Advanced echocardiography in characterization and management of patients with secondary mitral regurgitation

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Chapter six

Right ventricular - pulmonary artery coupling: prognostic value in patients with secondary mitral regurgitation

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Abstract

Background

Right ventricular (RV) dysfunction and pulmonary artery systolic pressure (PASP) are predictors of outcome in patients with secondary mitral regurgitation (MR). The right heart and the pulmonary circulation are however, interdependent and the relationship between RV contractility and afterload known as RV-PA coupling, can be estimated non-invasively. Accordingly, the purpose of this study is to investigate the incremental prognostic value of the ratio of tricuspid annular plane systolic excursion (TAPSE) and PASP (TAPSE/PASP) in patients with significant secondary MR.

Methods

A total of 591 patients (mean age 66±11 years, 67% male) with symptomatic secondary MR were included. The ratio TAPSE/PASP was measured and its association with the primary endpoint (all-cause mortality) was assessed.

Results

Based on spline curve analysis, a TAPSE/PASP ratio <0.35 was associated with an excess mortality. The patient population was divided into two groups: 229 (39%) patients with TAPSE/PASP<0.35 (impaired RV-PA coupling) and 362 (61%) with TAPSE/PASP≥0.35 (preserved RV-PA coupling). During a median follow-up of 54 [28, 105] months, 295 (50%) patients died. Patients with a TAPSE/PASP≥0.35 showed significantly better survival rates at 5-year follow-up than those with a TAPSE/PASP<0.35 (68% vs 53%, respectively, P= 0.001). On multivariable analysis, a TAPSE/PASP<0.35 remained independently associated with all-cause mortality (HR 1.283, 95% CI 1.008-1.633, P= 0.043).

Conclusions

In heart failure patients with secondary MR, TAPSE/PASP is independently associated with all-cause mortality and has an incremental prognostic value over TAPSE. By taking into account TAPSE/PASP ratio (as a measure for RV-PA coupling), it may improve further risk stratification of patients with secondary MR.

Introduction

Patients with heart failure (HF) and reduced left ventricular (LV) ejection fraction (EF) may develop secondary mitral regurgitation (MR) which leads to chronic volume overload, further LV and left atrial (LA) remodelling, LV dysfunction, distortion of the mitral valve apparatus and eventually increasing MR volume which constitutes a self-perpetuating cycle (1, 2). The chronic volume overload, LV dysfunction and increasing LV filling pressures lead to pulmonary hypertension (PH) and right ventricular (RV) dysfunction with an increased risk of morbidity and mortality (1). The emergence of transcatheter therapies has influenced the management of patients with severe secondary MR. However, two major trials evaluating transcatheter edge-to-edge mitral valve repair in HF patients with secondary MR demonstrated different results in survival and symptomatic improvement (3, 4). These conflicting results demonstrate that patient selection of those who might benefit from transcatheter treatment of MR remains challenging. RV dysfunction, assessed by tricuspid annular plane systolic excursion (TAPSE), has been demonstrated to provide strong prognostic value in patients with HF (5) and to be a major predictor of outcome in patients with moderate to severe secondary MR (6). PH also appears to be associated with increased risk of mortality in patients with secondary MR undergoing transcatheter edge-to-edge repair (7). RV dysfunction and pulmonary pressures are commonly evaluated as separate components. However, RV function is highly dependent on its afterload (8) and evaluation of RV systolic function should be corrected for pulmonary pressures. The ratio between TAPSE and pulmonary arterial systolic pressure (PASP) has been proposed to predict patient prognosis in several diseases (9, 10). This ratio, a measure of RV to pulmonary artery (RV-PA) coupling, assesses RV systolic function adjusted for the degree of afterload (11, 12) and has prognostic value in patients with HF (9) and those undergoing transcatheter aortic valve replacement (10). However, the potential utility of TAPSE/PASP has not yet been evaluated in HF patients with secondary MR. Accordingly, our objective herein was to investigate the prognostic value of RV-PA coupling as assessed by the TAPSE/PASP ratio in patients with secondary MR.

