VOLUME - 11, ISSUE - 08, AUGUST - 2022 • PRINT ISSN No. 2277 - 8160 • DOI : 10.36106/gjra

Original Research Paper

Cardiology

# PROGNOSTICATION BY RATIO OF TRICUSPID ANNULAR PLANE SYSTOLIC EXCURSION TO PULMONARY ARTERIAL SYSTOLIC PRESSURE BY ECHOCARDIOGRAPHY IN ACUTE PULMONARY EMBOLISM

| | |
|---|---|
| Dr. J. Nambirajan | Associate Professor & HOD, Department of Cardiology, Coimbatore medical |
| Dr. K. Moosa Saheer | Postgraduate Resident, Department of Cardiology, Coimbatore medical College, |
| Dr. D. Chakravarthy | Assistant Professor, Department of Cardiology, Coimbatore medical College, |

**ABSTRACT** Depending upon hemodynamic status and right ventricular dysfunction, In-hospital mortality of acute pulmonary embolism ranging from 0 to 50%. By assessing right ventricular function, we can predict the outcomes in patients with acute pulmonary embolism. In patients with acute pulmonary embolism (PE), right ventricular (RV) failure causes death due to a mismatch between RV systolic function and increased RV afterload. The aim of our study was to know whether the ratio of tricuspid annular plane systolic excursion (TAPSE)to pulmonary arterial systolic pressure (PASP) would predict adverse outcomes. This study was a retrospective analysis of a single Centre Pulmonary embolism register. After the confirmation of PE, patients taken a formal transthoracic echocardiography within 48 hours were included in this study. A 7-day composite outcome of death or hemodynamic deterioration was the primary end point of this study. The secondary endpoints of this study were 7- and 30- day all-cause mortality. A total of 67 patients were included; 14 met the primary composite outcome. In univariate analysis, the TAPSE/PASP was associated with our primary outcome [odds ratio = 0.027, 95% confidence interval (CI) 0.010–0.087; $P < 0.0001$], which was significantly better than either TAPSE or PASP alone ($P = 0.018$ and $P < 0.0001$, respectively). For predicting adverse outcome in PE, a TAPSE/PASP cut-off value of 0.4 was identified as the optimal value. Echocardiographic ratio of tricuspid annular plane systolic excursion to pulmonary arterial systolic pressure is superior in prediction of adverse outcome in acute PE. And also, it may improve risk stratification and identification of the patients that will suffer short-term deterioration after acute PE.

**KEYWORDS :** crumb rubber, utilization, compressive strength, low cost, sustainable

## INTRODUCTION

Utilization Cardiovascular diseases are the most common mortality worldwide, among this pulmonary embolism is at the third position. Right ventricular (RV) dysfunction and failure are the causes for death due to pulmonary embolism[1,2]. From the combined consequences of pulmonary arterial (PA) mechanical obstruction and vasoconstriction[3,5] causes the abrupt increases in RV afterload, which may exceed the ability of the ventricle to compensate[2,4,6].

Patients with acute PE, to predict adverse outcomes, minimally invasive investigations like biomarkers, electrocardiography, computed tomography, and especially transthoracic echocardiography (TTE)[2,7-9] are used. By measuring tricuspid annular plane systolic excursion (TAPSE), RV dilatation, inter-ventricular septal geometry, and pulmonary arterial systolic pressure (PASP)[10], general RV function is inferred using trans-thoracic echocardiography. These measures may help to predicts patients at high-risk of deterioration who merit advanced therapeutic options[11,12], even though patients may be initially normotensive. However, these adverse PE-related outcomes predicting tools sensitivity and specificity is limited to a range of 40–80%[9,13,14]. It improve the accuracy of outcome prediction, some additional measures are needed.

It is reasonable to investigate the RV and pulmonary circuit as unit, for accurate prognosis in PE[15]. The reason for fail to meet the standard for existing approaches may be the failure to do so. So, in this study, we try to define the RV and pulmonary circuit as one combined physical unit by deriving the echocardiographic index TAPSE/PASP. In left ventricular (LV) failure[16-22] a few studies of chronic pulmonary arterial hypertension (PAH)[23,24] this index already investigated. In this study we hypothesized that in patients with acute PE, the ratio of TAPSE/PASP is better than TAPSE or PASP individually to predict adverse clinical outcomes.

