Right Ventricular Energy Failure Predicts Mortality in Patients With Pulmonary Hypertension

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Right ventricular (RV) failure has a significant adverse impact on pulmonary hypertension (PH) prognosis. None of the currently used parameters directly assess whether RV fails to provide enough energy output to propel the blood through diseased pulmonary vascular system. Furthermore, most of the current parameters are affected by the volume status of the patient. We aimed to explore whether RV energy failure has a predictive power for mortality on top of the established prognostic risk parameters in patients with PH. We screened 723 cases from our database. A total of 3 sets of binary regression analyses were executed to determine the hazard ratios (HRs) of RV energy failure for 5-year mortality in clinical, echocardiographic, and hemodynamic context, using adjustment variables chosen according to previous studies. The final study population encompassed 549 cases. A total of 77 patients died during the 5-year follow-up (14%). RV energy failure was observed in 146 of 549 patients (26.6%). In the univariate model, RV energy failure strongly associated with increased long-term mortality (HR 4.25, 95% confidence interval [CI] 2.58 to 7.00, p <0.001). It also emerged as a significant predictor of long-term mortality in clinical and hemodynamic multivariate models (HR 2.59, 95% CI 1.43 to 4.67, p = 0.002 and HR 2.05, 95% CI 1.15 to 3.63, p = 0.015, respectively). In conclusion, our study indicates that the presence of RV energy failure independently predicts long-term mortality in PH. **(Am J Cardiol 2023;193:19−27)**

Abbreviations: 6MWT, six-minute walk test; NT pro-BNP, N-terminal pro-brain natriuretic peptide; PCWP, pulmonary capillary wedge pressure; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RA, right atrium; RHC, right heart catheterization; RV, right ventricle; sPAP, systolic pulmonary artery pressure ratio; TAPSE, tricuspid annular plane systolic excursion; WHO, World Heart Organization

Pulmonary hypertension (PH) is a mortal and disabling disease that affects approximately 1% of the population worldwide.[1] Although it occurs because of multiple causes, many of the underlying etiologies have a similar pathophysiologic progression. In a common path, increased pulmonary vascular resistance (PVR) and pulmonary pressures lead to an increased right ventricular (RV) afterload, which ultimately results in RV failure. RV failure aggravates symptoms and has a significant adverse prognostic impact.[2]

The diagnosis of RV failure is usually done with the evidence of increased right-sided filling pressures (right atrial [RA] or RV diastolic pressure) or decreased RV systolic performance (ejection fraction, fractional area change, systolic strain, tricuspid annular plane systolic excursion [TAPSE], and so on).[3] However, none of these parameters are directly indicative of whether RV energy output is enough to propel the blood through its respective pulmonary vascular system by overcoming PVR that is the primary cause of the RV failure in the first place. Furthermore, most of the aforementioned parameters if not all are affected by the volume status of the patient. Therefore, a more comprehensive approach focusing on the interaction between the RV and the pulmonary vasculature is needed.

Mechanistically, the RV generates potential energy during isovolumetric contraction and transfers it to the RV stroke volume during ejection, which is consumed for external work of passing the blood through PVR. In normal subjects, RV hydraulic energy output is the excess of the energy loss in pulmonary circulation. Thus, the blood arriving to the left atrium has a higher pressure per volume (i.e., hydraulic energy) than the blood in the RV at the beginning of RV systole. If RV energy output is less than the energy dissipated in pulmonary circulation (will be referred as RV energy failure), the blood loses more of its hydraulic energy and ends up in the left atrium with a lower pressure than RV diastolic pressure. This situation manifests itself with a left atrial (or pulmonary capillary wedge pressure [PCWP]) to RA pressure ratio ≤1 (Figure 1). Because both parts of this relation are determined by the same vascular volumes, the ratio itself is expected to be unaffected by the volume status of the patient. Furthermore, it gives more specific information about RV systolic performance relative to the patient's own pulmonary vascular status, irrespective of the absolute levels of PVR and RV systolic impairment. Therefore, we hypothesize that the presence of RV energy failure has a prognostic significance on top of the established prognostic risk parameters in patients with PH.

