm Hg had a significantly worse prognosis than those with higher TAPSE/PASP. These values in chronic pulmonary hypertension may be explained by the slower disease development, allowing the right ventricle to adapt over time. Ultimately, PASP can reach very high levels, resulting in a low TAPSE/PASP ratio. Our study meets most of the findings on the TAPSE/ PASP ratio in the previous research conducted in general Massachusetts hospital by Lynhe et al.[1]. Our studies differ in terms of the proportion and number of patients. The pervious study found that a TAPSE/PASP ratio was also significatively associated with adverse outcome, with a cut-off of 0.4 and that TAPSE/PASP predicted both 7- and 30-day all-cause mortality, while TAPSE and PASP did not. While a lower cut-off of 0.3 was determined in our study population.

Another study conducted by Vriz et al. found that the TAPSE/PASP ratio was reduced in patients with systemic hypertension and normal LV function suggesting RV-PA uncoupling in the context of a systemic disease [21].

Another study about the prognostic role of the echocardiographic TAPSE/PASP ratio and its relationship with NT-pro B NP plasma level in systemic sclerosis found that systemic sclerosis patients showed lower TAPSE/PASP ratio at baseline compared to healthy population and their data demonstrated that the TAPSE/PASP ratio might be more specific and accurate than other several indicators of RV function, as it better reflects the RV performance and the load-dependent status of the pulmonary circulation [22].

Our study concludes by suggesting that poor outcomes in PE may be predicted by a mismatch between right ventricular function and the acute PE-related vascular load, as reflected by a TAPSE/PASP ratio less than 0.3. This ratio should be further analyzed as it can be a useful tool for the stratification on risk in PE.

Limitations

Some limitations have to be addressed to the present study. At first, our analysis was of a single-center design, and uses observational non-randomized data, thus it is subject to selection bias.

Secondly, our study population was small as compared with a number of large-scale studies found in literature.

Besides, TTE was performed within seven days of acute PE presentation or diagnosis and this is an important time during which echocardiographic parameters can evolve. Furthermore, we did not perform risk stratification for PE which would have been interesting to evaluate this ratio in low or intermediate-risk Pulmonary embolisms.

Finally, it is possible that the present study is somewhat underpowered to accurately estimate the association between TAPSE/PASP ratio and adverse outcome in PE. Further studies with a larger population are needed to confirm our findings.

CONCLUSION

This study illustrates that the combined assessment of RV function and pulmonary pressure, as indicated by the echocardiographic ratio TAPSE/PASP, enhances the ability to predict adverse short-term and mid-term outcomes in patients with acute PE. To ensure the reliability and generalizability of these findings, an external validation of the TAPSE/PASP ratio, along with an exploration of its performance characteristics is deemed necessary.

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