Usefulness of Right Ventricular to Pulmonary Circulation Coupling as an Indicator of Risk for Recurrent Admissions in Heart Failure With Preserved Ejection Fraction

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In recent years, the study of right ventricular (RV) to pulmonary circulation (PC) coupling in heart failure with preserved ejection fraction (HFpEF) has been a matter of special interest. Tricuspid annular plane systolic excursion (TAPSE) to pulmonary artery systolic pressure (PASP) ratio has emerged as a reliable noninvasive index of RV to PC coupling. Thus, we hypothesized that TAPSE/PASP would be a predictor of readmission burden in HFpEF. One thousand one hundred and twenty seven consecutive HFpEF patients discharged for acute HF were included. In 367 patients (32.6%), PASP could not be accurately measured by echocardiography, leaving the final sample size to be 760 patients. Negative binomial regression method was used to evaluate the association between TAPSE/PASP ratio and recurrent admissions. Mean age of the cohort was 75.6 ± 9.7 years and 68.3% were women. At a median (interquartile range) follow-up of 2.0 (2.9) years, 352 (46.3%) patients died and 1,214 readmissions were registered in 482 patients (63.4%), being 506 of them HF-related. There was a stepwise increase in the rates of all-cause and HF readmissions by decreasing TAPSE/PASP ratio. After multivariable adjustment, TAPSE/PASP <0.36 was associated with a higher risk of HF-related recurrent admissions (incidence rate ratio [IRR] 1.51, 95% confidence interval [CI], 1.01 to 2.24; p = 0.040), whereas patients in the lowest quintile (TAPSE/PASP <0.28) exhibited the highest risk of both all-cause and HF-related recurrent admissions (IRR 1.40, 95% CI 1.04 to 1.87, p = 0.025; and IRR 1.85, 95% CI 1.22 to 2.80, p = 0.004, respectively). In conclusion, TAPSE/PASP ratio, as a noninvasive index of RV-PC coupling, emerges as a strong predictor of recurrent hospitalizations in HFpEF. **(Am J Cardiol 2019;124:567−572)**

Heart failure (HF) is a syndrome characterized by recurrent episodes of hospitalizations that deeply affect patients' quality of life, and account for large health care expenditures.[1,2] HF with preserved ejection fraction (HFpEF) represents approximately one-half of the patients admitted with acute HF (AHF). The readmission burden in HFpEF remains very high,[3,4] and identification of those patients at a high risk is still an unmet need.[5] HFpEF is a complex syndrome with multiple pathophysiological mechanisms implicated. In this regard, recent data have highlighted the growing importance of the right heart in clinical phenotyping and risk stratification.[5−10] Right ventricular (RV) dysfunction and pulmonary hypertension (PH) are common features in HFpEF and both are powerful predictor of outcomes.[8−10] Along this line, RV to pulmonary circulation (PC) coupling has emerged as a comprehensive index of global RV performance, better than each of these parameters separately.[11−13] Tricuspid plane annular systolic excursion (TAPSE) to pulmonary artery systolic pressure (PASP) ratio is a useful, simple, and noninvasive indicator of RV-PC coupling that has arisen in recent years.[12−15] We therefore hypothesized that TAPSE/PASP ratio could be a predictor of the readmission burden in HFpEF.

Methods

We prospectively included a consecutive cohort of 1,127 patients discharged with a diagnosis of AHF from the cardiology department of a tertiary-care teaching hospital in Valencia (Spain) since 2004 to 2014. Of them, in 367 patients (32.6%) PASP could not be measured accurately due to the lack of proper Doppler tricuspid regurgitation signal, leaving the final sample size to be 760 patients. AHF was defined according to Clinical Practice Guidelines.[1]