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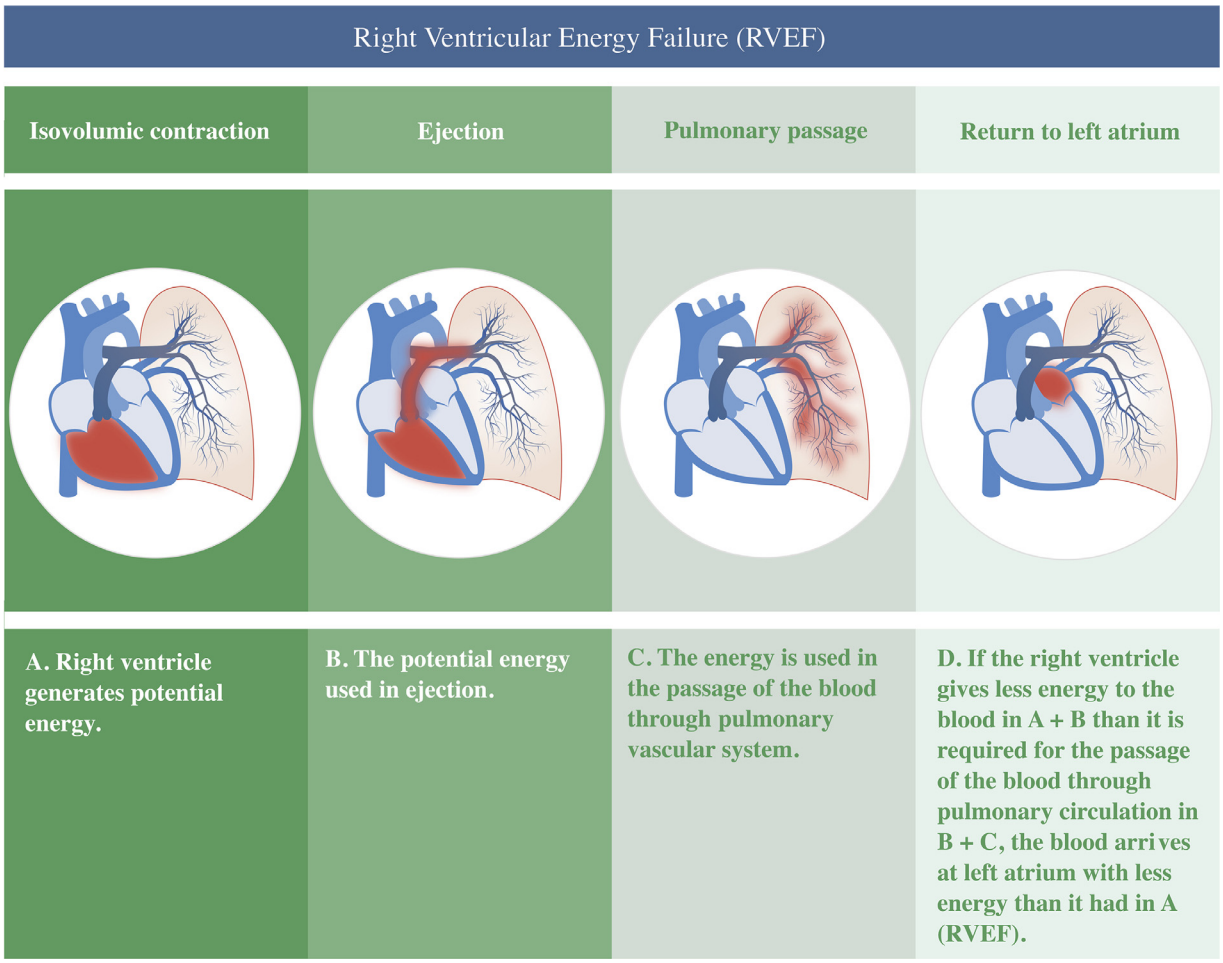


Figure 1. The concept of right ventricular energy failure. The RV generates potential energy during isovolumetric contraction (*A*) and transfers it to RV stroke volume during ejection (*B*), which is consumed during the passage of the blood through PVR (*B+C*). If the energy given by the RV is less than the energy consumed in the pulmonary passage, the blood arriving at the left atrium (*D*) has a lower hydraulic energy, and therefore pressure, compared with the blood in the RV at the beginning of RV systole. Therefore, we define this as RV energy failure where the right atrial pressure (as a surrogate for RV diastolic pressure) is higher than the left atrial pressure. RVEF = right ventricular energy failure.

Methods

The study was undertaken at Marmara University, Pendik Training and Research Hospital, a tertiary center for PH. A local ethical committee approval was obtained, and the study was undertaken in accordance with the Declaration of Helsinki. We retrospectively screened our hospital database for the patients with PH between 2015 and 2022. Only the patients with available right heart catheterization (RHC) results were included in the study.