## METHODS

### Design

This is a prospective study based on patients who were enrolled in our college Pulmonary embolism registry. The registry was approved by our Institutional ethical Committee.

Patients age more than 18 were included in this study if they had both PE confirmed and a formal TTE done within 48 hours. Our study period was from January 2020–January 2021. Patients who thrombolysis done prior to basic echo, or poor-quality images were excluded from our study.

### Outcomes

A 7-day composite outcome of death or hemodynamic deterioration was the primary end point of this study. The hemodynamic deterioration was defined as systemic systolic hypotension <90mmHg, need for inotropes or vasopressor, intubation with mechanical ventilation, or need for rescue therapy including systemic thrombolysis. The secondary endpoints of this study were 7- and 30- day all-cause mortality.

### Echocardiography

With consensus echocardiographic interpretation recommendations[10,26], and values averaged for at least three or more (in the case of an irregular rhythm) cardiac cycles, the analyses compiled. TAPSE measured as the difference in RV basal motion from peak systole to end-diastole on M-mode images. In case of no M-mode images recorded, manually measured from apical four chamber image view. To generate RV/LV ratio, in end diastole at the level of tip of the atrioventricular valve leaflets, RV and LV diameters were measured. To derive the right atrial (RA)–RV pressure gradient by simplified Bernoulli equation the maximal tricuspid regurgitation velocity (TRV) by continuous-wave Doppler was used. At the level of the hepatic veins, inferior vena cava (IVC) diameter was measured. RA pressure taken as recommended[26]. Then the sum of RAP and RA–RV pressure gradients calculated as PASP (as no patient had pulmonic valve Stenosis). From this the ratio TAPSE/PASP was derived.

### Other clinical parameters

As per routine clinical care, History, examination findings, and laboratory values were obtained. If Troponin level >_14 pg/mL and NT-pro BNP level >_600 pg/mL, was considered elevated. If either troponin or NT-pro BNP was elevated patient was considered biomarker positive.

### Statistics

Normality data were analyzed by Shapiro–Wilk test. For non-normally distributed parameters, like vital sign and echocardiographic parameters, median (interquartile ranges) are presented. Primary outcome among patients were compared by t-test or Mann– Whitney U test for numerical covariates and $X^2$ test or Fisher's exact test for categorical covariates, where appropriate. Logistic regression models were used to correlate between echocardiographic measurements and outcome. Adjusting for age, sex, smoking status, and past-medical history of chronic obstructive pulmonary disease, asthma, and pulmonary hypertension, Multivariate logistic regression analysis was done. <0.05 P-value, considered statistically significant.

## RESULTS

A total of 67 patients were included. 14(21%) patients met the primary composite outcome within 7 days, including 3(4.5%) deaths. 14(21%) patients systemic thrombolysis, and 2(2.9%) requiring vasopressor due to systemic hypotension. Some patients could have had more than one endpoint. 6(9%) patients died, at 30 days follow up.

### Demographics

In Table 1 the patients demographics data are given. In terms of past medical history and risk factors were generally comparable among the patients who met and did not meet the primary outcome.

**Table 1 Demographics stratified by primary outcome**

| | Patients who did not meet primary Outcome(n=53) | Patients who did meet primary Outcome (n=14) | P-value |
|---|---|---|---|
| Age (years) | 61±17 | 60±18 | 0.082 |
| Sex (female) | 26(49%) | 7 (47%) | 0.702 |
| Past medical history | 7 (13.2 %) | 2 (14.3%) | 0.552 |
| Coronary artery disease | 4 (8%) | 1 (7%) | 0.965 |
| Congestive heart failure | 4 (8%) | 1 (7%) | 0.067 |
| Stroke | 1 (2%) | 1 (7%) | 0.455 |
| Pulmonary hypertension | 6 (12%) | 1 (7%) | 0.033 |
| Asthma | 4 (8%) | 2 (14%) | 0.423 |
| COPD | 3 (5%) | 1 (7%) | 0.989 |
| Active cancer | 14 (26%) | 4 (28%) | 0.651 |
| Prior history of VTE | | | |
| Risk factors | 5 (9%) | 2 (17%) | 0.009 |
| Family history of VTE | 12 (22%) | 3 (23%) | 0.842 |
| Recent surgery | 14 (26%) | 4 (28%) | 0.724 |
| Recent hospitalization >_3 days | 3 (6%) | 1 (7%) | 0.471 |
| Recent trauma | 16 (30%) | 4 (29%) | 0.442 |
| Reduced mobility | 19 (36%) | 5 (36%) | 0.894 |
| Smoker | | | |

The clinical presentation of patients is given in table 2. Hypoxia, tachycardia, tachypnoea, and elevated biomarkers had frequently occurred among patients with adverse outcome.