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Either patients with new-onset or worsening HF were enrolled in the registry. By design, only patients discharged alive after the index hospitalization were included. Treatment strategies were individualized after established guidelines that were operating at the time patients were included in the registry. In all patients, a two-dimensional echocardiogram was performed during index hospitalization (96 ± 24 hours after admission), using the left lateral decubitus position. Two commercially available systems were used throughout the study, Agilent Sonos 5500 and ie33, (Philips, Massachusetts). PASP was estimated by measuring the maximum continuous Doppler-derived velocity of the tricuspid regurgitation jet, after established recommendations.[16] Right atrial pressure was according to inferior vena cava (IVC) size and its breathing-related collapsibility after a normal sniff, as follows: 3 mm Hg if IVC <21 mm that collapses >50%, 15 mm Hg if IVC >21 mm that collapses <50%, and 8 mm Hg in the situations in which IVC diameter and collapse did not fit this paradigm.[16] Left ventricular ejection fraction was assessed by the biplane Simpson method. TAPSE was tracked in the 4-chamber view per M-mode, as recommended.[16] RV-PC coupling was evaluated by calculating the ratio of TAPSE to PASP. TAPSE/PASP was evaluated as a continuous variable and as categorized per quintiles (Table 1). All-cause recurrent hospitalizations during follow-up were selected as the primary end point. HF-related recurrent hospitalizations were selected as secondary end points. All-cause mortality was selected as a sensitivity analysis. Only unplanned readmissions were included. Hospitalizations were adjudicated based on the paper-written and electronic discharge medical records review from every hospital of the Spanish healthcare system. These events were

Table 1
Baseline characteristics by TAPSE/PAPS ratio quintiles distribution

Variables	Quintile 1 (n = 152)	Quintile 2 (n = 152)	Quintile 3 (n = 152)	Quintile 4 (n = 152)	Quintile 5 (n = 152)	p Value
TAPSE/PAPs	<0.28	0.28−0.36	0.36−0.44	0.44−0.55	>0.55	
Age (years%)	76.2 (±8.1)	76.4 (±9.9)	75.8 (±9.0)	76.6 (±10.5)	73.4 (±10.7)	0.013
Women	109 (71.7%)	110 (72.4%)	116 (76.3%)	99 (65.1%)	85 (55.9%)	0.001
NYHA class ≥ III prior to admission	56 (36.8%)	27 (17.8%)	24 (15.8%)	19 (12.5%)	22 (14.5%)	<0.001
Hypertension	125 (82.2%)	121 (79.6%)	124 (81.6%)	127 (83.6%)	110 (72.4%)	0.116
Diabetes Mellitus	64 (42.4%)	62 (40.8%)	59 (38.8%)	50 (32.9%)	58 (38.2%)	0.505
Dyslipidemia	67 (44.1%)	69 (45.4%)	74 (48.7%)	77 (50.7%)	77 (50.7%)	0.693
