Right Ventricular Pulmonary Artery Coupling and Mortality in Cardiac Intensive Care Unit Patients

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BACKGROUND: Impaired right ventricular (RV) pulmonary artery coupling has been associated with higher mortality in patients with chronic heart disease, but few studies have examined this metric in critically ill patients. We sought to evaluate the association between RV pulmonary artery coupling, defined by the ratio of tricuspid annular peak systolic tissue Doppler velocity (TASV)/estimated RV systolic pressure (RVSP), and mortality in cardiac intensive care unit patients.

METHODS AND RESULTS: Using a database of unique cardiac intensive care unit admissions from 2007 to 2018, we included patients with TASV/RVSP ratio measured within 1 day of hospitalization. Hospital mortality was analyzed using multivariable logistic regression, and 1-year mortality was analyzed using multivariable Cox proportional-hazards analysis. We included 4259 patients with a mean age of 69±15 years (40.1% women). Admission diagnoses included acute coronary syndrome in 56%, heart failure in 52%, respiratory failure in 24%, and cardiogenic shock in 12%. The mean TASV/RVSP ratio was 0.31±0.14, and in-hospital mortality occurred in 7% of patients. Higher TASV/RVSP ratio was associated with lower in-hospital mortality (adjusted unit odds ratio, 0.68 per each 0.1-unit higher ratio; 95% CI, 0.58–0.79; P<0.001) and lower 1-year mortality among hospital survivors (adjusted unit hazard ratio, 0.83 per each 0.1-unit higher ratio; 95% CI, 0.77–0.90; P<0.001). Stepwise decreases in hospital and 1-year mortality were observed in each higher TASV/RVSP quintile. The TASV/RVSP ratio remained associated with mortality after adjusting for left ventricular systolic and diastolic function.

CONCLUSIONS: A low TASV/RVSP ratio is associated with increased short-term and long-term mortality among cardiac intensive care unit patients, emphasizing importance of impaired RV pulmonary artery coupling as a determinant of poor prognosis. Further study is required to determine whether interventions to optimize RV pulmonary artery coupling can improve outcomes.

Key Words: cardiac intensive care unit ■ Doppler ■ echocardiography ■ mortality ■ pulmonary hypertension ■ right heart failure ■ right ventricle
afterload is referred to as maintaining RV-PA coupling. 12 Echocardiographic measures of RV-PA coupling involve the ratio of RV longitudinal motion (ie, TAPSE or TASV)/the RV systolic pressure (RVSP) or PA systolic pressure. 3,12 Studies evaluating the TAPSE/RVSP ratio in patients with cardiovascular disease have shown associations between lower TAPSE/RVSP ratio (reflecting worse RV-PA coupling) and adverse outcomes. 12–19 Prior studies evaluating RV-PA coupling using the TASV/RVSP ratio have involved invasive measurements of PA systolic pressure, rather than noninvasive RVSP derived from Doppler transthoracic echocardiography (TTE). 20–24 To our knowledge, no published studies have examined the association between noninvasive measures of RV-PA coupling and outcomes using either the TAPSE/RVSP or TASV/RVSP ratio by TTE in critically ill patients. Because the TASV is potentially less load dependent than TAPSE, we sought to determine the association between RV-PA coupling, as determined by the TASV/RVSP ratio using Doppler TTE, and mortality in unselected cardiac intensive care unit (CICU) patients.

**METHODS**

**Study Population**

The authors declare that all supporting data are available within the article and its online supplementary files. This study was approved by the Institutional Review Board of Mayo Clinic (No. 16-000722) as posing minimal risk to patients, and was performed under a waiver of informed consent. We retrospectively analyzed a previously constructed database of consecutive unique adult patients, aged ≥18 years, admitted to the CICU at Mayo Clinic Hospital St. Mary's Campus between January 1, 2007, and April 30, 2018, to identify patients with a clinically indicated TTE performed during or within 1 day of hospitalization. 25,26 We excluded patients who did not have available data to calculate the TASV/RVSP ratio.

**Data Sources**

We recorded demographic, vital sign, laboratory, clinical, and outcome data, as well as procedures and therapies performed during the CICU and hospital stay; invasive hemodynamic data, physical examination, symptoms, imaging, and ECG data were not available. 27–31 All relevant data were extracted electronically from the medical record using the Multidisciplinary Epidemiology and Translational Research in Intensive Care Data Mart, a repository storing clinical data from all intensive care unit admissions at the Mayo Clinic Rochester. 32 The admission value of all vital signs, clinical measurements, and laboratory values was defined as either the first value recorded after CICU admission or the value recorded closest to CICU admission. 30 Admission diagnoses were defined as all *International Classification of Diseases, Ninth Revision (ICD-9)*, diagnostic codes...
on the day of CICU admission and 1 day before or after.\textsuperscript{25}

**Severity of Illness Scores**
The Acute Physiology and Chronic Health Evaluation III score, Acute Physiology and Chronic Health Evaluation IV, which predicted hospital mortality, and Sequential Organ Failure Assessment score were automatically calculated for all patients using data from the first 24 hours of CICU admission using previously validated electronic algorithms, with missing variables imputed as normal as the default.\textsuperscript{27–31} The Charlson Comorbidity Index and individual comorbidities were extracted from the medical record using a previously validated electronic algorithm.\textsuperscript{33}

**Echocardiographic Data**
The Mayo Clinic Echocardiography Database was queried, and the TTE performed closest to the date of CICU admission (either before or after) was identified. Vital signs at the time of the TTE were recorded. Numeric variables were extracted from the database, as listed in Table S1. One left ventricular ejection fraction (LVEF) value for each patient was determined using a hierarchical approach: volumetric LVEF, calculated using the Simpson biplane method, was preferred, followed by 2-dimensional and linear calculated LVEF, followed by visual estimation if these other methods were unavailable. The right atrial pressure (RAP) was estimated on the basis of the size and collapsibility of the inferior vena cava; if an invasive measurement of RAP was available at the time of TTE, this was substituted. The RVSP was estimated as follows: RAP\text{[}+\text{4×peak TR velocity]}\textsuperscript{2}, based on spectral Doppler (Table S2). The TASV/RVSP ratio was calculated as the ratio of TASV by tissue Doppler imaging (in cm/s)/the RVSP (in mm Hg). As a simplified version of the TASV/RVSP ratio, the ratio of TASV/TR velocity was also calculated. If TAPSE was available, the TAPSE/RVSP ratio was calculated.