**Table 2: - Clinical PE presentation, stratified by outcome**

| | Patients who did not meet primary Outcome (n=53) | Patients who met primary Outcome (n=14) | P-Value |
|---|---|---|---|
| Symptoms | 2 (4%) | 1 (7%) | 0.093 |
| Asymptomatic | 39 (74%) | 10 (71%) | 0.504 |
| Dyspnea | 6 (11%) | 1 (7%) | 0.072 |
| Chest pain | 13 (25%) | 4 (29%) | 0.789 |
| Chest pain (pleuritic) | 5 (10%) | 2 (15%) | 0.038 |
| Syncope | 2 (4%) | 1 (7%) | 0.388 |
| Hemoptysis | 9 (17%) | 2 (15%) | 0.737 |
| Cough | 5 (10%) | 1 (7%) | 0.527 |
| Palpitations | 10 (19%) | 2 (15%) | 0.321 |
| Leg pain | 14 (26%) | 3 (22%) | 0.895 |
| Leg swelling | 37 (70%) | 11 (79%) | 0.005 |
| Vitals and blood analysis | 105 (90–117) | 112 (96–128) | <0.001 |
| Hypoxia | 118 (102–132) | 112 (98–130) | 0.084 |
| Highest heart rate, beats/min | 20 (20–24) | 24 (20–30) | <0.001 |
| Lowest systolic blood pressure (mmHg) | 27 (51%) | 9 (65%) | <0.001 |
| Highest respiration rate, breaths/ Min | 28 (53%) | 8 (57%) | 0.042 |
| Troponin elevated | | | |
| NT-pro-BNP elevated | | | |

### Echocardiographic results

In Table 3, Echocardiographic measurements are given. ICC values were 0.95 for TAPSE/PASP, 0.94 for TAPSE, 0.96 for TRV and 0.95 for PASP, corroborating high degree of consistency in the intra-observer analyses.

**Table 3: - Echocardiographic measurements stratified by outcome**

| Echocardiographic variable | Patients who did not meet primary outcome (n-53) | Patients who did meet primary outcome (n-14) | P-Value |
|---|---|---|---|
| TAPSE (mm) | 16.9 (13.3–21.0) | 13.4 (9.3–16.6) | <0.001 |
| TRV (cm/s) | 2.7 (2.3–3.1) | 2.9 (2.6–3.2) | <0.001 |
| RA–RV pressure gradient (mmHg) | 28.7 (21.5–37.5) | 33.4 (26.8–41.7) | <0.001 |
| PASP (mmHg) | 34.1 (25.7–44.2) | 40.7 (32.7–51.6) | <0.001 |
| IVC (cm) | 1.7 (1.4–2.1) | 2.0 (1.6–2.3) | <0.001 |
| TAPSE/PASP (mm/mmHg) | 0.47 (0.33–0.70) | 0.29 (0.21–0.40) | <0.001 |
| McConnell sign present | 13 (24%) | 6 (43%) | <0.001 |
| Septal bowing | 14 (27%) | 7 (50%) | <0.001 |

It had noticed that, significantly lower TAPSE, higher TRV and higher PASP, larger IVC, and more frequently septal bowing and McConnell's sign were occurred, patients who experienced primary outcomes. The ratio of TAPSE/PASP also lower among these patients 0.27 (0.19–0.39), compared with those who did not meet the primary outcome [0.45 (0.32–0.68), P < 0.001].

By the index of TAPSE/PASP (<0.285, 0.285–0.419, 0.420–0.649, >0.649), We divided patients into quartiles; across these quartiles there was a significant trend associated with primary outcome (P< 0.0001). Compared with; 4/16 (25%), 3/21 (14%), and 2/15 (13%), respectively, in the higher quartiles, the lowest quartile, 6/15 (40%) of patients experienced adverse outcome.