Current smoker	6 (3.9%)	5 (3.3%)	9 (5.9%)	13 (8.6%)	19 (12.5%)	0.009
History of IHD	33 (21.7%)	30 (19.7%)	28 (18.4%)	33 (21.7%)	36 (23.6%)	0.826
History of pacemaker implantation	9 (5.9%)	4 (2.6%)	10 (6.6%)	10 (6.6%)	5 (3.3%)	0.331
History of atrial fibrillation	106 (70.7%)	105 (70%)	96 (63.2%)	94 (61.8%)	67 (44.1%)	<0.001
Charlson index > 2	118 (41.1%)	97 (33.7%)	92 (31.9%)	85 (29.5%)	90 (31.3%)	0.034
HR (bpm)	89.5 (±27.4)	98.8 (±29.6)	100.1 (±32.6)	98.1 (±32.2)	98.3 (±29.5)	0.196
Systolic blood pressure (mm Hg)	139.9 (±28.6)	144.9 (±32.6)	145.2 (±30.2)	148.5 (±30.2)	151.5 (±32.4)	0.301
Diastolic blood pressure (mm Hg)	74.7 (±17.4)	78 (±17.6)	79.3 (±18.6)	80.7 (±19.1)	80.5 (±18.9)	0.461
Hemoglobin (g/dl)	11.9 (±1.8)	11.8 (±1.7)	12 (±1.8)	12.1 (±1.9)	12.1 (±1.9)	0.458
Hematocrit (%)	36.7 (±5.2)	36.4 (±4.9)	36.7 (±5.1)	37.3 (±5.4)	37.2 (±5.2)	0.582
Transferrin saturation (%)	13.1 (8.5)	11.3 (9.7)	11.5 (10.8)	13.6 (11.6)	14.6 (11.1)	0.536
Ferritin (ng/mL)*	104.3 (87.9)	97.6 (75.6)	108.3 (97.1)	110.2 (88.5)	127.5 (139)	0.012
Leucocyte count (per ml)	8898.7 (±2943.5)	9075 (±3736.5)	9447.5 (±3258.4)	9114.1 (±3322.9)	9634.4 (±3734.1)	0.017
BUN (mg/dl)*	59.5 (28.9)	51.0 (38.0)	50.0 (36.0)	50 (26.5)	44.0 (28.5)	<0.001
Creatinine (mg/dl)	1.25 (±0.54)	1.25 (±0.61)	1.15 (±0.50)	1.16 (±0.49)	1.14 (±0.62)	0.003
eGFR (ml/min/1.73 m)	59.6 (±30.7)	62.6 (±49.9)	62.8 (±25.5)	63.4 (±25.5)	70.1 (±28.4)	<0.001
Serum sodium (mEq/l)	137.8 (±5.5)	138.5 (±5.3)	138.4 (±4.9)	138.8 (±4.2)	137.7 (±5.3)	0.827
NT-proBNP (pg/ml)*	4951 (5151)	3518 (4623)	3559 (5639)	3201 (4487)	2670 (3518)	<0.001
LV diastolic diameter (mm)	48.6 (±7.8)	49.9 (±7.7)	49.6 (±7.3)	49.6 (±7.5)	50.5 (±9.1)	0.395
LA (mm)	49.0 (± 7.7)	46.9 (±8.3)	45.7 (±8.8)	44.6 (±7.2)	42.5 (±6.7)	<0.001
DT (mm)	202.5 (± 59.9)	211.2 (± 66.1)	215.7 (± 53.4)	226.5 (± 64.6)	231 (± 59.0)	<0.001
TAPSE (mm)	16.3 (±2.8)	17.9 (±2.3)	18.5 (±2.3)	19.3 (±2.9)	21.6 (±3.5)	<0.001
Right ventricular S´(cm/s)	9.5 (± 2.4)	10.9 (±2.6)	10.4 (±2.3)	11.5 (±2.9)	12.5 (±2.6)	<0.001
PASP (mm Hg)	72.6 (±16.1)	54.2 (±7.3)	45.4 (±5.8)	38.8 (±6.3)	31.6 (±5.8)	<0.001
E/e' ratio	19.4 (14.5)	18.9 (13.8)	17.7 (10.4)	14.9 (10.3)	14.3 (10.3)	0.059
TR grade ≥ 3	78 (51.3%)	43 (28.3%)	29 (19.1%)	22 (14.5%)	13 (8.5%)	<0.001
Furosemide at discharge	110 (84%)	111 (79.3%)	115 (81.6%)	118 (81.9%)	117 (81.3%)	0.908
Thiazides at discharge	12 (9.2%)	14 (10%)	13 (9.2%)	11 (7.6%)	7 (4.9%)	0.540
Beta blockers at discharge	72 (54.6%)	91 (65%)	94 (64.4%)	102 (68.9%)	125 (83.9%)	<0.001
ACEI at discharge	36 (27.3%)	41 (29.5%)	50 (34.3%)	48 (32.4%)	45 (30.4%)	0.756
ARB at discharge	38 (28.6%)	45 (32.4%)	61 (41.8%)	45 (30.6%)	47 (31.8%)	0.149