A multidisciplinary PH team, including a cardiologist, a cardiothoracic surgeon, a pulmonologist, a rheumatologist, and a radiologist, evaluated all patients. All patients underwent a comprehensive examination, including medical assessment, transthoracic echocardiography, multislice computed tomography, ventilation/perfusion scintigraphy, RHC, and selective pulmonary angiography, as required. All patients were managed according to the European Society of Cardiology/European Respiratory Society (ESC/ERS) guidelines for the diagnosis and management of PH.[4,5]

The demographics and laboratory results were obtained through chart review and included complete blood count, kidney function tests, serum N-terminal probrain natriuretic peptide (NT-proBNP) levels, 6-minute walk test (6MWT) distance, and RHC measurements. The echocardiographic data were obtained using ultrasounds machines of the EPIQ series (Philips Medical Systems, Bothell, Washington). The RA area and TAPSE were measured from RV-oriented apical 4-chamber view. The systolic pulmonary artery pressure was estimated using the maximum velocity of tricuspid regurgitation jet and estimated RA pressure in accordance with the simplified Bernoulli equation. When possible, the echocardiographic data were retrieved from the institutional archive and blindly reanalyzed, if not, the reported measurements were taken from the original echocardiogram reports. RHC was performed through the right jugular vein using a Swan-Ganz catheter (Edwards Lifesciences, Irvine, California), and cardiac output was measured using the indirect Fick method. The pressure system calibration was checked before all tracing recordings with square-wave test. All pressure tracings were evaluated by visual exploration for physiologic accuracy, and the end-expiratory pressure values were taken. RV energy failure was defined as the mean PCWP to mean RA pressure ratio ≤ 1 (Figure 1).

Dead or alive status was checked using the national healthcare system.

The SPSS (version 26.0; SPSS Inc., Chicago, Illinois) statistics software was used for statistical analysis. Continuous variables were expressed as mean ± SD or median (interquartile range), and categorical variables were expressed in counts (percentages). The normality of continuous variables was assessed using visual inspection of histograms. The comparisons of the baseline parameters according to the presence or absence of RV energy failure subgroups were performed by chi-square, Student's *t* test, and Mann-Whitney *U* test, as appropriate. The diagnostic accuracy of RV energy failure was calculated using receiver operating characteristics analysis. After the univariate analysis, 3 sets of binary regression analyses were executed to determine the hazard ratio (HR) of RV energy failure for the 5-year mortality in clinical, echocardiographic, and hemodynamic context, using adjustment variables chosen according to previous studies.[1,5–10] Age, World Health Organization (WHO) functional class, 6MWT distance, and NT-proBNP level were used as adjustment variables in clinical model, whereas RA area, TAPSE to estimated systolic pulmonary artery pressure (sPAP) ratio, and the presence or absence of pericardial effusion were included in the echocardiographic model. In the hemodynamic model, RA pressure, cardiac index, stroke index, and mixed venous saturation were used. The cumulative risk of all-cause mortality was displayed using Kaplan–Meier plots and were compared using the log-rank test. A time-fixed Cox proportional hazard regression analysis was executed using age, WHO functional class, 6MWT distance, and NT-proBNP level as the adjustment variables. When the multivariable analyses were repeated for TAPSE to estimated sPAP ratio, a cutoff of 0.19 was used for dichotomization.[5] For all statistical analyses, a $p < 0.050$ was considered significant.

Results

A total of 723 cases was identified in our database; 174 patients were excluded because of incomplete clinical or hemodynamic data. The final study population encompassed 549 cases. The distribution of the patients according to PH subgroups was presented in Figure 2. Among the group IV patients, 143 had been operated for chronic thromboembolic PH (44.5%), 135 had been deemed as inoperable (42.2%), and 42 had undergone pulmonary balloon angioplasty (13.1%). The baseline characteristics are summarized in Table 1. The baseline echocardiographic and invasive hemodynamic parameters are presented in Table 2.

The median follow-up duration was 502 (712) days. A total of 77 patients died during the 5-year follow-up (14%). The 5-year mortality rate was 12.9% (19 of 147) in group I, 3.8% (2 of 53) in group II, 0% (0 of 6) in group III, and