Methods

Patient population

Through the departmental echocardiographic database (Imagevault EchoPAC, General Electric Vingmed Ultrasound, Norway) of Leiden University Medical Center, Leiden, The Netherlands, patients with HF and significant (moderate or severe) secondary MR were identified from April 1999 to July 2017 and included in this retrospective analysis. Patients with previous mitral valve intervention and missing echocardiographic data were excluded. Clinical and demographic characteristics at baseline were collected through the departmental clinical database (EPD-Vision 11.8.4.0; Leiden University Medical Center, Leiden, The Netherlands) and included cardiovascular comorbidities, New York Heart Association (NYHA) functional class, HF etiology and medication use. The institutional review board waved the need for written patient informed consent for this retrospective study with clinically acquired data.

Echocardiography

Using commercially available systems (General Electric Vingmed Ultrasound, Milwaukee, USA) equipped with 3.5 MHz or M5S transducers, transthoracic echocardiography data were acquired in hemodynamically stable patients in the left lateral decubitus position. Parasternal, apical, and subcostal views were acquired and two-dimensional images, M-mode and Doppler data were digitally stored for offline analysis (EchoPAC 201.0.0, General Electric Vingmed Ultrasound, Norway). LV volumes (end-systolic and end-diastolic) were measured in the apical 2- and 4-chamber views and LVEF was calculated according to Simpson's biplane method (13). LA volume was calculated at end-systole from the apical 4- and 2-chamber views (13). LV and LA volumes were indexed for body surface area. LV global longitudinal strain (GLS) was measured from standard 2-dimensional transthoracic echocardiography using the apical 4-chamber, 2-chamber, and long-axis views of the LV (14). LV GLS was determined offline using commercially available software (EchoPAC 201.0.0, General Electric Vingmed Ultrasound, Norway). According to current recommendations, an integrative approach (including qualitative, semiquantitative, and quantitative data) was used to grade MR severity given the following definitions: moderate (grade 2), moderate to severe (grade 3), and severe (grade 4) (15, 16). The vena contracta width was measured on the parasternal long-axis view at the narrowest part of the MR jet (17). The effective regurgitant orifice area (EROA) and regurgitant volume (RVol) were measured according to the proximal isovelocity surface area (PISA) method. An EROA of $\geq$20mm^2 and/or a RVol of $\geq$30 mL/beat defined prognostically severe MR (15, 18, 19). As a measure of LV filling pressures, the ratio between peak early diastolic transmitral flow velocity and peak early diastolic mitral annular tissue velocity ratio (E/e') was calculated (20). TAPSE was measured on the apical 4-chamber view using the M-mode to evaluate RV systolic function (21). The PASP was estimated using the peak velocity of the tricuspid regurgitant jet and the Bernoulli equation and, depending on the diameter and collapsibility of the inferior vena cava, 3, 8 or 15 mmHg were added (21). In patients with atrial fibrillation the average of 3 cardiac beats were calculated. As previously suggested (12), the TAPSE/PASP ratio was calculated as a measure of RV-PA coupling.

Follow-up

The primary endpoint was all-cause mortality. Survival data were obtained from the departmental cardiology information system (EPD-Vision 11.8.4.0; Leiden University Medical Center, Leiden, The Netherlands) which is linked to the governmental death registry database. Data at follow-up was complete for all patients.

Statistical analysis

Continuous data are presented as mean ± standard deviation when normally distributed or as median [Q1, Q3] when not normally distributed. Categorical data are presented as absolute numbers and percentages. Independent samples t-tests or Mann-Whitney U tests were used to compare continuous data, as appropriate. Categorical data were compared with the chi-square test. The changes in hazard ratio (HR) for all-cause mortality over a range of TAPSE/PASP (as a continuous variable) were investigated by a fitted spline curve. Kaplan-Meier analysis was performed to estimate cumulative survival rates for all-cause mortality and comparisons between groups were performed with the log-rank test. First the Kaplan-Meier analysis was performed with patients censored at the time of mitral valve interventions (i.e. Surgical mitral valve repair, surgical mitral valve replacement or transcatheter edge-to-edge mitral valve repair). Second the analyses was performed including the outcome after mitral valve interventions. Cox proportional hazards regression analysis was performed to identify the independent predictors of all-cause mortality. P-values <0.05 in univariable analysis were included in the multivariable model. HRs and 95% confidence intervals were calculated and reported. A likelihood ratio test was performed to investigate the incremental value of TAPSE/PASP over clinical and echocardiographic characteristics for the prediction of all-cause mortality. Changes in global chi-square values were calculated. All statistical analyses were performed using SPSS for Windows, version 23.0 (IBM, Armonk, NY, USA) and R version 3.4.4 (R Foundation for Statistical Computing, Vienna, Austria). A two-tailed p-value <0.05 was considered statistically significant for all analyses.