Values are mean ± standard deviation, median (interquartile range)* or n (%). ACEI = angiotensin-converting enzyme inhibitor; AHF = acute heart failure; ARB = angiotensin-II receptor blockers; BUN = blood ureic nitrogen; DT = deceleration time; E/e' = ratio of mitral peak velocity of early filling (E) to early diastolic mitral annular velocity (e'); eGFR = estimated glomerular filtration rate using the Modification of Diet in Renal Disease formula; HR = heart rate; IHD = ischemic heart disease; LA = left atrium; LV = left ventricular; NT-proBNP = N-terminal pro-brain natriuretic peptide; NYHA = New York Heart Association functional class; PASP = pulmonary artery systolic pressure; TAPSE = Tricuspid annular plane systolic excursion; TR = tricuspid regurgitation.

adjudicated by 2 researchers blinded to the TAPSE/PASP ratio. This was not an administrative database of codes based review. HF-related readmission was every hospitalization in which AHF or worsening HF was the main diagnosis at discharge. The study was prospectively designed, conformed to the principles outlined in the 1975 Declaration of Helsinki, and approved by the institutional local review ethical committee. All patients gave informed consent.

Continuous variables were expressed as mean ± standard deviation or median (interquartile range), whenever appropriate. Discrete variables were summarized as percentages. Baseline characteristics were compared among TAPSE/PASP categories with Pearsońs chi-square and p for trend tests for categorical or continuous variable, respectively. A descriptive analysis of recurrent hospitalizations was performed by counting the number of hospitalizations during the follow-up. Crude incidence rates (number of readmissions per 100 person-years) across TAPSE/PASP categories were calculated for all the readmission end points. The independent association between TAPSE/PASP ratio and recurrent hospitalizations was assessed through a multivariable negative binomial regression (NBreg) analysis, and estimates of risks were expressed as incidence rate ratio (IRR). As suggested by Rogers et al, each death was included as an additional event in the NBreg model but only if it occurred outside any rehospitalization.[17,18] All variables listed in Table 1 were evaluated as potential covariates in the NBreg model, independently of their p value. A backward stepwise selection, with a p value of 0.157 (AIC criterion) for variable inclusion, was used to achieve parsimonious models and prevent model's overfitting.[19,20] All the covariates and their estimates in the final multivariate NBreg models for all-cause and HF-related recurrent admissions are shown in Supplementary Table 1. The association between TAPSE/PASP and all-cause mortality during follow-up was evaluated by Kaplan-Meier and Cox regression analysis. A 2-sided p value of <0.05 was considered to be statistically significant for all analyses. All statistical analyses were performed using STATA 14.1 (StataCorp. 2014. Stata Statistical Software: Release 14.1. College Station, Texas: StataCorp LP).

Results

Mean age of the cohort was 75.6 ± 9.7 years, 519 patients (68.3%) were women and 351 (46.5%) had been previously admitted for AHF. One hundred and ninety five patients (25.7%) showed a TAPSE <17 mm and 591 (77.8%) had an estimated PASP >35 mm Hg. Mean value of TAPSE/PASP ratio was 0.43 ± 0.17. Table 1 summarizes the baseline characteristics stratified according to the TAPSE/PASP ratio per quintiles. Overall, there was a graded and significative association of TAPSE/PASP ratio with clinical, biochemical, and echocardiographic parameters related to the severity of the syndrome. Patients with RV-PC uncoupling were older, had more co-morbidities, and a higher proportion of atrial fibrillation. Likewise, low TAPSE/PASP ratios were associated with higher NT-proBNP, blood urea nitrogen, or serum creatinine. As expected, RV-PC coupling declined progressively along with RV systolic dysfunction and a higher degree of echo-derived PH. Furthermore, TAPSE/PASP was negatively associated with functional tricuspid regurgitation severity and features of left ventricular diastolic dysfunction (left atrium size, deceleration time or E/e´ ratio).

At a median follow-up of 2.0 years (interquartile range 0.74 to 3.6), 352 patients (46.3%) died. By Kaplan-Meier analysis, patients in the lower quintiles of TAPSE/PASP ratio showed the highest risk of mortality (Figure 1). In multivariate analysis, the continuum of TAPSE/PAPS ratio was inverse and linearly associated with the risk of mortality. Thus, patients in the lowest quintile of TAPSE/PASP (<0.28) showed the highest mortality risk (hazard ratio 2.57, confidence interval [CI] 95% 1.73 to 3.84, $p < 0.001$).

A cumulative total of 1,214 all-cause readmissions were encountered in 482 patients (63.4%). Of note, 176 (36.5%) and 63 (13.1%) patients were readmitted ≥3 or ≥ 5 times along the follow-up, respectively. Overall, there was a stepwise increase in the rates of readmissions with decreasing TAPSE/PASP ratio. Hence, patients in the lowest quintile had the highest readmission burden (p value for trend <0.001). Crude incidence rates per 100 person/years for recurrent all-cause hospitalizations according to TAPSE/PASP ratio quintiles are shown in Figure 2. In univariate analysis, evaluating TAPSE/PASP ratio as a continuous variable, it was associated with the risk of recurrent admissions (IRR 0.36, 95% CI 0.19 to 0.66, $p = 0.026$). In comparison to patients in the upper quintile, there was a stepwise increase of all-cause recurrent admissions with low TAPSE/PASP ratios. In multivariable analysis, only patient in the lowest quintile (TAPSE/PASP <0.28) exhibited a significant increase of risk of recurrent all-cause hospitalizations (Table 2). Figure 3 shows the gradient of readmissions risks across the continuum of RV-PC coupling index. Univariate and fully-adjusted IRRs for all TAPSE/PASP categories are shown in Table 2.