**Statistical Analysis**
CICU, hospital, and 1-year mortality were determined using electronic review of health records. Because there is no commonly accepted normal range or established cutoff for the TASV/RVSP ratio, patients were grouped by TASV/RVSP quintiles. Categorical variables are reported as number (percentage), and the Pearson χ\textsuperscript{2} test was used to compare groups; trends across TASV/RVSP quintiles were analyzed using the Cochran-Armitage trend test. Continuous variables are reported as mean±SD, and the Wilcoxon rank-sum test was used to compare groups. Trends across TASV/RVSP quintiles were analyzed using linear regression. Pearson \textit{r} correlation coefficients were calculated between TASV/RVSP and other TTE variables. Logistic regression was used to determine the association between the TASV/RVSP ratio and hospital mortality, and receiver-operator characteristic curves were constructed to determine area under the receiver-operator characteristic curve (AUC) values, with 95% CIs generated using 1000-sample bootstrapping; the optimal cutoff for predicting hospital mortality was defined as the highest value of the Youden J index (sensitivity+specificity−1). AUC values were compared using the De Long test. Multivariable analysis was performed using logistic regression, with 24 clinically relevant covariates selected a priori, including demographics, comorbidities, illness severity, admission diagnoses, and the use of critical care therapies and procedures. Separate multivariable logistic regression models were generated, using either the TASV/RVSP ratio itself (per 0.1 unit) or the TASV/RVSP quintile as a continuous variable. Interaction terms between the TASV/RVSP ratio and admission diagnoses of interest were added to the multivariable logistic regression model. Survival up to 1 year was evaluated using Kaplan-Meier survival analysis, with TASV/RVSP quintiles compared using the log-rank test. Cox proportional-hazards analysis was used to determine predictors of postdischarge mortality up to 1 year in hospital survivors, adjusting for the same variables as the multivariable logistic regression model. The proportional-hazards assumption was confirmed on the basis of the final multivariable Cox model. Two-tailed \textit{P}<0.05 was considered statistically significant. Statistical analyses were performed using JMP Pro version 14.1.0 (SAS Institute, Cary, NC).

**RESULTS**

**Study Population**
Of 12 428 potentially eligible unique CICU patient admissions, 8169 were excluded (2138 without a TTE during or within 1 day before or after hospitalization and 6031 whose TTE did not have available data for TASV/RVSP ratio), leaving 4259 patients in the final study population (Figure 1). Patients who were included in the final study population differed significantly from patients who were excluded from the study (Table 1); in particular, included patients were older, had a higher prevalence of acute coronary syndrome (ACS) and heart failure (HF), and had greater use of coronary angiography and percutaneous coronary intervention. The mean age of the final study population was 69.3±14.6 years, and 40.1% were women. Admission diagnoses (not mutually exclusive) in the final study population included ACS in 55.5%, HF in 51.5%, respiratory failure in 24.4%,
cardiogenic shock in 12.4%, cardiac arrest in 11.0%, and sepsis in 6.3% (Table 1).

Definition of TASV/RVSP Quintiles
The TASV/RVSP ratio quintiles were defined as follows: quintile 1, <0.18; quintile 2, 0.18 to 0.25; quintile 3, 0.25 to 0.33; quintile 4, 0.33 to 0.43; and quintile 5, ≥0.43 (with higher TASV/RVSP reflecting better RV-PA coupling); the mean TASV/RVSP ratio was 0.31±0.14, with a median of 0.29 (interquartile range, 0.19–0.4). Patient characteristics differed significantly across quintiles of TASV/RVSP ratio (Table 2). Patients with better RV-PA coupling (ie, higher TASV/RVSP quintiles) were younger and less likely to be women, had lower severity of illness and less use of critical care therapies, and had fewer comorbidities and critical care admission diagnoses (Table 2).

Cardiac Structure and Function by TTE
TTE was performed within 1 day of CICU admission in 3498 (82.1%) patients, including 1492 (35.0%) with TTE performed on the day of CICU admission. Measured TTE variables differed substantially across TASV/RVSP ratio quintiles (Table 3), with trends reflecting better biventricular function and lower biventricular filling pressures at higher TASV/RVSP ratio quintiles (Figure S1A and S1B). TASV/RVSP ratio varied as a function of admission diagnosis, being highest in patients with ACS and lower in patients with HF, cardiogenic shock, sepsis, or respiratory failure. TAPSE was available in 1231 (28.9%) patients, and TAPSE correlated with TASV (Pearson r=0.70; P<0.001). As expected, the TAPSE/RVSP ratio correlated strongly with TASV/RVSP ratio (Pearson r=0.88; P<0.001; Figure S2). Qualitative RV function was reported for 2787 (65.4%) patients (Table 3), including 855 (30.7%) with moderate or greater RV dysfunction. As expected, the prevalence of qualitative RV dysfunction increased with lower TASV/RVSP quintile (P<0.001).

Hospital Mortality: Univariable Analyses
Hospital mortality occurred in 306 (7.2%) patients, including 191 (4.5%) who died in the CICU. Patients who died in the hospital had a lower TASV/RVSP ratio (0.21±0.11 versus 0.31±0.15; P<0.001), resulting from...
### Table 1. Baseline Characteristics, Comorbidities, Admission Diagnoses, Therapies, Selected Echocardiographic Variables, and Outcomes of Patients Who Were Included and Excluded From the Final Study Population