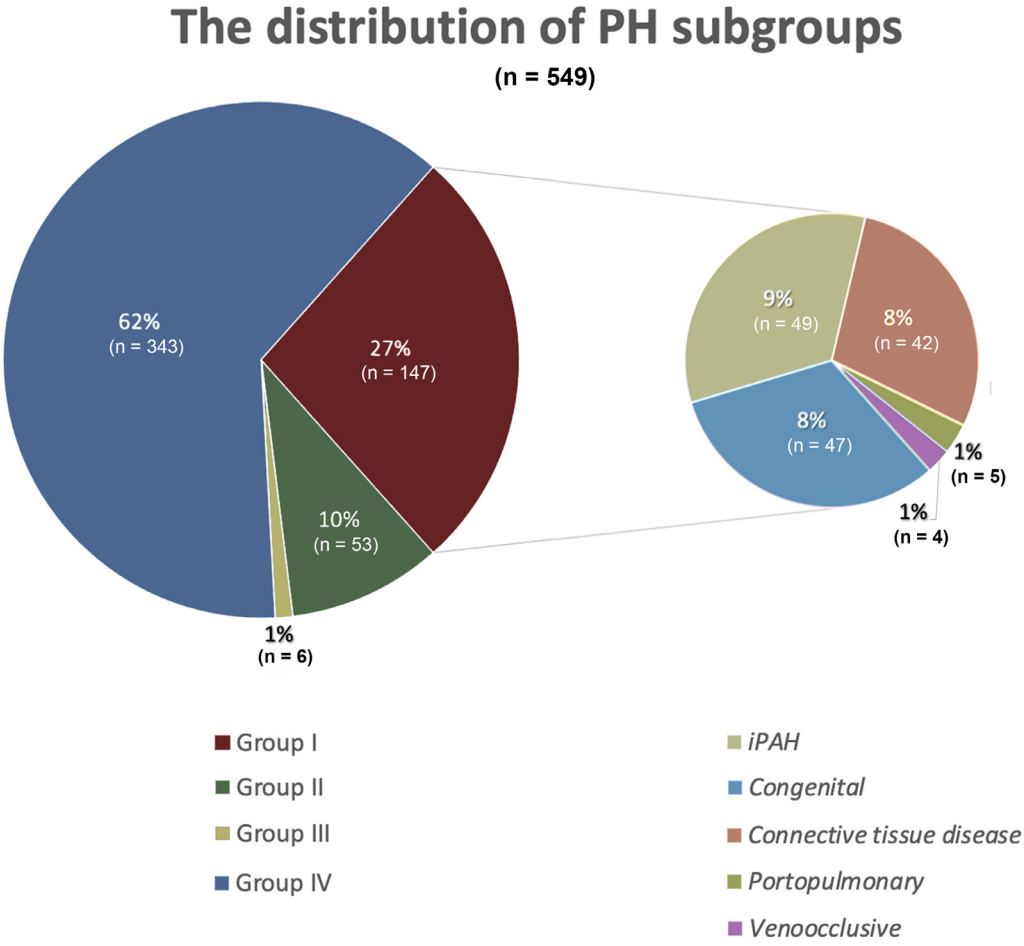


Figure 2. The distribution of pulmonary hypertension subgroups. iPAH = idiopathic pulmonary arterial hypertension.

Table 1
Baseline characteristics

	All (n = 549)	RVEF (n = 146)	No RVEF (n = 403)	p Value
Demographics				
Age, years	56.0±16.0	51.7±16.9	57.5±15.3	<0.001
Female, %	343 (62.5)	265 (65.9)	78 (53.4)	0.021
BMI, $kg.m^{-2}$	28.9±8.5	28.8±12.6	28.9±6.4	0.902
Heart rate, $beats.min^{-1}$	81±15	82±15	81±16	0.303
SBP, mm Hg	132±25	129±25	133±24	0.083
Comorbidities				
Hypertension, n (%)	271 (49.4)	66 (45.2)	205 (50.9)	0.241
Diabetes, n (%)	79 (14.4)	16 (11.0)	63 (15.6)	0.168
Dyslipidemia, n (%)	87 (15.8)	19 (13.0)	68 (16.9)	0.274
CAD, n (%)	90 (16.4)	22 (15.1)	68 (16.9)	0.606
CKD, n (%)	61 (11.1)	20 (13.7)	41 (10.2)	0.246
Thyroid disorders, n (%)	99 (18)	32 (21.9)	67 (16.6)	0.154
Laboratory parameters				
GFR, $mL.min^{-1}.m^2$	104±53	104±52	104±56	0.981
Hemoglobin, $g.dL^{-1}$	12.8±2.8	13.0±1.7	13.1±1.8	0.468
hs-troponin T, $ng.L^{-1}$	12±12	9±10	17±14	<0.001
NT-proBNP, $ng.L^{-1}$	1,365±2,149	1,996±2,442	1,138±1,988	<0.001
Functional class				
WHO class I, n (%)	161 (29.3)	20 (13.7)	141 (35.0)	<0.001
WHO class II, n (%)	244 (44.3)	67 (45.9)	177 (43.9)	
WHO class III, n (%)	135 (24.6)	52 (35.6)	83 (20.6)	
WHO class IV, n (%)	9 (1.6)	7 (4.8)	2 (0.5)	
6MWT, m	340±118	304±117	352±116	<0.001
PH group				
Group I, n (%)	147 (26.8)	42 (28.8)	105 (26.1)	0.283
Group II, n (%)	53 (9.7)	2 (1.4)	51 (12.7)	
Group III, n (%)	6 (1.1)	2 (1.4)	4 (1)	
Group IV, n (%)	343 (62.5)	100 (68.5)	243 (60.3)	
Treatment				
Supportive therapies				
Anticoagulants, n (%)	420 (76.5)	116 (79.5)	304 (75.6)	0.349
Diuretics, n (%)	356 (64.8)	119 (81.5)	237 (59.0)	<0.001
Statins, n (%)	88 (16.0)	21 (14.4)	67 (16.6)	0.552
CCB, n (%)	6 (1.1)	1 (0.7)	5 (1.2)	0.583
PH specific therapy				
PDE5i	15 (2.7)	1 (0.7)	14 (3.5)	0.077
ERA	49 (11.2)	10 (9.7)	39 (6.8)	0.304
Riociguat	258 (46.8)	95 (65.5)	163 (40.5)	<0.001
ERA + PDE5i or Riociguat	82 (14.9)	34 (23.3)	48 (11.9)	0.001
ERA + PDE5i + PCA	29 (5.3)	16 (11.0)	13 (3.2)	<0.001
Follow-up				
Days, median (IQR)	502 (712)	613 (789)	488 (691)	0.190