A cumulative total of 506 HF-related hospitalizations were registered in 294 patients (39.0%). Similarly to all-cause readmissions, we found a stepwise increased incidence of HF readmissions with decreasing TAPSE/PASP ratios. Crude incidence rates per 100 person/years according to TAPSE/PASP quintiles are presented in Figure 2.

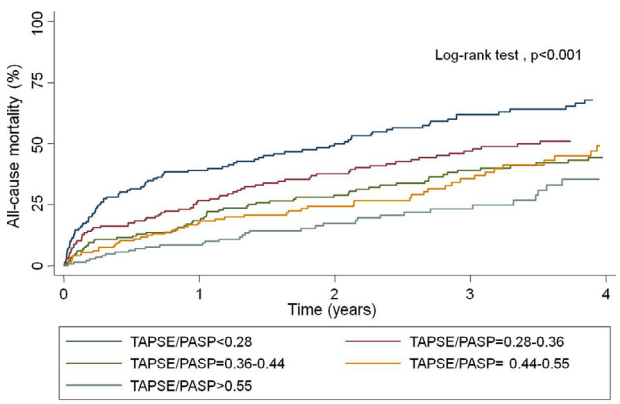

Figure 1. Kaplan-Meier curves for all-cause mortality according to TAPSE/PAPS ratio quintiles. PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

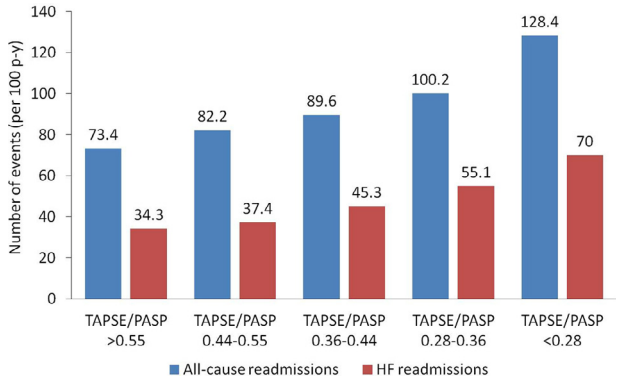

Figure 2. Crude incidence rate of all-cause and HF-related rehospitalizations according to TAPSE/PASP ratio quintiles. HF = heart failure; PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

In univariate analysis, evaluating TAPSE/PASP ratio as a continuous variable, this index was strongly associated with the risk of HF-related recurrent admissions (IRR 0.23, 95% CI 0.09 to 0.57, p = 0.002). In multivariable analysis, patients with TAPSE/PASP <0.36, and particularly those with <0.28, showed an independent and significant increase of risk of HF-related hospitalizations. Univariate and fully adjusted IRRs for all TAPSE/PASP categories are shown in Table 2. Figure 3 shows the gradient of HF-related readmission risks across the continuum of this RV-PC coupling index.

In a sensitivity analysis (using the same set of covariates plus adjusting for atrial fibrillation, LA size, and E/e´ ratio) TAPSE/PASP remained showing an independent increased risk of all-cause and HF-related recurrent admissions (p = 0.041 and p = 0.012, respectively), as it is shown in Supplementary Figure 1.

Discussion

The study of the right heart and its clinical implications in HFpEF is nowadays an attractive field of investigation.[5,21] The novel finding of our study is that TAPSE/PASP ratio, as a noninvasive index of RV-PC coupling and global RV performance, was strongly related to the rehospitalization burden in patients with HFpEF. Thus, after an episode of AHF, using this index before discharge could help in identifying patients at a high risk of recurrent admissions, with potential implications for transitional models and/or potential targeted therapies.