### Association with adverse outcome

The index of TAPSE/PASP were associated with the primary endpoint with an odds ratio (OR) = 0.026 [95% confidence interval (CI) 0.010–0.085, P< 0.0001] per unit change, in univariate analysis. There is no gender difference was noted. When separately analyzing TAPSE and PASP with the primary outcome (Table 4). However, to predict primary endpoint, in ROC analysis TAPSE/PASP had an AUC of 0.730 (95% CI 0.693–0.779), whereas TAPSE and PASP separately showed significantly lower AUC. Based on the ROC, we identified the optimal value for TAPSE/PASP ratio as 0.376 (95% CI 0.298–0.413) to predict the outcome in PE.

**Table 4: - Correlation between echocardiographic estimates of RV function and afterload and the endpoints**

| Correlation to primary, composite outcome | OR | 95% CI | P-value |
|---|---|---|---|
| TAPSE (univariate) | 0.878 | 0.844–0.913 | <0.0001 |
| PASP (univariate) | 1.033 | 1.020–1.047 | <0.0001 |
| TAPSE/PASP (univariate) | 0.028 | 0.010–0.087 | <0.0001 |
| TAPSE (multivariate) | 0.873 | 0.838–0.910 | <0.0001 |
| PASP (multivariate) | 1.034 | 1.020–1.048 | <0.0001 |
| TAPSE/PASP (multivariate) | 0.026 | 0.008–0.080 | <0.0001 |
| Correlation (univariate) to 7 days all-cause mortality | 0.901 | 0.835–0.974 | 0.0082 |
| TAPSE | 1.018 | 0.992–1.044 | 0.1780 |
| PASP | 0.060 | 0.007–0.527 | <0.0001 |
| TAPSE/PASP | 0.955 | 0.909–1.005 | 0.0744 |
| Correlation (univariate) to 30 days all-cause mortality | 1.009 | 0.991–1.027 | 0.3322 |
| TAPSE | 0.326 | 0.118–0.895 | 0.0297 |
| PASP | | | |
| TAPSE/PASP | | | |

In multivariate analysis, the index of TAPSE/PASP was independently associated with primary outcome with an OR 0.026 per unit change (95% CI 0.008–0.080, P < 0.0001). With the primary endpoint, TAPSE and PASP separately were also independently associated (Table 4).

Patients with higher TAPSE/PASP was associated with lower 7-day all-cause mortality with OR 0.050 (95% CI 0.006–0.517, P< 0.0001) per unit change, for secondary outcomes of all-cause mortality. TAPSE or PASP individually not predicting 30-day all-cause mortality with OR 0.315 (95% CI 0.107–0.884, P= 0.0276) per unit change (Table 4).

The percentage of events for both primary and the two secondary outcomes also stratified by high vs. low TAPSE/PASP with the 0.387 as optimal cut-off. In the low TAPSE/PASP group, significantly more events occurred, during the first 7 days.

## DISCUSSION

The echocardiographic index of TAPSE/PASP is a method to integrate estimates of RV function relative to RV afterload. This study shows that this index is independently related to adverse PE outcome. Compared with two parameters separately, this index gives strong predictor for adverse outcome. In intermediate-risk PE patients, even when adjusting for elevated biomarkers or other echocardiographic findings of RV dysfunction, this index gives a stronger predictor of adverse outcome.

In the management of PE, it is critical to stratify the patients according to their risk. This helps which patients are risk for hemodynamic decompensation and will helps to invasive therapy[2, 12]. Previously PE risk stratifications are mainly based on isolated parameters. These are like RV/LV ratio on CTPA or TTE[9,27,28] or regional or global RV dysfunction on TTE[29-32]. The important drawback of this measures is a restricted focus on the RV consequences without accounting for the RV afterload. Whereas some other parameters are focused on the pulmonary vascular characteristics without giving importance to the RV function, like early systolic notching in the pulmonary artery Doppler in PE due to pulmonary obstruction and vasoconstriction[33]. A number of studies of potential imaging prognostic measures in PE did not robustly predict outcome is because of failure to consider the RV–PA unit as a whole[13,34,35].