Values are mean±standard deviation or number (percentage), unless specified otherwise.

BMI = body-mass index; CAD = coronary artery disease; CCB = calcium channel blockers; CKD = chronic kidney disease; CRP = C-reactive protein; ERA = endothelin receptor antagonists; GFR = glomerular filtration rate; hs-TnT = high-sensitivity cardiac troponin T; IQR = interquartile range; MWT = 6-min walk test; NT-proBNP = N-terminal probrain natriuretic peptide; PCA = prostacyclin analogues; PDE5i = phosphodiesterase-5 inhibitors; PH = pulmonary hypertension; RVEF = right ventricular energy failure; SBP = systolic blood pressure.

16.3% (56 of 343) in group IV patients. RV energy failure was observed in 26.6% (146 of 549) in the whole cohort and 28.6% (42 of 147) in group I, 3.8% (2/53) in group II, 33.3% (2 of 6) in group III, and 29.2% (100 of 343) in group IV. The difference in baseline characteristics according to the presence or absence of RV energy failure are summarized in Tables 1 and 2.

The presence of RV energy failure had a sensitivity 28.8% and specificity of 91.3% for the 5-year mortality, respectively (area under curve [AUC] 0.663; 95% confidence interval [CI] 0.593 to 0.732; p <0.001). The diagnostic accuracy did not differ when the analysis was limited to group I (AUC 0.699, 95% CI 0.565 to 0.833, p = 0.005) and group IV patients (AUC 0.646, 95% CI 0.563 to 0.729, p = 0.001). No gender-based difference was observed in the diagnostic accuracy of RV energy failure. When the respective predictive capabilities of RV energy failure components (i.e., PCWP and RA pressure) were separately analyzed, the RA pressure retained its significant predictive power (AUC 0.727, 95% CI 0.670 to 0.784, p <0.001), whereas PCWP did not turn out to have a discriminative accuracy (AUC 0.547, 95% CI 0.488 to 0.605, p = 0.187). However, RV energy failure retained its predictive accuracy in patients with moderately (10 to 19 mm Hg;

Table 2
Echocardiographic and hemodynamic parameters

	All (n = 549)	RVEF (n = 146)	No RVEF (n = 403)	p Value
Echocardiographic parameters				
LVEF, %	58±6	59±5	58±6	0.853
RA area, cm^2	21.4±5.8	25.7±5.3	19.8±5.3	<0.001
TR V_{max}, $m.s^{-1}$	3.8±1.4	4.2±0.6	3.6±1.6	<0.001
sPAP, mm Hg	64±27	83±25	57±24	<0.001
TAPSE, mm	18.7±4.4	15.7±4.1	19.8±4	<0.001
TAPSE/sPAP, $mm.mmHg^{-1}$	0.38±0.26	0.22±0.13	0.44±0.27	<0.001
RV MPI	0.31±0.07	0.27±0.06	0.33±0.07	<0.001
RV TDI S-velocity, $cm.sec^{-1}$	11.3±3.1	9.2±3.1	12.1±2.8	<0.001
Pulmonary acceleration time, ms	117.3±30.7	102.2±30.8	122.7±28.9	<0.001
Pericardial effusion, n (%)	152 (27.7)	79 (54.5)	73 (18.1)	<0.001
Invasive hemodynamic parameters				
PA systolic pressure, mm Hg	64±26	83±25	57±23	<0.001
PA diastolic pressure, mm Hg	24±12	32±13	21±10	<0.001
PA mean pressure, mm Hg	40±16	52±16	35±14	<0.001
Ao systolic pressure, mm Hg	132±25	129±25	133±24	0.083
Ao diastolic pressure, mm Hg	81±33	82±38	79±15	0.363
Ao mean pressure, mm Hg	98±17	97±17	98±16	0.503
RA mean pressure, mm Hg	11±6	15±5	9±5	<0.001
PCWP, mm Hg	12±5	10±3	13±6	<0.001
PVR, woods	6.1±4.6	9.8±5.0	4.8±3.7	<0.001
SVR, woods	18.6±7.9	19.1±6.7	18.5±8.4	0.453
PVR/SVR	0.33±0.23	0.53±0.25	0.26±0.18	<0.001
SaO_2, %	94±5	92±6	94±5	<0.001
MvO_2, %	65.1±9.6	61±10	67±9	<0.001
CO, $L.min^{-1}$	4.9±1.6	4.4±1.6	5.1±1.5	<0.001
CI, $L.min^{-1}.m^{-2}$	2.7±0.9	2.6±1.8	3.1±4.3	0.485
SV, ml	62±22	55±20	65±22	<0.001
SI, $mL.min^{-1}$	34±12	31±11	36±12	<0.001

Values are mean±standard deviation or number (percentage).