| Variable | Final Study Population (n=4529) | Excluded Patients (n=8169) | P Value |
|----------|---------------------------------|--------------------------|--------|
| **Demographics and outcomes** | | | |
| Age, y | 69.3±14.6 | 66.7±15.4 | <0.001 |
| Female sex | 1706 (40.1) | 2980 (36.5) | <0.001 |
| White race | 3941 (92.5) | 7525 (92.1) | 0.41 |
| **Echocardiographic Variables** | | | |
| CICU length of stay, d | 2.6±1.8 | 2.4±1.5 | <0.001 |
| Hospital length of stay, d | 7.6±10.3 | 8.2±14.7 | 0.03 |
| CICU mortality | 191 (4.5) | 525 (6.4) | <0.001 |
| Hospital mortality | 306 (7.2) | 843 (10.3) | <0.001 |
| 1-y mortality | 976 (21.6) | 1920 (23.2) | 0.02 |
| **Comorbidities** | | | |
| Charlson Comorbidity Index | 2.3±2.6 | 2.4±2.7 | <0.001 |
| History of MI | 746 (16.7) | 1554 (19.1) | 0.04 |
| History of HF | 755 (17.8) | 1766 (21.7) | <0.001 |
| History of DM | 1153 (27.1) | 2391 (29.3) | 0.01 |
| History of lung disease | 795 (18.7) | 1615 (19.8) | 0.14 |
| History of CKD | 812 (19.1) | 1749 (21.4) | 0.002 |
| Prior dialysis | 167 (3.9) | 453 (5.6) | <0.001 |
| **Admission diagnoses** | | | |
| ACS | 2342 (51.5) | 2896 (35.8) | <0.001 |
| HF | 2173 (51.5) | 3835 (47.4) | <0.001 |
| Shock | 638 (15.1) | 1221 (15.1) | 0.96 |
| CS | 524 (12.4) | 974 (12.0) | 0.53 |
| Cardiac arrest | 484 (11.0) | 1015 (12.5) | 0.01 |
| Respiratory failure | 1031 (24.4) | 1955 (24.1) | 0.73 |
| Sepsis | 268 (6.3) | 512 (6.3) | 0.95 |
| **Procedures and therapies** | | | |
| Vasopressors | 808 (19.0) | 1864 (22.8) | <0.001 |
| Inotropes | 330 (7.7) | 820 (10.0) | <0.001 |
| Invasive ventilator | 582 (13.7) | 1452 (18.2) | <0.001 |
| Noninvasive ventilator | 661 (15.5) | 1262 (15.4) | 0.92 |
| Dialysis in CICU | 176 (4.1) | 418 (5.0) | 0.01 |
| CRRT | 39 (2.1) | 155 (1.9) | 0.46 |
| IABP in CICU | 356 (8.4) | 695 (8.5) | 0.78 |
| PAC in CICU | 383 (9.0) | 815 (10.0) | 0.08 |
| Coronary angiogram | 2744 (64.4) | 4510 (55.3) | <0.001 |
| PCI | 1777 (41.7) | 2543 (31.1) | <0.001 |
| RBC transfusion | 410 (9.6) | 983 (12.0) | <0.001 |
| In-hospital CPR | 95 (2.2) | 222 (2.7) | 0.09 |
| **Severity of illness scores** | | | |
| APACHE-III score | 60.2±23.7 | 61.0±25.8 | 0.54 |
| APACHE-IV predicted mortality, % | 16.4±18.6 | 17.1±20.3 | 0.09 |
| Day 1 SOFA score | 3.3±3.1 | 3.6±3.2 | <0.001 |
| Braden skin score | 17.9±3.2 | 17.6±3.4 | <0.001 |
| **Vital signs at TTE** | | | |
| TTE within 1 d of hospitalization | 4259 (90.0) | 1786 (22.8) | <0.001 |
| TTE within 1 d of CICU admission | 3498 (82.1) | 3946 (48.3) | <0.001 |

(Continued)
Table 2. Baseline Characteristics, Comorbidities, Admission Diagnoses, and Therapies of Patients, According to TASV/RVSP Quintiles, Where Higher Quintiles Reflect Better RV-PA Coupling

| Variable                              | Quintile 1 (n=852) | Quintile 2 (n=829) | Quintile 3 (n=848) | Quintile 4 (n=895) | Quintile 5 (n=835) | P Value |
|---------------------------------------|--------------------|--------------------|--------------------|--------------------|--------------------|---------|
| **Demographics**                      |                    |                    |                    |                    |                    |         |
| Age, y                                | 71.3±14.5          | 72.5±14.4          | 71.2±14.0          | 68.1±13.7          | 63.5±14.8          | <0.001  |
| Female sex                            | 367 (43.1)         | 359 (43.3)         | 354 (41.8)         | 339 (37.9)         | 287 (34.4)         | <0.001  |
| White race                            | 762 (89.4)         | 765 (92.3)         | 800 (94.3)         | 835 (93.3)         | 779 (93.3)         | 0.002   |
| **Comorbidities**                     |                    |                    |                    |                    |                    |         |
| Charlson Comorbidity Index            | 3.3±2.9            | 2.7±2.6            | 2.3±2.4            | 1.7±2.1            | 1.4±2.1            | <0.001  |
| History of MI                         | 186 (21.9)         | 172 (20.8)         | 150 (17.7)         | 139 (15.6)         | 99 (11.9)          | <0.001  |
| History of HF                         | 329 (38.7)         | 195 (23.6)         | 113 (13.4)         | 79 (8.8)           | 39 (4.7)           | <0.001  |
| History of DM                         | 331 (38.9)         | 255 (30.8)         | 222 (26.2)         | 205 (23.0)         | 140 (16.8)         | <0.001  |
| History of lung disease               | 214 (25.2)         | 198 (23.9)         | 156 (18.4)         | 132 (14.8)         | 95 (11.4)          | <0.001  |
| History of CKD                        | 284 (33.4)         | 207 (25.0)         | 155 (18.3)         | 104 (11.6)         | 62 (7.4)           | <0.001  |
| Prior dialysis                        | 63 (7.4)           | 51 (6.2)           | 19 (2.2)           | 19 (2.1)           | 15 (1.8)           | <0.001  |
| **Admission diagnoses**               |                    |                    |                    |                    |                    |         |
| ACS                                   | 305 (35.8)         | 391 (47.5)         | 493 (58.7)         | 580 (65.5)         | 573 (69.7)         | <0.001  |
| HF                                    | 714 (83.9)         | 562 (68.3)         | 419 (49.9)         | 301 (34.5)         | 177 (21.5)         | <0.001  |
| Shock                                 | 180 (21.2)         | 182 (22.1)         | 125 (14.9)         | 88 (9.9)           | 63 (7.7)           | <0.001  |
| CS                                    | 153 (18.0)         | 152 (18.5)         | 104 (12.4)         | 65 (7.3)           | 50 (6.1)           | <0.001  |
| Cardiac arrest                        | 93 (10.9)          | 109 (13.2)         | 101 (12.0)         | 96 (10.8)          | 65 (7.9)           | 0.015   |
| Respiratory failure                   | 320 (37.6)         | 283 (34.4)         | 209 (24.9)         | 149 (16.8)         | 70 (8.5)           | <0.001  |
| Sepsis                                | 74 (8.7)           | 77 (9.4)           | 57 (6.8)           | 41 (4.6)           | 19 (2.3)           | <0.001  |
| **Severity of illness scores**        |                    |                    |                    |                    |                    |         |
| APACHE-III score                      | 70.3±23.9          | 67.4±24.1          | 60.8±22.5          | 54.2±21.3          | 48.7±19.5          | <0.001  |
| APACHE-IV predicted hospital mortality, % | 23.7±21.0         | 21.3±20.8          | 16.4±17.8          | 11.9±15.0          | 8.8±12.5           | <0.001  |
| Day 1 SOFA score                      | 4.8±3.3            | 4.1±3.3            | 3.2±2.9            | 2.5±2.5            | 1.9±2.2            | <0.001  |
| Braden skin score                     | 16.9±3.2           | 17.3±3.3           | 17.8±3.2           | 18.5±3.0           | 19.1±2.8           | <0.001  |
| **Outcomes**                          |                    |                    |                    |                    |                    |         |
| CICU length of stay, d                | 3.5±6.3            | 3.0±4.4            | 2.4±2.1            | 2.1±1.9            | 1.8±1.7            | <0.001  |
| Hospital length of stay, d            | 11.0±14.0          | 9.5±11.7           | 7.0±9.3            | 5.7±7.1            | 4.7±6.1            | <0.001  |
| CICU mortality                        | 93 (10.9)          | 40 (4.8)           | 34 (4.0)           | 17 (1.9)           | 7 (0.8)            | <0.001  |
| Hospital mortality                    | 131 (15.4)         | 84 (10.1)          | 47 (5.5)           | 33 (3.7)           | 11 (1.3)           | <0.001  |
| 1-y Mortality                         | 359 (42.1)         | 234 (28.2)         | 162 (19.1)         | 103 (11.5)         | 61 (7.3)           | <0.001  |