As done via the TAPSE/PASP ratio, the importance of jointly analyzing RV function and the pulmonary circuit as a unit has been emphasized[15,36]. The normal values is in the range of 0.8-1.8 which may vary with higher ages but not with gender[36-38]. A higher ratio indicates that the RV is functioning well given the afterload. The ratio will decrease as PASP increases or TAPSE decreases as RV dysfunction. As afterload is the most dynamic factor compared with contractility in the time following acute intermediate-risk PE in an animal model, it is speculated that changes in PASP is the main determinant in TAPSE/PASP changes[39]. Noting TAPSE does not account for ventricular force or contractility as it does not contain information on ventricular mass or a time consideration, TAPSE/PASP ratio is not a measure of function but rather a proxy for VA-coupling. Even though these concerns in this ratio, it is valuable in the evaluation of pulmonary hypertension, tricuspid regurgitation, and LV dysfunction[16-18, 20,22,40,41]. This ratio now extent to evaluate the PE also.

Even though the ratio was derived in a reciprocal manner, it has been investigated in a smaller European cohort that the combination of RV function and afterload in acute PE showed promising results[42]. TAPSE/PASP values were decreased even to lower values than the report in acute PE, in chronically progressive pulmonary hypertension[23,24]. In chronic pulmonary hypertension compared with acute PE, lower values of TAPSE/PASP observed might be explained by slower disease development where the RV has an opportunity to adapt[15] and ultimately PASP can reach very high levels yielding a low ratio.

In our study, it is found that the ratio of TAPSE/PASP < 0.4, suggest that poor outcomes in PE may be heralded by a mismatch between RV function and an acute PE-related vascular load manifestation. Depending on the speed of disease progression, as well as prior RV comorbidities the effect of this mismatch can vary that may generate pulmonary hypertension and RV compensation.

TAPSE is only an estimate of RV longitudinal contraction of the RV basal myocardium, and this may not reflect the global state of RV contraction, even though overall ventricular contraction is mostly longitudinal in the RV[6]. Like that, PASP is not necessarily integrating load dependencies or changes in flow patterns, vascular adaptabilities, and impedance, but it is only an estimate of RV afterload[4,44]. For the accurate measurement of RV contractility and after load, more thorough investigations are required, which will include pressure-volume loop recording. That will help to define the end-systolic pressure–volume relationship (Ees) as the independent measure of contractility and the arterial elastance (Ea) as the afterload. So, the Ees/Ea ratio will reflect ventriculo–arterial coupling. Which would describe the force of the ventricle matches the afterload faced[6,44]. Other methods to estimates RV afterload by non-invasive method, like pulmonary vascular resistance or Ea, though both require additional and more advanced measurements with uncertain assumptions[45,46]. To investigate whether such methods improve risk stratification further without limiting feasibility, further research is needed.

In most of the moderate to severe pulmonary thromboembolism, they can induce RV-PA uncoupling. To accurately evaluate this pressure-volume loop is needed. But in practice, its measurements are invasive, expensive, rarely available, and thus not clinically relevant in acute settings.

So, in acute settings instead of the RV–PA coupling, the TAPSE/ PASP ratio may be used as the echocardiographic counterpart[43]. In many studies, it has been proved that TAPSE/PASP well correlate with actual RV–PA coupling[18]. It also correlates with invasively measured RAP, pulmonary vascular resistance, and LV end-diastolic pressure[22].

As echocardiography is easy to perform, inexpensive, harmless, and widely available, the ratio of TAPSE/ PASP could be implemented in near real-time acute clinical risk stratification systems. In critically ill patients that cannot co-operate standard TTE positioning, where RV function can be assessed by measuring IVC, TRV, and TAPSE, in supine position in subcostal views[47,48].

To identify PE patients at risk of deterioration, we have retrospectively established TAPSE/PASP ratio cut-off of 0.4. Recent studies are suggested, in moderate-severe tricuspid regurgitation a cut-off of 0.49 is an optimal TAPSE/PASP, which is comparable in PE[40]. To investigate efficacy of this cut-off to trigger more aggressive management of patients with acute PE, a prospective study should be designed. To investigate the TAPSE/PASP ratio in a larger, unselected PE population and to assess if the ratio is suitable for long-term prognosis or in prediction of chronic thromboembolic pulmonary hypertension, further research is also warranted.