Ao = aortic; CI = cardiac index; CO = cardiac output; LVEF = left ventricular ejection fraction; MPI = myocardial performance index; MvO_2 = mixed venous oxygen saturation; PA = pulmonary artery; PCWP = pulmonary capillary wedge pressure; PVR = pulmonary vascular resistance; RA = right atrium; RV = right ventricular; RVEF = right ventricular energy failure; S_AO_2 = systemic oxygen saturation; SI = stroke index; sPAP = estimated systolic pulmonary artery pressure; SV = stroke volume; SVR = systemic vascular resistance; TAPSE = tricuspid annular plane systolic excursion; TDI = tissue Doppler imaging; TR = tricuspid regurgitation; V_{max} = maximum velocity.

sensitivity 29.8%, specificity 85.3%; AUC 610, 95% CI 0.521 to 0.700, p = 0.018) or severely (≥20 mm Hg) increased RA pressure subgroups (sensitivity 46.4%, specificity 93.8%; AUC 714, 95% CI 0.561 to 0.868, p = 0.023).

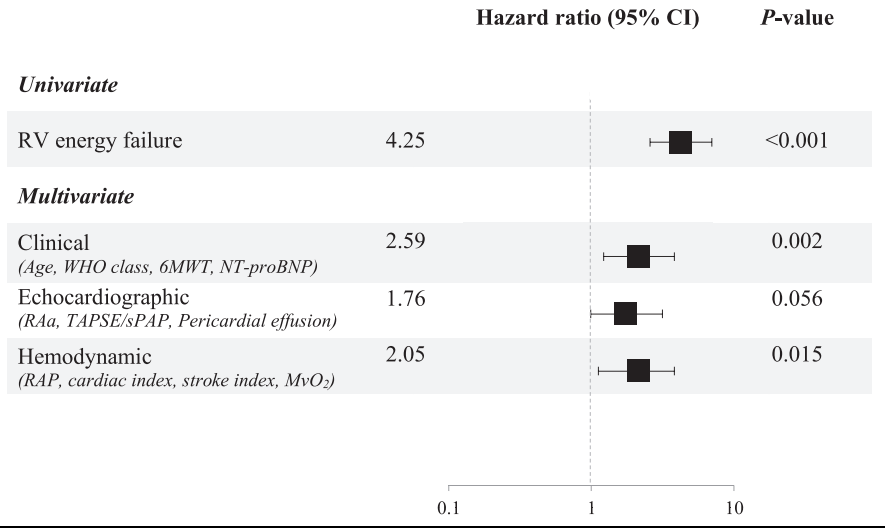
In the univariate model, RV energy failure was strongly associated with increased long-term mortality (HR 4.25, 95% CI 2.58 to 7.00, p <0.001). Although marginally losing its statistical significance in the echocardiographic multivariate model (HR 1.76, 95% CI 0.99 to 3.15, p = 0.056), it again emerged as a significant predictor of long-term mortality in both clinical and hemodynamic multivariate models (HR, 2.59; 95% CI 1.43 to 4.67, p = 0.002 and HR 2.05, 95% CI 1.15 to 3.63, p = 0.015, respectively; Table 3). As a competing variable, a low TAPSE to estimated sPAP ratio was found to be a significant predictor of long-term mortality in the univariate model (HR 2.77, 95% CI 1.69 to 4.56, p <0.001) but lost its significance in all multivariate models, including clinical (HR 1.66, 95% CI 0.91 to 3.02, p = 0.099), echocardiographic (HR 0.61, 95% CI 0.31 to 1.19, p = 0.147), and hemodynamic models (HR 1.61, 95% CI 0.92 to 2.80, p = 0.093).

The Kaplan−Meier survival estimates showed that the presence of RV energy failure was significantly associated with worse survival (p <0.001; Figure 3). This association was preserved when the analysis was limited to group I (p = 0.004) and group IV (p = 0.001). In the Cox proportional hazards model, RV energy failure also appeared as a significant factor for predicting mortality (HR 1.88, 95% CI 1.17 to 3.05, p = 0.010) even after adjusting for age, WHO class, 6MWT distance, and NT-proBNP level (Figure 3). As a competing variable, a low TAPSE to estimated sPAP ratio did not turn out to be a significant predictor of long-term mortality in the same model (HR 1.60, 95% CI 0.98 to 2.64, p = 0.062).