Results

Patient population

A total of 591 patients (mean age 66±11 years, 67% male) were included. Ischemic heart failure was present in 51% of the patient population. The majority of patients had NYHA II and III heart failure symptoms. The mean LVEF was 29±11% whereas the median

LV GLS was -7.3% [-9.9, -5.2]. The mean TAPSE was 16±5 mm and the mean PASP was 30±13 mmHg for the total population. During a median follow-up of 35 [17, 63] months, mitral valve intervention was performed in 258 (43.7%) patients, including 168 (28.4%) surgical mitral valve repairs, 2 (0.3%) surgical mitral valve replacements, and 88 (14.9%) transcatheter mitral valve repairs. Baseline clinical and echocardiographic characteristics are summarized in Tables 1 and 2.

Table 1. Baseline clinical characteristics according to TAPSE/PASP ratio.

	Total population (n= 591)	TAPSE/PASP ratio < 0.35 (n= 229)	TAPSE/PASP ratio ≥ 0.35 (n= 362)	p-value
Age (years)	66 ± 11	68 ± 10	65 ± 11	0.008
Male, n (%)	395 (67)	165 (72)	230 (64)	0.032
BSA (m^2)	1.92 ± 0.21	1.92 ± 0.21	1.93 ± 0.21	0.773
Prior CABG	101 (17)	53 (23)	48 (13)	0.002
Atrial fibrillation, n (%)	248 (42)	120 (52)	128 (35)	<0.001
Hypertension, n (%)	240 (41)	98 (43)	142 (39)	0.390
Diabetes mellitus, n (%)	138 (23)	57 (25)	81 (22)	0.481
COPD, n (%)	68 (12)	29 (13)	39 (11)	0.483
eGFR (mL/min/1.73m^2)	62 ± 24	58 ± 23	65 ± 24	0.001
Ischemic heart failure, n (%)	304 (51)	131 (57)	173 (78)	0.026
NYHA class, n (%)				0.121†
I	31 (5)	12 (5)	19 (5)	
II	145 (25)	51 (22)	94 (26)	
III	343 (58)	192 (56)	214 (59)	
IV	72 (12)	37 (16)	35 (10)	
Medication, n (%)				
Beta-blockers	419 (71)	163 (71)	256 (71)	0.904
Diuretics	496 (84)	210 (92)	286 (79)	<0.001
ACEi/ARB	480 (81)	177 (77)	303 (84)	0.052
Device therapy, n (%)				
ICD	94 (16)	53 (15)	41 (18)	0.291
CRT*	401 (68)	148 (65)	253 (70)	0.182

Continuous data are presented as mean ± SD or median [Q1, Q3]. Categorical data are presented as numbers and percentages. *CRT at baseline and follow-up. † overall P-value. ACE = angiotensin-converting enzyme; ARB = angiotensin receptor blocker; BSA = body surface area; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; NYHA = New York Heart Association.

Table 2. Baseline echocardiographic characteristics according to TAPSE/PASP ratio.

	Total population (n= 591)	TAPSE/PASP ratio < 0.35 (n= 229)	TAPSE/PASP ratio ≥ 0.35 (n= 362)	p-value
LVEDVi (mL/m^2)	105 ± 40	103 ± 37	107 ± 42	0.260
LVESVi (mL/m^2)	77 ± 36	76 ± 34	78 ± 38	0.606
LVEF (%)	29 ± 11	28 ± 12	29 ± 10	0.160
LV GLS (%)	-7.3 [-9.9, -5.2]	-6.5 [-9.2, -4.7]	-7.6 [-10.2, -5.8]	<0.001
LAVI (mL/m^2)	37 ± 18	42 ± 21	35 ± 16	<0.001
VC width (mm)*	6 ± 2	6 ± 2	6 ± 3	0.927
EROA (mm^2)†	22 ± 11	22 ± 11	21 ± 11	0.599
RVol (mL)‡	31 ± 15	30 ± 14	31 ± 16	0.305
TAPSE (mm)	16 ± 5	13 ± 3	18 ± 4	<0.001
PASP (mmHg)	30 ± 13	49 ± 13	34 ± 10	<0.001
E/e’	25 ± 23	26 ± 19	24 ± 25	0.382

Continuous data are presented as mean ± SD or median [Q1, Q3]. Categorical data are presented as numbers and percentages. *VC width available in 511 patients; †EROA available in 415 patients; ‡RVol available in 414 patients.