Data displayed as number (percentage) for categorical variables or mean±SD for continuous variables. P value is for the Cochran-Armitage trend test (categorical variables) or linear regression (continuous variables) across TASV/RVSP ratio quintiles. ACS indicates acute coronary syndrome; APACHE, Acute Physiology and Chronic Health Evaluation; CICU, cardiac intensive care unit; CKD, chronic kidney disease; CPR, cardiopulmonary resuscitation; CRRT, continuous renal replacement therapy; CS, cardiogenic shock; DM, diabetes mellitus; HF, heart failure; IABP, intra-aortic balloon pump; MI, myocardial infarction; PA, pulmonary artery; PAC, PA catheter; PCI, percutaneous coronary intervention; RBC, red blood cell; RV, right ventricular; RVSP, RV systolic pressure; SOFA, Sequential Organ Failure Assessment; and TASV, tricuspid annular peak systolic tissue Doppler velocity.

*Admission diagnoses are not mutually exclusive and sum to >100%.
both lower TASV (10.1±3.9 versus 11.6±3.4 cm/s; 
\textit{P}<0.001) and higher RVSP (50.9±18.1 versus 42.1±15.5 mm Hg; 
\textit{P}<0.001). Patients in the lowest 2 quintiles of TASV/RVSP ratio accounted for most inpatient deaths (quintile 1, 42.8%; and quintile 2, 27.4%), whereas only 3.6% of inpatient deaths were in TASV/RVSP ratio quintile 5. A clear stepwise decrease in CICU and hospital mortality was observed with increasing TASV/RVSP ratio quintile (unadjusted odds ratio [OR], 0.560 per each higher TASV/RVSP quintile; 
95% CI, 0.507–0.617; \textit{P}<0.001; Figure S3).

TASV/RVSP ratio was inversely associated with hospital mortality (unadjusted unit OR, 0.516 per each 0.1 higher TASV/RVSP ratio; 
95% CI, 0.461–0.578; \textit{P}<0.001; AUC, 0.719; 95% CI, 0.690–0.744), with an optimal cutoff value of 0.25 for prediction of hospital mortality corresponding
Inverse relationships between TASV/RVSP ratio and mortality were observed in patients with each admission diagnosis (Figure 2). The association between TASV/RVSP ratio and mortality differed as a function of admission diagnosis (Table 4), being strongest (AUC, 0.73) for patients with ACS and weakest (AUC, 0.58; \( P = 0.08 \)) for patients with sepsis.

**Hospital Mortality Discrimination by TTE**

The AUC value for hospital mortality for the TASV/RVSP ratio was higher than that for TASV (AUC, 0.64; 95% CI, 0.61–0.68; \( P < 0.001 \) by De Long test), RVSP (AUC, 0.68; 95% CI, 0.65–0.71; \( P = 0.004 \) by De Long test), or TASV/TR velocity ratio (AUC, 0.69; 95% CI, 0.65–0.72; \( P < 0.001 \) by De Long test). Among the 1231 (28.9%) with available data for the TAPSE/RVSP ratio, the AUC value for hospital mortality (0.68; 95% CI, 0.63–0.73) was similar to that observed for the TASV/RVSP ratio in this group (\( P = 0.47 \) by De Long test). Addition of the TASV/RVSP ratio to the Acute Physiology and Chronic Health Evaluation III score alone resulted in an improvement in discrimination for hospital mortality (AUC, 0.822 versus 0.764; \( P < 0.001 \) by De Long test).

**Hospital Mortality: Multivariable Analyses**

After multivariable adjustment (Table 5), TASV/RVSP ratio remained inversely associated with hospital mortality (adjusted unit OR, 0.676 per each 0.1 higher; 95% CI, 0.582–0.786; \( P < 0.001 \)). Discrimination for hospital mortality by the multivariable model was excellent with or without inclusion of the TASV/RVSP ratio in the model (AUC, 0.914 versus 0.909, respectively; \( P = 0.11 \) by De Long test). Each higher TASV/RVSP ratio quintile was associated with lower adjusted hospital mortality (adjusted OR, 0.714 per each higher TASV/RVSP ratio quintile; 95% CI, 0.627–0.814; \( P < 0.001 \)); each other TASV/RVSP quintile had lower hospital-adjusted mortality than quintile 1 (all \( P < 0.001 \); Figure 3A).

**Figure 2.** Hospital mortality as a function of tricuspid annular peak systolic tissue Doppler velocity (TASV)/right ventricular systolic pressure (RVSP) ratio among patients, according to admission diagnosis.

A higher TASV/RVSP ratio reflects better RV-PA coupling. All \( P < 0.001 \) for trends. ACS indicates acute coronary syndrome; CA, cardiac arrest; CS, cardiogenic shock; and HF, heart failure.
Table 4. Discrimination for Hospital Mortality by the TASV/RVSP Ratio (per Each 0.1 Higher TASV/RVSP Ratio) Among Patients, According to Admission Diagnosis (Admission Diagnoses Were Not Mutually Exclusive)

| Admission Diagnosis       | Unadjusted OR per 0.1 | 95% CI       | AUC     | P Value |
|---------------------------|-----------------------|--------------|---------|---------|
| Acute coronary syndrome   | 0.489                 | 0.412–0.580  | 0.734   | <0.0001 |
| Cardiac arrest            | 0.604                 | 0.490–0.733  | 0.686   | <0.0001 |
| Cardiogenic shock         | 0.636                 | 0.518–0.781  | 0.648   | <0.0001 |
| Heart failure             | 0.650                 | 0.564–0.748  | 0.626   | <0.0001 |
| Respiratory failure       | 0.654                 | 0.556–0.770  | 0.621   | <0.0001 |
| Sepsis                    | 0.806                 | 0.633–1.027  | 0.583   | 0.08    |
| Shock (any type)          | 0.666                 | 0.560–0.792  | 0.634   | <0.0001 |

Data displayed as unadjusted OR and 95% CI values, with the AUC and P value for patients with each admission diagnosis. AUC indicates area under the receiver-operator characteristic curve; OR, odds ratio; RVSP, right ventricular systolic pressure; and TASV, tricuspid annular peak systolic tissue Doppler velocity.