## LIMITATIONS

Even though this study analyzed a large population of acute PE patients from a prospective cohort with robust clinical correlates and well phenotype patients with complete data ascertainment, there is some limitations for this study. As our cases are from a tertiary center PE registry, most patients are intermediate-and high-risk group at a single institution, so generalizability may be limited. Secondly, the echocardiographic metrics of RV–PA coupling is relying on known correlation between the TAPSE/PASP ratio and invasive measurements, not derived invasively[18]. TAPSE only measure longitudinal RV function, but some conditions radial and apical RV function also affected. Many RV function are qualitative measures, so which might introduce higher degree of inter-observer variability and therefore would depend on echocardiographer experience. Lastly, patients who were received rescue therapies prior to an echocardiogram are excluded from this study, so some high-risk patients are not included in this study.

## CONCLUSION

In this study it is demonstrated that the echocardiographic ratio TAPSE/PASP can estimate, a combination of RV function and pulmonary pressure which improves prediction of adverse short-term outcome in patients with acute non-low-risk PE.

## REFERENCES:


1. Cohen A, Agnelli G, Anderson F, Arcelus J, Bergqvist D, Brecht J, for the VTE Impact Assessment Group in Europe (VITAE) et al. Venous thromboembolism (VTE) in Europe. Thromb Haemost 2007;98:756–64.
2. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geersing G-J, Harjola V-P, ESC Scientific Document Group 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.
3. Bernard S, Namasivayam M, Dudzinski DM. Reflections on echocardiography in pulmonary embolism-literally and figuratively. J Am Soc Echocardiogr 2019;32: 807–10.
4. Konstam MA, Kiernan MS, Bernstein D, Bozkurt B, Jacob M, Kapur NK et al. Evaluation and management of right-sided heart failure: a scientific statement from the American Heart Association. Circulation 2018;137:e578–e622.
5. Lyhne MD, Kline JA, Nielsen-Kudsk JE, Andersen A. Pulmonary vasodilation in acute pulmonary embolism—a systematic review. Pulm Circ 2020;10:1–16.
6. Sanz J, Sa´nchez-Quintana D, Bossone E, Bogaard HJ, Naeije R. Anatomy, function, and dysfunction of the right ventricle: JACC state-of-the-art review. J Am Coll Cardiol 2019;73:1463–82.
7. Cho JH, Sridharan GK, Kim SH, Kaw R, Abburi T, Irfan A et al. Right ventricular dysfunction as an echocardiographic prognostic factor in hemodynamically stable patients with acute pulmonary embolism: a meta-analysis. BMC Cardiovasc Disord 2014;14:1–9.
8. Barco S, Mahmoudpour SH, Planquette B, Sanchez O, Konstantinides SV, Meyer G. Prognostic value of right ventricular dysfunction or elevated cardiac biomarkers in patients with low-risk pulmonary embolism: a systematic review and meta-analysis. Eur Heart J 2019;40:902–10.
9. Dudzinski DM, Hariharan P, Parry BA, Chang Y, Kabrhel C. Assessment of right ventricular strain by computed tomography versus echocardiography in acute pulmonary embolism. Acad Emerg Med 2017;24:337–43.
10. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. J Am Soc Echocardiogr 2010;23:685–713.
11. Dudzinski DM, Giri J, Rosenfield K. Interventional treatment of pulmonary embolism. Circ Cardiovasc Interv 2017;10:1–10.
12. Rivera-Lebron B, McDaniel M, Ahrar K, Alrifai A, Dudzinski DM, Fanola C et al. Diagnosis, treatment and follow up of acute pulmonary embolism: consensus practice from the PERT Consortium. Clin Appl Thromb Hemost 2019;25:1–25.
13. Barrios D, Morillo R, Lobo JL, Nieto R, Jaureguizar A, Portillo AK et al. Assessment of right ventricular function in acute pulmonary embolism. Am Heart J 2017;185:123–9.
14. Sanchez O, Trinquart L, Colombet I, Durieux P, Huisman MV, Chatellier G et al. Prognostic value of right ventricular dysfunction in patients with haemodynamically stable pulmonary embolism: a systematic review. Eur Heart J 2008;29: 1569–77.
15. Vonk Noordegraaf A, Haddad F, Chin KM, Forfia PR, Kawut SM, Lumens J et al. Right heart adaptation to pulmonary arterial hypertension: physiology and pathobiology. J Am Coll Cardiol 2013;62:D22–33.