E = peak early diastolic transmitral flow velocity; e’ = peak early diastolic mitral annular tissue velocity; EROA = effective regurgitant orifice area; LAVI = left atrial volume index; LVEF = left ventricular ejection fraction; LVEDVi = left ventricular end-diastolic volume index; LVESVi = left ventricular end-systolic volume index; LV GLS = left ventricular global longitudinal strain; PASP = pulmonary artery systolic pressure; RVol = regurgitant volume; TAPSE = tricuspid annular plane systolic excursion; VC = vena contracta.

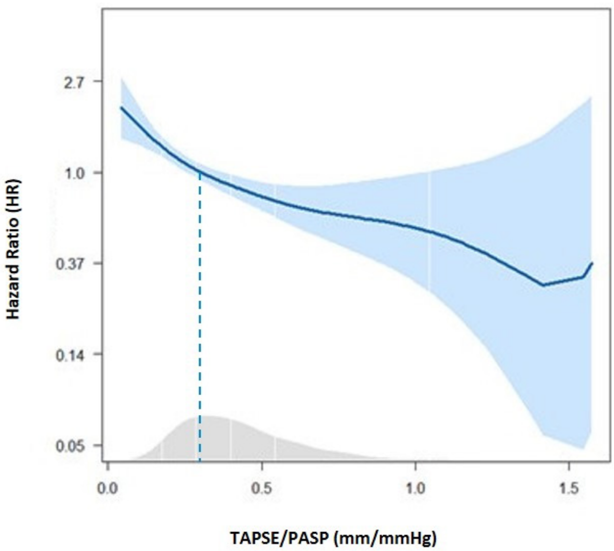

Figure 1. Spline curve for all-cause mortality according to TAPSE/PASP ratio.
All-cause mortality across the range of TAPSE/PASP ratio, plotted as a cubic spline on a log-hazard scale with overlaid 95% confidence intervals. The histogram representing the distribution of TAPSE/PASP ratio in the population is plotted on the X-axis. The shaded light blue region

represents the 95% confidence interval range for each hazard ratio. The vertical dotted line representing the cut-off value TAPSE/PASP 0.35. PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

Survival analysis

During a median follow-up of 54 [28, 105] months, 295 patients (49.9%) died. Based on spline curve analysis, a threshold of TAPSE/PASP ratio <0.35 was associated with an excess risk of all-cause death (Figure 1). The assumption of linearity was not violated (χ^2: 4.236, P= 0.13). This cut-off value was used to identify the patients with more RV-PA uncoupling.

Tables 1 and 2 show the baseline clinical and echocardiographic characteristics for patients with more impaired RV-PA uncoupling (n=229 [38.7%] TAPSE/PASP ratio <0.35) vs. those with more preserved RV-PA coupling (n=362 [61.3%] TAPSE/PASP ≥0.35). Patients with a TAPSE/PASP <0.35 were slightly older, were more frequently male, had a higher prevalence of atrial fibrillation and more impaired renal function compared to patients with a TAPSE/PASP ≥0.35. Patients with a TAPSE/PASP <0.35 were more symptomatic and were more frequently using diuretics compared to those with a TAPSE/PASP ≥0.35.

In terms of echocardiographic characteristics, patients with a TAPSE/PASP ≥0.35 had less impaired LV systolic function assessed by LV GLS. However, there were no significant differences in LV volumes and LVEF, E/e' ratio or MR severity. Patients with a TAPSE/PASP <0.35 had a larger left atrial volume index compared to those with a TAPSE/PASP ≥0.35.

Survival analysis censored for occurrence of mitral valve intervention showed that patients with a TAPSE/PASP ≥0.35 had better survival rates as compared to patients with a TAPSE/PASP <0.35 (5-year estimated survival rates 81.1% vs. 66.7% respectively, P=0.002; Figure 2, panel A). Patients with a TAPSE/PASP ≥0.35 also had better survival rates than those with a TAPSE/PASP<0.35 when all patient follow-up data was analyzed, including after the performance of mitral valve intervention (5-year estimated survival rates 68.3% vs. 52.6% respectively, P=0.001; Figure 2, panel B). After correcting for age, male sex, impaired renal function, diabetes mellitus, ischemic aetiology, the use of diuretics, LV GLS and the performance of mitral valve intervention, by Cox proportional hazards modelling a TAPSE/PASP <0.35 was independently associated with all-cause mortality (HR 1.28, 95% CI 1.01-1.63, P=0.04) (Table 3).