A higher TASV/RVSP ratio remained associated with lower hospital mortality in patients with (adjusted OR, 0.741; 95% CI, 0.617–0.890; P=0.001) and without (adjusted OR, 0.563; 95% CI, 0.423–0.749; P<0.001) left ventricular (LV) systolic dysfunction. Likewise, the TASV/RVSP ratio remained associated with hospital mortality after adjusting for LVEF and mitral ratio of peak early transmitral spectral Doppler velocity to peak early diastolic tissue Doppler velocity (E/e' ratio) (adjusted OR, 0.759; 95% CI, 0.639–0.902; P=0.002); neither LVEF nor mitral E/e' ratio was associated with adjusted hospital mortality (P>0.1). We observed a significant statistical interaction (P=0.01) between an admission diagnosis of sepsis and TASV/RVSP for prediction of hospital mortality on multivariable logistic regression; there were no significant interactions with other admission diagnoses.

One-Year Mortality: Univariable Analyses

A total of 919 (21.6%) patients died within 1 year after CICU admission, including 613 (15.5%) of the 3953 hospital survivors plus the 306 patients who died during hospitalization; 428 (10.0%) had <1 year of follow-up. The TASV/RVSP ratio was inversely associated with 1-year mortality in hospital survivors (unadjusted unit hazard ratio [HR], 0.604 per each 0.1 higher TASV/RVSP ratio; 95% CI, 0.562–0.647; P<0.001). One-year survival was progressively higher in each higher TASV/RVSP quintile by Kaplan-Meier analysis, both in the entire cohort and among hospital survivors (P<0.001 by log-rank; Figure 4).

One-Year Mortality: Multivariable Analyses

After multivariable adjustment (Table 6), the TASV/RVSP ratio remained inversely associated with 1-year mortality in hospital survivors (adjusted unit HR, 0.829 per each 0.1 higher; 95% CI, 0.767–0.895; P<0.001). Each higher TASV/RVSP quintile was associated with lower adjusted 1-year mortality among hospital survivors than quintile 1 (all P<0.01; Figure 3B). A higher TASV/RVSP ratio remained associated with lower 1-year mortality in hospital survivors with (adjusted HR, 0.793 per each 0.1 higher; 95% CI, 0.714–0.879; P<0.001), but not those without (adjusted HR, 0.912 per each 0.1 higher; 95% CI, 0.806–1.031; P=0.14) LV systolic dysfunction. Likewise, the TASV/RVSP ratio remained associated with 1-year mortality among hospital survivors after adjusting for LVEF and mitral E/e' ratio (adjusted HR, 0.877; 95% CI, 0.804–0.957; P=0.003); mitral E/e' ratio (P=0.049) was nominally associated with higher adjusted 1-year mortality, but LVEF was not (P=0.13).

DISCUSSION

This is the first study examining RV-PA coupling by TTE in a cohort of critically ill patients, and one of the first studies examining the prognostic associations of the TASV/RVSP ratio by TTE. The ratio of TASV/RVSP, reflecting RV-PA coupling, is strongly and inversely related to hospital and 1-year postdischarge mortality across a broad range of patients receiving care in the CICU. Our results emphasize the importance of both PH and RV function, as reflected by impaired RV-PA coupling measured using Doppler TTE, as determinants of in-hospital and postdischarge outcomes in hospitalized patients with cardiovascular disease. Patients with higher TASV/RVSP ratio, reflecting better load-adjusted RV function, were less likely to die, even after adjusting for severity of illness and other factors known to predict outcomes. The TASV/RVSP ratio remained associated with mortality after adjustment for LV function, although the association between TASV/RVSP ratio and mortality was stronger in patients without LV systolic dysfunction. The association between TASV/RVSP ratio and mortality varied as a function of admission diagnosis, being strongest among patients with ACS and not significantly associated among patients with sepsis. This study validates the TASV/RVSP ratio as a much-needed imaging biomarker of RV-PA coupling that can be used for risk stratification in this critically ill population. Further study is required to determine whether therapeutic interventions to optimize impaired RV-PA coupling may improve outcomes in this population.

This analysis adds to a growing literature on both the importance of 2-dimensional and Doppler echocardiography and noninvasive hemodynamics for risk stratification and the adverse prognosis associated with RV dysfunction and PH in critically ill patients.4–8,10,11,34 Prior studies have shown PH and/or RV...
dysfunction to be associated with worse outcomes in patients with sepsis or unselected medical intensive care unit patients.6–8,10,11,34 The only recent study we identified examining RV-PA coupling in critically ill patients used invasive measurements to define this parameter in surgical intensive care unit patients.34 To our knowledge, this is the first study examining the prognostic impact of noninvasively assessed PH or RV function in a mixed CICU population, further underscoring the importance of Doppler TTE assessment in patients with acute cardiovascular disease. Our results demonstrate that the TASV/RVSP ratio improves hospital mortality discrimination beyond established measures of illness severity, although the incremental improvement over a fully adjusted multivariable model is modest.

The concept of RV-PA coupling describes the adaptation of the RV to alterations in afterload.3,35 With preserved RV-PA coupling during the early phase of chronic PH, the RV can compensate for the increased afterload by increasing its contractility, often with associated RV hypertrophy and dilatation but initially preserved systolic function.3,35 With progression of chronic PH leading to RV failure, RV-PA uncoupling leads to a decrease in RV systolic function associated with a loss of RV longitudinal motion.3,35 Therefore,