Discussion

Pulmonary hemodynamics has always been an uncharted territory and its pathophysiology, especially related to PH, is still not completely understood. The pulmonary hemodynamic parameters show remarkable variations compared with their systemic counterparts. For example, PVR in PH may increase by a factor of 5 compared with about 50% in systemic hypertension.[11] Similarly, the RV is capable of increasing its contractility fourfold to fivefold before RV failure becomes manifest,

Table 3
Hazard ratios of RV energy failure for mortality in different models



6MWT = 6-min walk test; CI = confidence interval; MvO_2 = mixed venous oxygen saturation; NT-proBNP = N-terminal probrain natriuretic peptide; RAa = right atrial area; RAP = right atrial pressure; RV = right ventricular; sPAP = estimated systolic pulmonary artery pressure; TAPSE = tricuspid annular plane systolic excursion; WHO = World Health Organization.

such a significant degree and long course of adaptation is not possible for left ventricular failure.[12] Therefore, it is necessary to assess the RV contractile performance in the context of its own afterload rather than focusing on 1 side of this relation in isolation.[11–13]

Contrary to the intuition, many hemodynamic parameters have failed to show an important prognostic power in isolation, including pulmonary artery pressure itself that gives its name to the disease.[4] Despite their interdependence and contradicting significance in different studies,[14–17] a few parameters, such as RA pressure, cardiac index, stroke index, and mixed venous saturation, have been shown to have some predictive power and incorporated into the recent ESC/ERS risk classification scheme.[5] Nevertheless, these parameters actually indicate a different dimension of the disease and path to mortality, such as a high RA pressure implying excessive water sparing because of highly active neurohormonal system and a low cardiac or stroke index or low mixed venous saturation signifying a cardiac output that cannot meet the demands of the body.[18] Therefore, they do not depict a complete picture of PH hemodynamics because they do not provide any information about the RV-pulmonary vascular system integration. Correspondingly, our results indicate that the presence of RV energy failure predicts long-term mortality even after the correction for these parameters and provides additional prognostic information not captured by them.

Ventriculoarterial coupling has been a popular parameter to assess the RV-pulmonary vascular bed interaction and is calculated as the ratio of end-systolic elastance to arterial elastance, which should be between certain limits for both the maximum and the most efficient energy transfer from ventricle to its vascular bed.[19] Although this concept was adapted from the studies on the left ventricle, it has also been studied in PH,[20–23] and its noninvasive surrogates have been proposed for clinical use.[24–29] Recently, ESC/ERS guidelines incorporated the TAPSE to estimated sPAP into the recommended risk classification scheme as a noninvasive marker of RV ventriculoarterial coupling.[5] Interestingly, the same guidelines did not recommend more reliable volume- or pressure-based methods for its calculation with echocardiography, magnetic resonance imaging, or RHC.[21,25,30,31] This reservation may reflect the limitations of the concept originating from its complicated nature and the assumptions needed for its calculation. Aside from its impracticality, ventriculoarterial coupling may also have a limited predictive power for mortality because of the considerable RV coupling reserve that sustains enough energy transfer for the maintenance of the normal circulation until the later stages of the disease.[32]

Our novel parameter, RV energy failure, is a different approach to the relation between the RV and the pulmonary circulation and implies a worse scenario, where the RV is incapable of propelling the blood from the pulmonary circulation. In addition to being a definite definition of RV failure in energetical sense, RV energy failure also represents the turning point from a dominant right-sided cardiac disease into a biventricular disorder because the circulatory pathophysiology resembles the Fontan circulation without adequate energy input from RV, where the fate of circulation becomes critically dependent on left ventricular energy output. This may partly explain why the presence of RV energy failure picks a patient subgroup with a disturbing hemodynamic profile with lower cardiac output and cardiac index. Also, it partially explains why RV energy failure is seen less frequently in group II patients in our study and in other studies.[33,34] A double ventricular "energy failure" situation would be a rare occurrence because it is expected to have dire consequences.