Table 3. Univariate and multivariable cox regression analysis to identify associates of all-cause mortality.

	Univariate analysis			Multivariable analysis		
Variable	**HR**	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Age	1.030	1.019-1.043	<0.001	1.021	1.008-1.034	0.002
Male	1.582	1.224-2.046	<0.001	1.470	1.117-1.936	0.006
BSA (m^2)	1.172	0.689-1.995	0.558			
eGFR <60 (mL/min/1.73m^2)	2.845	2.242-3.611	<0.001	2.372	1.840-3.058	<0.001
Hypertension	0.936	0.741-1.183	0.581			
Diabetes mellitus	1.362	1.045-1.774	0.022	1.294	0.988-1.697	0.062
Atrial fibrillation	1.209	0.961-1.522	0.106			
Ischaemic aetiology	1.340	1.064-1.688	0.013	1.111	0.870-1.418	0.398
NYHA classification ≥ II	1.098	0.629-1.915	0.743			
Diuretics	2.204	1.493-3.253	<0.001	1.799	1.206-2.682	0.004
MV intervention*	1.148	0.906-1.455	0.253			
LV GLS (%)	1.090	1.051-1.131	<0.001	1.067	1.027-1.109	0.001
E/e'	1.002	0.997-1.007	0.406			
TAPSE/PASP ratio <0.35	1.637	1.300-2.061	<0.001	1.283	1.008-1.633	0.043

BSA = body surface area; CI = confidence interval; E = peak early diastolic transmitral flow velocity; e' = peak early diastolic mitral annular tissue velocity; eGFR = estimated glomerular filtration rate; LV GLS = left ventricular global longitudinal strain; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

*Surgical mitral valve repair, surgical mitral valve replacement or transcatheter edge-to-edge mitral valve repair, compared to optimal medical therapy alone

Incremental prognostic value of TAPSE/PASP

A likelihood ratio test was performed to determine the incremental prognostic value of TAPSE alone and TAPSE/PASP over clinical and echocardiographic parameters, both as a continuous variable and as a dichotomous variable. No significant increase in the chi-square value was observed after the addition of TAPSE alone (as a continuous variable) to the baseline model ($\chi 2$ difference = 0.29, P= 0.790, Figure 3, Panel A). However, addition of TAPSE/PASP (as a continuous variable) to the baseline model did show a significant increase in the chi-square value ($\chi 2$ difference = 8.48, P= 0.002, Figure 3, Panel A). Similarly, introducing TAPSE alone as a dichotomous variable (<17 mm, according to contemporary guidelines)(13) did not significantly increase the chi-square value (χ2 difference = 0.02, P= 0.95, Figure 3, Panel B). However, adding TAPSE/PASP <0.35 resulted in a significant increase in the chi-square value (χ2 difference = 5.65, P=0.04, Figure 3, Panel B), demonstrating the incremental prognostic value of TAPSE/PASP.

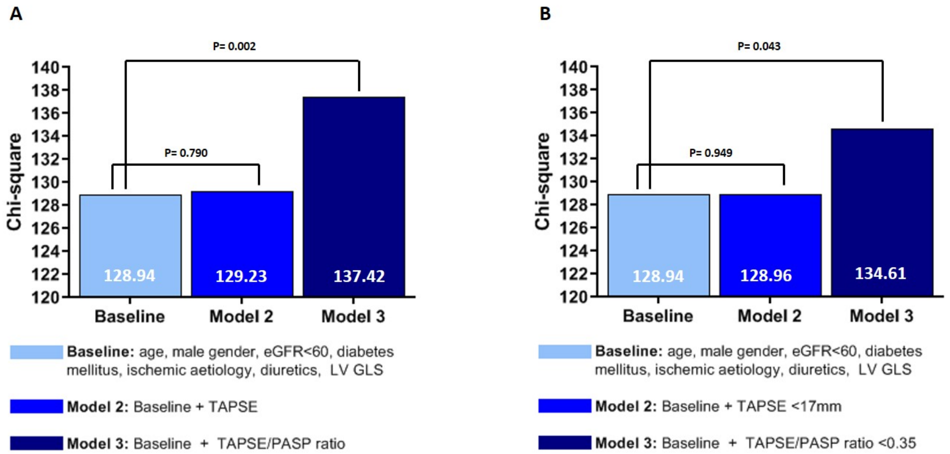

Figure 3. Incremental prognostic value of TAPSE/PASP ratio.
The incremental value of TAPSE/PASP ratio, as a continuous value *(A)* and dichotomized *(B)*, over clinical and echocardiographic parameters for the prediction of all-cause mortality.
eGFR = estimated glomerular filtration rate; LV GLS = left ventricular global longitudinal strain; PASP = pulmonary artery systolic pressure; TAPSE = tricuspid annular plane systolic excursion.