16. Braganc¸a B, Tre^pa M, Santos R, Silveira I, Fontes-Oliveira M, Sousa MJ et al. Echocardiographic assessment of right ventriculo-arterial coupling: clinical correlates and prognostic impact in heart failure patients undergoing cardiac resynchronization therapy. J Cardiovasc Imaging 2020;28:109–20.
17. Guazzi M, Bandera F, Pelissero G, Castelvecchio S, Menicanti L, Ghio S et al. Tricuspid annular plane systolic excursion and pulmonary arterial systolic pressure relationship in heart failure: an index of right ventricular contractile function and prognosis. Am J Physiol Heart Circ Physiol 2013;305:H1373–81.
18. Guazzi M, Dixon D, Labate V, Beussink-Nelson L, Bandera F, Cuttica MJ et al. RV contractile function and its coupling to pulmonary circulation in heart failure with preserved ejection fraction: stratification of clinical phenotypes and outcomes. JACC Cardiovasc Imaging 2017;10:1211–21.
19. Sultan I, Cardounel A, Abdelkarim I, Kilic A, Althouse AD, Sharbaugh MS et al. Right ventricle to pulmonary artery coupling in patients undergoing transcatheter aortic valve implantation. Heart 2019;105:117–21.
20. Gorter TM, van Veldhuisen DJ, Voors AA, Hummel YM, Lam CSP, Berger RMF et al. Right ventricular–vascular coupling in heart failure with preserved ejection fraction and pre- vs. post-capillary pulmonary hypertension. Eur Heart J Cardiovasc Imaging 2018;19:425–32.
21. Martens P, Verbrugge FH, Bertrand PB, Verhaert D, Vandervoort P, Dupont M et al. Effect of cardiac resynchronization therapy on exercise-induced pulmonary hypertension and right ventricular–arterial coupling. Circ Cardiovasc Imaging 2018; 11:e007813.
22. Acar RD, Acar S¸, Do_gan C, Bayram Z, Karaduman A, Uysal S et al. The TAPSE/ PASP ratio and MELD score in patients with advanced heart failure. Herz 2020; 305:H1373–7.
23. Tello K, Axmann J, Ghofrani HA, Naeije R, Narcin N, Rieth A et al. Relevance of the TAPSE/PASP ratio in pulmonary arterial hypertension. Int J Cardiol 2018;266: 229–35.
24. French S, Amsallem M, Ouazani N, Li S, Kudelko K, Zamanian RT et al. Non-invasive right ventricular load adaptability indices in patients with sclerodermaassociated pulmonary arterial hypertension. Pulm Circ 2018;8:1–11.
25. Kabrhel C, Jaff MR, Channick RN, Baker JN, Rosenfield K. A multidisciplinary pulmonary embolism response team. Chest 2013;144:1738–9.
26. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015;28: 1–39.
27. Zhang LJ, Lu GM, Meinel FG, McQuiston AD, Ravenel JG, Schoepf UJ. Computed tomography of acute pulmonary embolism: state-of-the-art. Eur Radiol 2015;25:2547–57.
28. Lyhne MD, Schultz JG, MacMahon PJ, Haddad F, Kalra M, Tso DM-K 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.
29. Kabrhel C, Okechukwu I, Hariharan P, Takayesu JK, MacMahon P, Haddad F et al. Factors associated with clinical deterioration shortly after PE. Thorax 2014;69: 835–42.
30. Lobo JL, Holley A, Tapson V, Moores L, Oribe M, Barro´n M, the PROTECT and the RIETE investigators et al. Prognostic significance of tricuspid annular displacement in normotensive patients with acute symptomatic pulmonary embolism. J Thromb Haemost 2014;12:1020–7.
31. Grifoni S, Olivotto I, Cecchini P, Pieralli F, Camaiti A, Santoro G et al. Shortterm clinical outcome of patients with acute pulmonary embolism, normal blood pressure, and echocardiographic right ventricular dysfunction. Circulation 2000; 101:2817–22.
32. Schmid E, Hilberath JN, Blumenstock G, Shekar PS, Kling S, Shernan SK et al. Tricuspid annular plane systolic excursion (TAPSE) predicts poor outcome in patients undergoing acute pulmonary embolectomy. Heart Lung Vessel 2015;7: 151–8.
33. Afonso L, Sood A, Akintoye E, Gorcsan J, Rehman MU, Kumar K et al. A Doppler echocardiographic pulmonary flow marker of massive or submassive acute pulmonary embolus. J Am Soc Echocardiogr 2019;32:799–806.
34. Hofmann E, Limacher A, Me´an M, Kucher N, Righini M, Frauchiger B et al. Echocardiography does not predict mortality in hemodynamically stable elderly patients with acute pulmonary embolism. Thromb Res

2016;145:67–71.