| Table 5. Predictors of Hospital Mortality Using Unadjusted and Multivariable-Adjusted Logistic Regression |
|--------------------------------------------------------|---------------------------------|----------------|---------------------------------|
| Variable                                              | Unadjusted Logistic Regression  |             | Multivariable-Adjusted Regression |
|                                                      | OR  | 95% CI       | P Value | OR  | 95% CI | P Value |
| Demographics and comorbidities                        |     |              |         |     |        |         |
| Age (per y)                                           | 1.016 | 1.007–1.025 | <0.001 | 1.019 | 1.006–1.031 | 0.004* |
| Female sex                                            | 0.948 | 0.747–1.204 | 0.67   | 0.860 | 0.640–1.154 | 0.31   |
| White race                                            | 0.668 | 0.454–0.982 | 0.04   | 0.720 | 0.431–1.204 | 0.21   |
| Charlson Comorbidity Index                            | 1.142 | 1.100–1.186 | <0.001 | 1.041 | 0.988–1.098 | 0.13   |
| Prior dialysis                                        | 2.388 | 1.535–3.715 | <0.001 | 0.951 | 0.519–1.742 | 0.87   |
| Admission diagnoses                                   |     |              |         |     |        |         |
| ACS                                                   | 0.561 | 0.433–0.710 | <0.001 | 1.021 | 0.724–1.440 | 0.91   |
| HF                                                    | 3.656 | 2.768–4.828 | <0.001 | 1.009 | 0.693–1.467 | 0.96   |
| CA                                                    | 6.260 | 4.847–8.085 | <0.001 | 3.039 | 2.074–4.455 | <0.001* |
| Shock                                                 | 9.807 | 7.667–12.543 | <0.001 | 2.662 | 1.853–3.825 | <0.001* |
| Respiratory failure                                   | 7.233 | 5.640–9.275 | <0.001 | 1.682 | 1.166–2.427 | 0.005* |
| Sepsis                                                | 7.846 | 5.866–10.494 | <0.001 | 1.982 | 1.349–2.910 | <0.001* |
|Severity of illness                                    |     |              |         |     |        |         |
| APACHE-III score                                      | 1.043 | 1.039–1.048 | <0.001 | 1.012 | 1.005–1.019 | <0.001* |
| Braden skin score                                     | 0.750 | 0.723–0.777 | <0.001 | 0.915 | 0.868–0.964 | <0.001* |
| Procedures and therapies                              |     |              |         |     |        |         |
| Coronary angiogram                                     | 0.437 | 0.346–0.552 | <0.001 | 0.516 | 0.366–0.727 | <0.001* |
| PCI                                                   | 0.383 | 0.291–0.504 | <0.001 | 0.860 | 0.584–1.269 | 0.45   |
| IABP                                                  | 2.940 | 2.162–4.000 | <0.001 | 1.124 | 0.705–1.792 | 0.62   |
| PAC                                                   | 3.154 | 2.347–4.239 | <0.001 | 0.907 | 0.592–1.388 | 0.65   |
| Invasive ventilator                                    | 8.344 | 6.528–10.667 | <0.001 | 0.712 | 0.458–1.106 | 0.13   |
| Non invasive ventilator                               | 2.648 | 2.044–3.429 | <0.001 | 1.111 | 0.788–1.567 | 0.55   |
| No. of vasoactive drugs                               | 2.789 | 2.495–3.117 | <0.001 | 1.282 | 1.107–1.486 | <0.001* |
| RBC transfusion                                       | 3.362 | 2.527–4.473 | <0.001 | 0.776 | 0.519–1.161 | 0.22   |
| Dialysis                                              | 8.309 | 5.937–11.631 | <0.001 | 1.931 | 0.959–3.890 | 0.07   |
| CRRT                                                  | 15.317 | 9.924–23.642 | <0.001 | 3.111 | 1.342–7.212 | 0.008* |
| CRRT                                                  | 10.141 | 6.616–15.546 | <0.001 | 4.138 | 2.348–7.292 | <0.001* |
| TASV/RVSP ratio (per 0.1)                             | 0.516 | 0.461–0.578 | <0.001 | 0.676 | 0.582–0.786 | <0.001* |

Data are displayed as unit OR and 95% CI values. The final multivariable logistic regression model area under the receiver-operator characteristic curve value was 0.914 for hospital mortality. ACS indicates acute coronary syndrome; APACHE, Acute Physiology and Chronic Health Evaluation; CA, cardiac arrest; CRRT, continuous renal replacement therapy; HF, heart failure; IABP, intra-aortic balloon pump; IHCA, in-hospital CA; OR, odds ratio; PAC, pulmonary artery catheter; PCI, percutaneous coronary intervention; RBC, red blood cell; RVSP, right ventricular systolic pressure; and TASV, tricuspid annular peak systolic tissue Doppler velocity.

*All listed variables were included in the final multivariable model, and * denotes variables that had P<0.05 in the final multivariable model.
Figure 3. Forest plot demonstrating adjusted odds ratio values for hospital mortality using logistic regression (A) and adjusted hazard ratio values for 1-year mortality among hospital survivors using Cox proportional-hazards (B), according to tricuspid annular peak systolic tissue Doppler velocity (TASV)/right ventricular systolic pressure (RVSP) ratio quintile, with quintile 1 as referent.
TASV/RVSP quintiles are numbered 1 to 5, with a higher TASV/RVSP ratio quintile reflecting better right ventricular pulmonary artery coupling. All P<0.001.
the TASV/RVSP (or TAPSE/RVSP, which is strongly correlated with TASV/RVSP and performed similarly for mortality discrimination in this cohort) provides a metric reflecting RV-PA coupling by integrating both RV systolic longitudinal motion and RV afterload.\textsuperscript{12} The TASV/RVSP ratio by Doppler TTE is easier to obtain than other proposed invasive and noninvasive measures of RV-PA coupling, including the ratio of RV end-systolic elastance/PA elastance or the ratio of RV fractional area change, end-systolic area, free wall strain, or ejection fraction using advanced imaging modalities to RVSP.\textsuperscript{3,34,36–38} The TASV/RVSP ratio can be measured at bedside in most patients using standard equipment, permitting assessment of RV physiological features at bedside that can offer insights into prognosis even when 2-dimensional

**Figure 4.** Kaplan-Meier curves demonstrating survival up to 1 year after cardiac intensive care unit admission as a function of tricuspid annular peak systolic tissue Doppler velocity (TASV)/right ventricular systolic pressure (RVSP) ratio quintile in the overall population (A) and among hospital survivors (B). TASV/RVSP quintiles are numbered 1 to 5, with a higher TASV/RVSP ratio quintile reflecting better right ventricular pulmonary artery coupling. $P<0.001$ by log-rank.
image quality is suboptimal and more sophisticated imaging methods are not feasible. 9

The use of the TAPSE/RVSP ratio by echocardiography, as a proposed marker of RV-PA coupling, has been well established, and our results extend prior studies by demonstrating that the TASV/RVSP ratio by Doppler TTE is clinically feasible and useful for outcome prediction.12 Studies have consistently associated a low TAPSE/RVSP ratio with worse outcomes in patients with systemic hypertension,19 pulmonary arterial hypertension,17,18 and HF with either preserved or reduced LVEF.12–16 The invasively measured TASV/RVSP ratio has been associated with symptoms, hemodynamic compromise, and outcomes in patients with HF and preserved LVEF, including patients undergoing transcatheter aortic valve replacement.20–24 Our study further validates these studies, and emphasizes that RV-PA coupling, as measured noninvasively using the TASV/RVSP ratio, is an important prognostic marker, even among critically ill CICU patients. Indeed, we found that the TASV/RVSP ratio, as measured by Doppler TTE, was among the strongest predictors of 1-year mortality among hospital survivors; the idea that a single Doppler TTE measurement during hospitalization can prognosticate long-term, even among hospital survivors, is remarkable and warrants prospective examination for validation. Notably, most studies

