Echocardiographic estimation of right ventricular wall tension: haemodynamic comparison and long-term follow-up

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Abstract

Prognosis in pulmonary hypertension is strictly linked to right ventricle failure, which results from uncoupling between right ventricle function and its afterload. This study sought to describe how to estimate with echocardiography right ventricular wall tension, its correlation with right ventricle haemodynamics and its prognostic role. A total of 190 patients without overt right ventricle failure but with suspected pulmonary hypertension on a previous echocardiogram underwent right heart catheterization and nearly-simultaneous echocardiography. Right ventricular wall tension was estimated according to Laplace's law as right ventricle length × tricuspid regurgitation peak gradient and it was correlated with right ventricle haemodynamic profile; its potential prognostic impact was tested along with canonical right ventricle function parameters. Right ventricular wall tension correlated significantly with invasive estimation of right ventricle end-diastolic pressure (R: 0.343, $p < 0.001$) and with several other haemodynamic variables, such as mean pulmonary artery pressure, pulmonary artery compliance, transpulmonary gradient, pulmonary vascular resistance, right atrial pressure and right ventricle stroke work index (all $p < 0.001$). At a mean follow-up of five years and three months, only right ventricular wall tension was associated to all-cause mortality ($p = 0.036$), while tricuspid annular plane systolic excursion ($p = 0.536$), right ventricle fractional area change ($p = 0.383$), right ventricle fractional area change ($p = 0.076$), tricuspid regurgitation peak gradient ($p = 0.107$) and tricuspid annular plane systolic excursion/tricuspid regurgitation peak gradient ($p = 0.181$) could not. We identified a novel bedside echocardiographic predictor of altered right ventricle haemodynamics, which is precociously altered in patients without overt right ventricle failure and is associated to all-cause mortality at a long-term follow-up. Further studies are needed to confirm its role in pulmonary hypertension patients.

Introduction

Pulmonary hypertension (PH) is a severe disease with a poor prognosis,[1] which may originate from a primary pulmonary vascular dysfunction or from right ventricle (RV) pressure overload secondary to left heart disease.[2] In both cases, the natural history of the disease evolves into progressive RV failure that represents the main determinant of PH prognosis.[3,4]

Several studies have focused on the coupling between RV function and pulmonary artery (PA) resistance, hence shaping a pathophysiological background that accurately describes how RV haemodynamics adapt to the pressure overload that accompanies PH.[5–8] According to this model, RV–PA coupling is mainly defined by Ees/Ea, where Ees represents end-systolic RV elastance and Ea

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describes PA elastance; Ees is defined as the slope between the end-systolic pressure versus the end-systolic volume in pressure–volume loop under different loading status, while Ea is defined as the ratio between end-systolic pressure and stroke volume (SV).[6–8]

PH is characterized by an initial increase of Ea, to which the RV responds with enhanced inotropism, thus leading to higher Ees; since both factors increase in a similar fashion, in this first phase Ees/Ea will remain normal or nearly normal. Nevertheless, this adaptive mechanism occurs at the cost of increased right ventricular end-diastolic pressure (RVEDP), which translates into raised RV wall tension (RVWT) and altered RV energetics.[6,9] While PH progresses and PA elastance increases, Ea will eventually reach a critical point that cannot be further tolerated by the RV; as RVEDP rises beyond this point, Ees/Ea will then decrease and signs and symptoms of RV failure will be manifest.[10]

We investigated RVWT, derived from transthoracic echocardiography, in comparison with contemporary available methods estimating RV haemodynamics, and we assessed whether it can stratify prognosis in a precocious phase of PH, when canonical echocardiographic parameters are expected to be normal or nearly normal.

Methods

Study population

The study population of the present work was selected from the RIGHT1 study,[11] a prospective, blinded study designed to compare the performance of several echocardiographic indices of pulmonary haemodynamics. RIGHT1 was conducted between July 2011 and November 2013, enrolling 200 patients with a generic indication for right heart catheterization (RHC) referred to the Haemodynamic Laboratory of the AOU Città della Salute e della Scienza of Turin. Exclusion criteria included ongoing infusion of inotropes, overt heart failure, known pulmonary stenosis or ventilatory support.