Our results indicate that despite selecting a very high-risk patient subpopulation, the presence of RV energy failure still preserves its prognostic impact after adjusting for

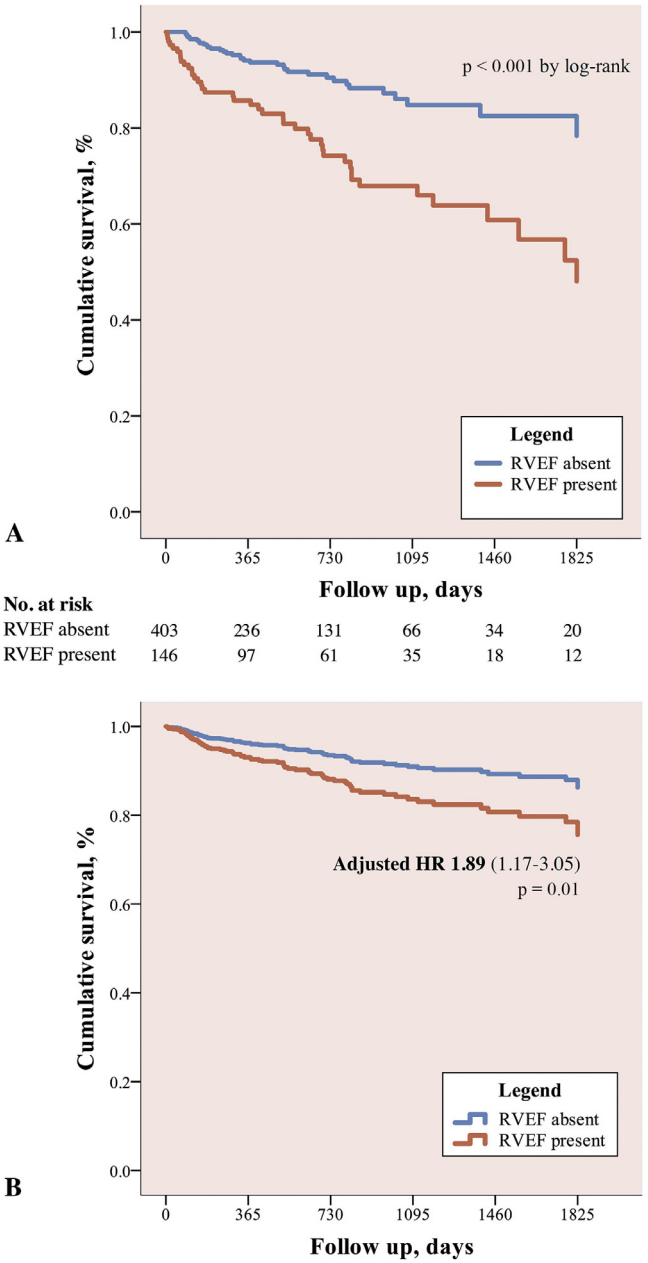


Figure 3. Kaplan−Meier (*A*) and Cox proportional hazard (*B*) curves for mortality according to the presence or absence of RVEF. RVEF = right ventricular energy failure.

age, WHO functional class, 6MWT distance, and NT-proBNP level in the clinical model. These adjustment variables have been proposed as the most significant prognostic parameters by the ESC/ERS guidelines and incorporated in many risk prediction systems, such as the ESC/ERS,[4,5] REVEAL,[6] REVEAL Lite[8], and COMPERA[10] risk scores. Therefore, RV energy failure seems to have incremental value over the currently recommended risk classification schemes.

The concept of RV energy failure is more straightforward than its counterparts assessing ventriculoarterial coupling and does not rely on complicated assumptions and can be easily obtained. Furthermore, the RV energy failure concept is expected to be volume-independent because the same stroke volume is used for the calculation of both generated and wasted hydraulic energy. Correspondingly, our results indicate that RV energy failure has a stronger prognostic predictive value than ventriculoarterial coupling, as assessed noninvasively by the ratio of TAPSE to estimated sPAP. Although it is beyond the scope of this study, whether RV energy failure performs better than invasively defined ventriculoarterial coupling in mortality prediction is worth elucidating in further studies.

Our study has several limitations. As a tertiary center specialized on chronic thromboembolic PH, our PH cohort had a different distribution in terms of PH subgroups, which showed dominance of group IV patients. Although this may affect the predictive power of RV energy failure, it should be noted that RV energy failure also predicted long-term mortality in group I patients. The RA pressure to PCWP ratio was previously studied in group I patients with PH as an indicator of RV failure and lower values were found to be associated with a worse 1-year survival rate.[35] Therefore, the inclusion of other PH groups with a higher proportion actually extends previous observations. Many of the adjustment parameters used in the regression analyses have been less extensively studied in group 4 patients; therefore, the effect of these corrections may differ in various PH cohorts. Overall mortality rate in our cohort was slightly lower than in previous studies, which might have limited the diagnostic accuracy of RV energy failure. Although we used several adjustment models, the possibility of collinearity between the presence of RV energy failure and other prognostic parameters cannot be excluded.

In conclusion, our study indicates that the presence of RV energy failure nearly doubles the mortality of PH even after correction for many established prognostic parameters. Whether the addition of this hemodynamic parameter to the current risk scores would increase their predictive power should be tested in prospective trials.

Disclosures

The authors have no conflicts of interest to declare.

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