HFpEF is a complex and heterogeneous syndrome,[5,6,21] but evidence is growing recently about the importance of the right heart and PC.[21] RV dysfunction and PH are both common features in HFpEF, ranging from to 26% to 49%, and from 46% to 83%, respectively.[8,10] This is similar to our data, in which 26% of patients had TAPSE <17 mm and echo-derived PH was high, with up to 78% of patients showing PASP >35 mm Hg. A key factor is that both parameters are strongly interconnected, because RV systolic function is markedly dependent on afterload. In HFpEF, the coupling of RV for a given overload pressure is commonly impaired,[11] so RV contractility gets worse with progressively higher vascular loading. Thus, RV-PC coupling has emerged as a global index of RV performance and right length-force relation,[10] beyond the information provided per each variable in isolation. Guazzi et al proposed a noninvasive index of RV-PC coupling with widely available echo parameters, such as TAPSE and PASP,[12] that has shown to have an excellent correlation with invasively PA compliance, distributes along the exponential relation between PA compliance and PC resistance,[15,22] and has been increasingly adopted ever since.[15,21,23]

TAPSE/PASP has been previously linked to a reduced functional capacity and impaired exercise performance in

Table 2
Association between TAPSE/PASP ratio and the risk of all-cause and heart failure-related recurrent admissions

NBreg models	IRR (95% CI)	p Value	IRR (95% CI)	p Value
	All-cause recurrent admissions			
	Unadjusted		Adjusted	
TAPSE/PASP >0.55 (reference)				
TAPSE/PASP = 0.44−0.55	1.12 (0.82 to 1.53)	0.481	1.07 (0.80 to 1.43)	0.634
TAPSE/PASP = 0.36−0.44	1.22 (0.92 to1.62)	0.167	1.16 (0.88 to 1.53)	0.301
TAPSE/PASP = 0.28−0.36	1.36 (1.03 to 1.81)	0.033	1.17 (0.90 to 1.54)	0.238
TAPSE/PASP <0.28	1.75 (1.29 to 2.37)	<0.001	1.40 (1.04 to 1.87)	0.025
	Heart failure-related recurrent admissions			
	Unadjusted		Adjusted	
TAPSE/PASP >0.55 (referent)				
TAPSE/PASP = 0.44−0.55	1.09 (0.71 to 1.67)	0.696	1.05 (0.70 to 1.56)	0.806
TAPSE/PASP = 0.36−0.44	1.32 (0.89 to 1.95)	0.165	1.34 (0.92 to 1.95)	0.128
TAPSE/PASP = 0.28−0.36	1.60 (1.07 to 2.41)	0.022	1.51 (1.01 to 2.24)	0.042
TAPSE/PASP <0.28	2.04 (1.33 to 3.12)	<0.001	1.85 (1.22 to 2.80)	0.004

CI = confidence interval; IRR = incidence rate ratio; NBreg = negative binomial regression; PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion. Models adjusted for: age, gender, previous heart failure admissions, Charlson index, serum hemoglobin, blood urea nitrogen and N-terminal probrain natriuretic peptides.