35. Park J-H, Kim JH, Lee J-H, Choi SW, Jeong J-O, Seong I-W. Evaluation of right ventricular systolic function by the analysis of tricuspid annular motion in patients with acute pulmonary embolism. J Cardiovasc Ultrasound 2012;20:181–8.
36. Forton K, Motoji Y, Caravita S, Faoro V, Naeije R. Exercise stress echocardiography of the pulmonary circulation and right ventricular-arterial coupling in healthy adolescents. Eur Heart J Cardiovasc Imaging 2020;73:987.
37. Wolsk E, Bakkestrøm R, Kristensen CB, Aagaard Myhr K, Thomsen JH, Balling L et al. Right ventricular and pulmonary vascular function are influenced by age and volume expansion in healthy humans. J Card Fail 2019;25:51–9.
38. Ferrara F, Rudski LG, Vriz O, Gargani L, Afilalo J, D'Andrea A et al. Physiologic correlates of tricuspid annular plane systolic excursion in 1168 healthy subjects. Int J Cardiol 2016;223:736–43.
39. Lyhne MD, Schultz JG, Kramer A, Mortensen CS, Nielsen-Kudsk JE, Andersen A. Right ventricular adaptation in the critical phase after acute intermediate-risk pulmonary embolism. Eur Heart J Acute Cardiovasc Care 2020. E-pub ahead of print. doi: 10.1177/2048872620925253
40. Saeed S, Smith J, Grigoryan K, Lysne V, Rajani R, Chambers JB. The tricuspid annular plane systolic excursion to systolic pulmonary artery pressure index: association with all-cause mortality in patients with moderate or severe tricuspid regurgitation. Int J Cardiol 2020. Epub ahead of print. doi: 10.1016/j.ijcard.2020.05.093
41. Bosch L, Lam CSP, Gong L, Chan SP, Sim D, Yeo D et al. Right ventricular dysfunction in left-sided heart failure with preserved versus reduced ejection fraction. Eur J Heart Fail 2017;19:1664–71.
42. Ciurzy_nski M, Kurnicka K, Lichodziejewska B, Kozłowska M, Pływaczewska M, Sobieraj P et al. Tricuspid regurgitation peak gradient (TRPG)/tricuspid annulus plane systolic excursion (TAPSE)—a novel parameter for stepwise echocardiographic risk stratification in normotensive patients with acute pulmonary embolism. Circ J 2018;82:1179–85.
43. Vriz O, Pirisi M, Bossone E, Fadl ElMula FEM, Palatini P, Naeije R. Right ventricular-pulmonary arterial uncoupling in mild-to-moderate systemic hypertension. J Hypertens 2020;38:274–81.
44. Champion HC, Michelakis ED, Hassoun PM. Comprehensive invasive and noninvasive approach to the right ventricle-pulmonary circulation unit: state of the art and clinical and research implications. Circulation 2009;120:992–1007.
45. Tampakakis E, Shah SJ, Borlaug BA, Leary PJ, Patel HH, Miller WL et al. Pulmonary effective arterial elastance as a measure of right ventricular afterload and its prognostic value in pulmonary hypertension due to left heart disease. Circ Heart Fail 2018;11:1308–9.
46. Abbas AE, Franey LM, Marwick T, Maeder MT, Kaye DM, Vlahos AP et al. Noninvasive assessment of pulmonary vascular resistance by Doppler echocardiography. J Am Soc Echocardiogr 2013;26:1170–7.
47. Main AB, Braham R, Campbell D, Inglis AJ, McLean A, Orde S. Subcostal TAPSE: a retrospective analysis of a novel right ventricle function assessment method from the subcostal position in patients with sepsis. Ultrasound J 2019;11: 19–8.
48. Barthe´le´my R, Roy X, Javanainen T, Mebazaa A, Chousterman BG. Comparison of echocardiographic indices of right ventricular systolic function and ejection fraction obtained with continuous thermodilution in critically ill patients. Crit Care 2019;23:312.