Discussion

In the present study, we evaluated the prognostic value of TAPSE/PASP (an echocardiographic surrogate of RV-PA coupling) in HF patients with significant secondary MR (Figure 4). Our findings demonstrated an independent association of TAPSE/PASP with all-cause mortality and an incremental prognostic value of the TAPSE/PASP ratio compared with use of individual parameters of RV systolic function not corrected for afterload.

Secondary MR and prognosis: role of pulmonary hypertension and right ventricular function

Secondary MR results from an imbalance between closing and tethering forces on the mitral valve due to LV dilation and dysfunction (22, 23). The chronic volume overload caused by secondary MR leads to a self-perpetuating cycle characterized by LV dilation and dysfunction, distortion of the mitral valve apparatus and increasing MR volume which can lead to pulmonary congestion, increased pulmonary pressures and RV dilation and dysfunction (1, 2). PH is observed in approximately 40% of patients with secondary MR (24) and is associated with adverse outcomes, even after correcting MR with surgical or transcatheter edge-to-edge mitral valve repair (7, 25). In addition, RV dysfunction has been associated with an increased risk of mortality in patients with HF (5) and is a major predictor of outcome specifically in patients with secondary MR (6, 26). However, RV systolic function is highly dependent on pulmonary pressures and different afterload conditions can significantly influence its estimation (2). Integration of PH (assessed by PASP) and RV function (assessed by TAPSE) using the TAPSE/PASP ratio enables an estimation of RV-PA coupling. Until recently, measures for RV-PA coupling were evaluated invasively. A study by Tello *et al*. (12) validated TAPSE/PASP ratio as a surrogate of RV-PA coupling in 52 patients with PH. A TAPSE/PASP <0.31 mm/mmHg defined RV-PA uncoupling and was associated with poor outcome. Guazzi *et al*. (9) investigated the TAPSE/PASP ratio in 293 HF patients with both preserved and reduced LVEF. A TAPSE/PASP ratio <0.36 mm/mmHg was the best cutoff value associated with prognosis (area under the curve 0.78; 95% CI 0.75-0.86; P<0.001). The TAPSE/PASP cutoff values most strongly associated with mortality in these prior studies were similar to that observed in the current large-scale study of patients with secondary MR. In the present population, a TAPSE/PASP <0.35 mm/mmHg was independently associated with long-term mortality. In contrast, TAPSE alone was not an independent predictor of long-term outcomes.

Clinical implications of TAPSE/PASP in secondary MR

The use of transcatheter mitral valve repair in HF patients with secondary MR is increasing. Two major trials that evaluated the prognostic impact of transcatheter edge-to-edge mitral valve repair in HF patients with secondary MR reported varying results in terms of mortality and symptomatic improvement (3, 4). Although patients were selected for these trials according to contemporary guidelines (18, 27), their conflicting results highlight the challenge of identifying patients who may benefit from intervention. In this regard baseline RV dysfunction has been shown to be an important predictor of outcomes after mitral valve intervention (28, 29). Osterech *et al*. (30) demonstrated higher all-cause mortality in patients with compared without baseline RV dysfunction (assessed by TAPSE) in 130 patients with secondary MR undergoing transcatheter mitral valve repair. However, RV dysfunction is significantly affected by afterload and the sole use of TAPSE may provide an imprecise estimation of RV contractility. As demonstrated in the present study, by taking into account loading conditions the TAPSE/PASP ratio (reflecting RV-PA coupling) may further improve risk stratification of patients with secondary MR. Patients with a lower TAPSE/PASP (indicating RV-PA uncoupling) may be considered to have more advanced disease as the RV is not able to further increase its contractility (TAPSE) to cope with the increased afterload (PASP). In such patients RV function might recover less from the afterload reduction following correction of the MR. In this regard, in our study a TAPSE/PASP <0.35 was independently associated with worse outcomes in patients with secondary MR. However, future prospective studies are warranted to investigate whether the selection of candidates for valvular interventions would be improved by considering this measure of RV-PA uncoupling. Nonetheless, the present study confirms the importance of assessing RV function in HF patients with secondary MR and has demonstrated that correcting for RV afterload when evaluating RV performance (e.g. with the TAPSE/PASP ratio) provides greater prognostic utility than considering RV performance alone (e.g. TAPSE). The prognostic utility of TAPSE/PASP ratio is even confirmed in patients with significant secondary tricuspid regurgitation (TR) (31).