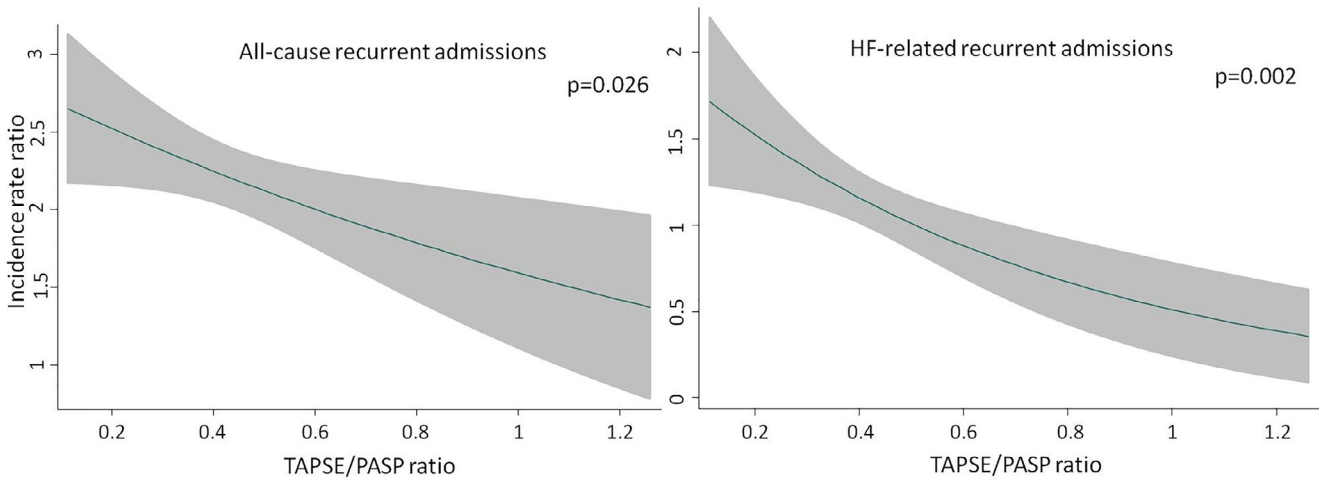

Figure 3. Gradient of risks of all-cause and heart failure-related recurrent admissions across the continuum of TAPSE/PASP ratio, expressed as incident rate ratios. HF = heart failure; PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

HFpEF.[14] Moreover, it has been previously associated with a high risk of mortality in different cohorts.[12,14,23,24] Our study confirms this data, showing that RV-PC uncoupling is strongly associated with a reduced survival in HFpEF. However, the evidence endorsing the role of TAPSE/PASP for predicting the risk of hospitalizations is scarce. In a cohort of 378 ambulatory HFpEF patients, those with TAPSE/PASP <0.35 showed a 2.2-fold increase in the hazard of first HF readmission.[14] From a methodological point of view, "time-to-first" risk analyses, although are well recognized, probably do not accurately reflect the hospitalization burden in a chronic disease such as HF. Nowadays, some experts recommend evaluating all rehospitalizations that occur during follow-up.[17,18,25] Indeed, recurrent admissions has been selected as a primary end point in important ongoing clinical trials in HFpEF, such as the PARAGON-HF trial.[26] A prognostic cut-off of <0.36 has been postulated.[21] This cut-off strongly predicts the risk of HF-related recurrent admissions in our study, although the lower the ratio the highest the risk of both all-cause and HF readmissions. Hence, the present study expands previous data with regarding readmission risks in a large cohort of HFpEF patients, and in an acute clinical scenario.

There is increasing data on the presence of a precapillary component in PH-related HF.[10,27] This "reactive" form of PH is characterized by increased vascular resistance and transpulmonary pressure gradients and it is associated with adverse outcomes.[10,15,27] Recently, Gorter et al have described that TAPSE/PASP ratio has a good accuracy to identify patients with precapillary component of PH.[15] This is an important topic that may explain the robust prognostic value associated with this noninvasive index. We also observed that RV-PC uncoupling was related to global features of advanced HF, such as previous HF hospitalizations, a higher prevalence of atrial fibrillation, renal dysfunction, or worsening diastolic dysfunction. Some of these factors could be related to the genesis and/or progression of RV-PC uncoupling but definitely represents a more advance stage of the syndrome. In this regard, similar findings have been previously reported.[14,15,28] In addition, women showed lower TAPSE/PASP ratios than men. Recently Beale et al reported that women have a lower PA compliance than men, and may have intrinsic differences in PC reactivity, so it may help to explain why RV-PC coupling can get more impaired in women.[29]

Several limitations of our study need to be acknowledged. First, this is a single-center observational study in which hidden bias might be operating. Second, echocardiographic studies were not reviewed by an independent core laboratory external to the investigators. Third, TAPSE definitely has its caveats and limitation as an index of RV systolic function.[16] Nonetheless, it is a widely available parameter recommended in HFpEF given its evidence and simplicity.[21] Advanced imaging techniques, such as RV strain does not seem to increase the prognostic value of this ratio.[23] Fourth, repeated-events methods in the HF field is relatively new, and consequently, there are areas still subjected to controversy, as it is the case of calibration and discrimination analyses. However, it seems to portrait a more accurate evaluation of the morbidity burden than the traditional "time-to-first event" end points.[17,18,25]

In conclusion, TAPSE/PASP ratio, as a noninvasive index of RV-PC coupling, was strongly related to mortality risk, and identified a subset of HFpEF patients at a high risk of all-cause and HF-related recurrent hospitalizations. This data supports the clinical use of this index for risk stratification in HFpEF, and prospect considering RV to PC coupling as a potential target of interventions in HFpEF.

Disclosures

The authors have no conflict of interest to disclose.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2019.05.024.

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