### Table 6. Predictors of 1-Year Mortality Among Hospital Survivors Using Unadjusted and Multivariable-Adjusted Cox Proportional-Hazards Analysis

| Variable                        | Unadjusted Cox |                      |                      |                      |                      |                      |                      |                      |                      |
|---------------------------------|----------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|----------------------|
|                                 | HR             | 95% CI               | P Value              | HR                   | 95% CI               | P Value              | HR                   | 95% CI               | P Value              |
| Demographics and comorbidities  |                |                      |                      |                      |                      |                      |                      |                      |                      |
| Age (per y)                     | 1.042          | 1.035–1.048          | <0.001               | 1.024                | 1.016–1.032          | <0.001*              |                      |                      |                      |
| Female sex                      | 1.028          | 0.876–1.208          | 0.73                 | 0.845                | 0.716–0.996          | 0.05*                |                      |                      |                      |
| White race                      | 0.977          | 0.712–1.342          | 0.89                 | 0.835                | 0.600–1.161          | 0.28                 |                      |                      |                      |
| Charlson Comorbidity Index      | 1.219          | 1.192–1.246          | <0.001               | 1.105                | 1.074–1.136          | <0.001*              |                      |                      |                      |
| Prior dialysis                  | 2.914          | 2.198–3.862          | <0.001               | 1.231                | 0.899–1.686          | 0.20                 |                      |                      |                      |
| Admission diagnoses             |                |                      |                      |                      |                      |                      |                      |                      |                      |
| ACS                             | 0.637          | 0.544–0.747          | <0.001               | 1.263                | 1.043–1.528          | 0.02*                |                      |                      |                      |
| HF                              | 4.164          | 3.434–5.049          | <0.001               | 2.039                | 1.638–2.538          | <0.001*              |                      |                      |                      |
| CA                              | 0.961          | 0.723–1.276          | 0.78                 | 0.811                | 0.582–1.218          | 0.21                 |                      |                      |                      |
| Shock                           | 1.146          | 1.137–1.762          | 0.002                | 0.688                | 0.514–0.922          | 0.01*                |                      |                      |                      |
| Respiratory failure             | 2.527          | 2.146–2.975          | <0.001               | 1.290                | 1.041–1.599          | 0.02*                |                      |                      |                      |
| Sepsis                          | 2.324          | 1.777–3.039          | <0.001               | 1.029                | 0.765–1.384          | 0.85                 |                      |                      |                      |
| Severity of illness             |                |                      |                      |                      |                      |                      |                      |                      |                      |
| APACHE-III score               | 1.026          | 1.023–1.029          | <0.001               | 1.012                | 1.006–1.017          | <0.001*              |                      |                      |                      |
| Braden skin score               | 0.867          | 0.847–0.887          | <0.001               | 0.933                | 0.903–0.963          | <0.001*              |                      |                      |                      |
| Procedures and therapies        |                |                      |                      |                      |                      |                      |                      |                      |                      |
| Coronary angiogram              | 0.432          | 0.369–0.506          | <0.001               | 0.661                | 0.546–0.801          | <0.001*              |                      |                      |                      |
| PCI                             | 0.407          | 0.339–0.488          | <0.001               | 0.722                | 0.582–0.895          | 0.003*               |                      |                      |                      |
| IABP                            | 0.924          | 0.678–1.260          | 0.82                 | 0.832                | 0.588–1.180          | 0.30                 |                      |                      |                      |
| PAC                             | 1.534          | 1.194–1.971          | <0.001               | 1.082                | 0.802–1.458          | 0.61                 |                      |                      |                      |
| Invasive ventilator             | 1.733          | 1.398–2.149          | <0.001               | 0.672                | 0.495–0.911          | 0.01*                |                      |                      |                      |
| Noninvasive ventilator          | 2.207          | 1.840–2.647          | <0.001               | 1.026                | 0.832–1.264          | 0.81                 |                      |                      |                      |
| No. of vasoactive drugs         | 1.327          | 1.225–1.430          | <0.001               | 1.132                | 1.004–1.277          | 0.04*                |                      |                      |                      |
| RBC transfusion                 | 1.753          | 1.391–2.120          | <0.001               | 0.959                | 0.744–1.235          | 0.74                 |                      |                      |                      |
| Dialysis                        | 3.001          | 2.208–4.078          | <0.001               | 1.475                | 0.922–2.361          | 0.11                 |                      |                      |                      |
| CRRT                            | 4.459          | 2.913–6.828          | <0.001               | 1.509                | 0.808–2.819          | 0.20                 |                      |                      |                      |
| IHCA                            | 1.805          | 1.063–3.066          | 0.03                 | 1.565                | 0.874–2.801          | 0.13                 |                      |                      |                      |
| TASV/RVSP ratio (per 0.1)       | 0.604          | 0.562–0.647          | <0.001               | 0.829                | 0.767–0.895          | <0.001*              |                      |                      |                      |

Data are displayed as unit HR and 95% CI values. ACS indicates acute coronary syndrome; APACHE, Acute Physiology and Chronic Health Evaluation; CA, cardiac arrest; CRRT, continuous renal replacement therapy; HF, heart failure; HR, hazard ratio; IABP, intra-aortic balloon pump; IHCA, in-hospital CA; PAC, pulmonary artery catheter; PCI, percutaneous coronary intervention; RBC, red blood cell; RVSP, right ventricular systolic pressure; and TASV, tricuspid annular peak systolic tissue Doppler velocity.

*All listed variables were included in the final multivariable model, and * denotes variables that had P<0.05 in the final multivariable model.
examining RV-PA coupling using either the TAPSE/RVSP or the TASV/RVSP ratio have included primarily patients with chronic PH and RV dysfunction rather than patients with acute RV strain attributable to pulmonary embolism or acute RV injury attributable to RV infarction in whom PA pressures may be reduced because of low RV stroke volume. Although not previously examined, it is likely that disease chronicity can influence not only the measured TASV/RVSP ratio, but also the association of RV-PA coupling with clinical outcomes.

The robust associations between impaired RV-PA coupling (ie, a low TASV/RVSP ratio) and higher mortality suggest that interventions to improve coupling may improve outcomes. Such therapeutic interventions might include treatments to reduce RA and PA pressure using either diuretics or interventions that act directly on the pulmonary vasculature. Fluid removal can improve PA pressures and RV-PA coupling through a reduction in filling pressures, which can decrease right heart dilation and alleviate pericardial restraint. Alternatively, severely decompensated patients may benefit from short-term inotropic support to enhance RV-PA coupling during the short-term and allow for recovery from acute insults. Notably, reduced RV-PA coupling correlated with impaired LV systolic and diastolic dysfunction, emphasizing the importance of right-sided heart disease among patients with left-sided heart failure and suggesting the need to optimize biventricular function in many patients. Serial measurement of the TASV/RVSP ratio using bedside Doppler TTE could help to understand the effects of treatments on RV-PA coupling, and potentially to monitor for adverse heart-lung interactions in mechanically ventilated patients. Further study is required to examine whether currently available therapies for PH and RV failure can improve RV-PA coupling and outcomes in CICU patients.