Study limitations

The single center and retrospective nature of this study limits the generalizability of the results. Data on BNP or NT-proBNP were not systematically acquired in our centre. A recent study by Karam et al. (32) also evaluated RV-PA coupling in patients with secondary MR undergoing transcatheter mitral valve repair (TMVR). Although the results are similar, our study evaluated the prognostic value of RV-PA coupling in all patients with SMR and not only the patients requiring intervention. Pressure-volume loops derived from right heart catheterization are the gold standard to measure ventricular and arterial elastances and RV-PA coupling (33), and there are inherent limitations to the use of non-invasive measures of contractility and total (pulsatile and resistive) afterload. Although the evaluation of RV function with TAPSE might be considered a limitation of the current study, TAPSE is a robust and recommended parameter to assess longitudinal RV function (21). In addition, the pulsatile component of afterload contributes only ~23% to total afterload in normal patients and those with arterial PH (34) supporting the use of PASP for this analysis. Finally correcting TAPSE for PASP as an index of RV-PA coupling had been demonstrated to be the best echocardiographic indicator of RV-PA coupling against invasive measurements (11, 12).

Conclusions

In the present large-scale study of HF patients with significant secondary MR treated medically and with mitral valve interventions, RV-PA uncoupling as assessed by the TAPSE/PASP ratio was independently associated with long-term all-cause mortality and had incremental prognostic utility compared with TAPSE alone.

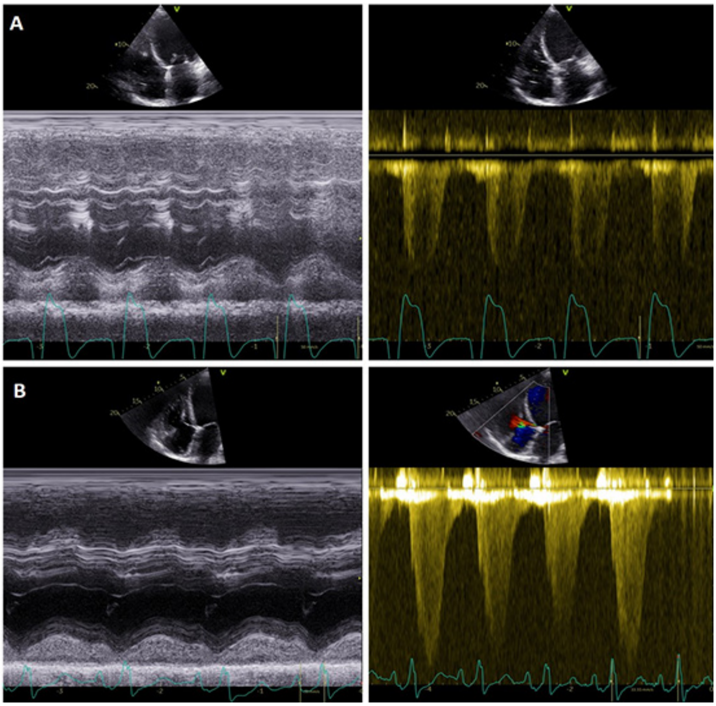

Figure 4. TAPSE/PASP ratio in patients with secondary MR

(A) A patient with severe secondary MR, TAPSE of 20 mm and PASP of 32.37 mmHg. This patient had a TAPSE/PASP ratio of 0.62 (more preserved RV-PA coupling) and did not die during follow-up. **(B)** A patient with severe secondary MR, TAPSE of 17 mm and PASP of 67.55 mmHg. This patient had a TAPSE/PASP ratio of 0.25 (more impaired RV-PA coupling) and died during follow-up. Despite both patients having preserved RV function according to TAPSE, the TAPSE/PASP ratio and outcome were significantly different. MR = mitral regurgitation; PA = pulmonary arterial; PASP = pulmonary artery systolic pressure; RV = right ventricular; TAPSE = tricuspid annular plane systolic excursion.

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