**Limitations**

This analysis carries the same limitations common to all retrospective observational studies, and cannot infer causation. Missing TTE data could have influenced the results and introduced bias, particularly considering that fewer than half of patients with a TTE had data available for calculating the TASV/RVSP ratio and that the baseline characteristics and outcomes differed significantly between included and excluded patients. Poor imaging windows in sicker patients could have prevented complete data acquisition, leading to bias, and TTE data were obtained without the objectives of this study in mind. It is likely that TASV and TAPSE were preferentially measured among patients with abnormal RV structure or function, and RVSP can only be estimated among patients with sufficient TR to acquire a Doppler signal; our institution measures TASV more frequently than TAPSE, limiting our ability to compare these 2 related measures robustly. Serial TTE data were not available, preventing us from assessing changes in RV-PA coupling over time. Likewise, we did not have invasive hemodynamic data to correlate with and corroborate measured Doppler TTE hemodynamic values, nor did we have data on symptoms, physical examination, imaging, or ECG, which limits our ability to draw firm inferences. In addition, we were not able to determine the acuity or specific cause of PH and RV dysfunction, precluding us from determining whether abnormal values of TASV/RVSP reflected acute or chronic pathological features. A potential limitation of the TASV/RVSP ratio is that echocardiographic estimation of RAP has demonstrated only modest correlations with invasive measurements in patients receiving positive-pressure ventilation, and echocardiography may underestimate RAP and PA pressures when RAP is high. However, the simplified TASV/TR velocity ratio, which does not depend on RAP, had an AUC for hospital mortality that was only modestly lower than the TASV/RVSP ratio. We could not determine the therapies that patients were receiving at the time of TTE (such as vasoactive drugs), preventing us from inferring the relationship between medical treatments and RV-PA coupling. Given the numerous potential confounders that can affect late mortality after hospitalization in CICU patients, our 1-year mortality analysis should be considered exploratory and interpreted with caution.

**CONCLUSIONS**

In the largest human study of RV-PA coupling in an unselected CICU cohort, our findings suggest a robust inverse association between TASV/RVSP ratio and mortality risk during and following hospitalization. This study emphasizes the potential usefulness of Doppler TTE measurements for characterizing the prognostically important hemodynamic abnormalities that are common in CICU patients. Future prospective studies will be needed to confirm the association between the TASV/RVSP ratio and outcomes in CICU patients and to determine whether its prognostic value is influenced by cause and response to short-term therapy, to provide further insights into how this easily obtained bedside imaging biomarker can be integrated into clinical practice.

**ARTICLE INFORMATION**

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SUPPLEMENTAL MATERIAL
### Table S1. Measured and derived echocardiographic variables of interest.

| Variable                                                                 |
|--------------------------------------------------------------------------|
| Systolic blood pressure                                                  |
| Diastolic blood pressure                                                 |
| Mean blood pressure                                                      |
| Pulse pressure                                                           |
| Heart rate                                                              |
| Shock index                                                             |
| Heart rhythm (sinus rhythm or atrial fibrillation)                       |
| Left ventricular ejection fraction (LVEF)                                |
| Wall motion score index                                                  |
| Left ventricular outflow tract (LVOT) peak velocity                      |
| LVOT velocity-time integral (VTI)                                        |
| Stroke volume (SV)                                                       |
| Stroke volume index (SVI)                                                |
| Cardiac output (CO)                                                      |
| Cardiac index (CI)                                                       |
| Lateral mitral annulus peak systolic tissue Doppler (s’) velocity        |
| Early mitral diastolic (E) velocity                                     |
| Mitral atrial diastolic (A) velocity                                    |
| Mitral E/A velocity ratio                                               |
| Medial mitral annulus early diastolic tissue Doppler (e’) velocity      |
| Mitral E/e’ velocity ratio                                              |
| Right atrial pressure (RAP)                                             |
| Tricuspid regurgitation (TR) peak systolic velocity                     |
| Tricuspid annulus peak systolic velocity (TASV)                         |
| Tricuspid annular plane systolic excursion (TAPSE)                      |
Table S2. Formulas used for echocardiographic hemodynamic parameters, using data from the time of the echocardiogram.

| Echocardiographic parameter          | Formula                                                                 |
|--------------------------------------|--------------------------------------------------------------------------|
| Mean arterial pressure (MAP)          | \([SBP + (2 \times DBP)] / 3\)                                          |
| Stroke volume (SV)                   | \((\pi/4) \times LVOT VTI \times (LVOT diameter)^2\)                    |
| Stroke volume index (SVI)            | \(SV / BSA\)                                                            |
| Cardiac output (CO)                  | \(SV \times HR\) (at time of LVOT VTI acquisition)                      |
| Cardiac index (CI)                   | \(CO / BSA = SVI \times HR\)                                            |
| Cardiac power output (CPO)           | \((CO \times MAP) / 451\)                                               |
| Pressure-adjusted heart rate (PAHR)  | \((HR \times RAP) / MAP\)                                               |
| Right ventricular systolic pressure (RVSP) | \(RAP + [4 \times (peak TR velocity)^2]\)                             |
| TASV/RVSP ratio                      | \(TASV / RVSP\)                                                         |
| TAPSE/RVSP ratio                     | \(TAPSE / RVSP\)                                                        |
| TASV/TR velocity ratio               | \(TASV/TR velocity\)                                                    |

BSA, body surface area; DBP, diastolic blood pressure; HR, heart rate; LVOT, left ventricular outflow tract; RAP, right atrial pressure; SBP, systolic blood pressure; VTI, velocity-time integral.
Figure S1. Tricuspid annulus systolic velocity (TV s’) by tissue Doppler imaging (TDI) (A) and estimated right ventricular systolic pressure (RVSP) by continuous-wave Doppler (B) as a function of TV s’ to RVSP ratio decile.
Figure S2. Tricuspid annular plane systolic excursion (TAPSE) to right ventricular systolic pressure (RVSP) ratio as a function of tricuspid annulus systolic velocity (TASV) to RVSP ratio decile.
Figure S3. CICU and hospital mortality as a function of TASV/RVSP ratio quintile. A higher TASV/RVSP ratio quintile reflects better RV-PA coupling, and each higher TASV/RVSP quintile was associated with lower hospital mortality (unadjusted OR 0.560 per each higher quintile, 95% CI 0.507-0.617, p <0.001). All p <0.001 for trends across