Haemodynamic assessment

RHC was performed through femoral or jugular access according to operator's preference. Right atrial pressure, RV pressure, PA pressure and pulmonary capillary wedge pressure were acquired. The zero reference level was always set at the midthoracic level. Cardiac output was evaluated using Fick's method and/or thermodilution. PA compliance was calculated according to the single element model as SV/PA pulsatory pressure (namely, systolic–diastolic PA pressure).[12] All measurements were made at end-expiration, and values used in our analysis were a mean of three acquisitions, in case sinus rhythm was present, or five in case of atrial fibrillation. Physicians performing the RHC were blinded to the results of the transthoracic echocardiography.

Hemodynamic values were interpreted according to international consensus.[13,14]

Echocardiographic assessment

All patients underwent a complete transthoracic echocardiography within 30 min prior to RHC; RHC was started immediately after echocardiography. A Philips IE33 machine (Philips Medical Systems, Andover, MA) with a S5 probe was used for all 2D and Doppler acquisitions. All echocardiographic examinations were performed with a respirometer for the precise timing of respiratory cycles. Patients were instructed to breathe normally. All morphologic and functional chamber evaluations were made according to the international guidelines available in 2013[15,16]; multiple indexes of RV diastolic and systolic function were acquired accordingly. Two operators (C.M. and E.A.) performed most of the exams. All measurements were obtained offline using a dedicated software (ComPACS; MediMatic S.R.L., Genoa, Italy) by an experienced operator, blinded to the RHC results.

Right ventricular wall tension

RVWT, based on Laplace–Young's law, was calculated as follows

$$RVWT = TRPG \times RVD3$$

TRPG represents transtricuspid pressure gradient, defined as the maximum gradient across the tricuspid valve, and it was acquired according to international guidelines.[15,16] Multiple measurements were made from different echocardiographic windows and the highest peak gradient recorded was used in the analysis. RVD3 represents end-diastolic RV length: this index was preferred to other RV diameters because the systolic motion of the RV occurs mainly along its length, and therefore the RV motion vector runs more parallel to RVD3 than to other RV diameters. However, we are aware that this may be an oversimplification of the complex RV geometry. RVD3 was measured in the RV dedicated four-chamber-view, as suggested by current guidelines.[15,16] RV wall thickness was not included in the traditional Laplace equation due to its significant inter- and intra-observer variability, which could harmfully confound the results.[17]

Follow-up

The participants in this study were retrospectively investigated for all-cause death via a dedicated software used in our centre (TrakCare, InterSystems Corporation, Cambridge, MA, USA); when an event could not be traced this way, a telephonic follow-up was performed. Follow-up was censored at death occurrence or at last contact with the patient, be it either clinical or by telephone.

Statistical analysis

Data were presented as mean ± standard deviation or as median and interquartile range when appropriate. The parametric distribution of variables was analysed using the Shapiro–Wilk test. Differences between means were examined using the Student t test or analysis of variance for normally distributed variables. The results of the Wilcoxon rank-sum test or the Kruskal–Wallis test were analysed for non-normally distributed variables. The relationship between the echocardiographic estimates and RHC values was tested using Pearson correlation and linear regression. Fisher's R-to-Z transformation was used to examine the statistical significance of the differences between correlations. Kaplan–Meier cumulative survival was calculated. In order to assess the cut-off value for RVWT, a receiver operating characteristic (ROC) analysis was performed and Youden's index was used. Two-tail p-value < 0.05 was considered statistically significant. Statistical analysis was conducted using SPSS, version 21.

Results

Study population

Two-hundred patients were enrolled in this study; 10 patients were excluded due to technical issues during catheterization, inconclusive catheterization results or because echocardiography could not be performed. One-hundred and ninety patients were included in the baseline data analysis; 157 (83%) patients underwent RHC for diagnostic purposes, 27 (14%) for known PH follow-up and 6 (3%) for cardiac transplantation follow-up. Basic anthropometric, haemodynamic and echocardiographic characteristics are summarized in Table 1. Mean age was 61.9 ± 13.7 years; 103 (54%) were male; and 21 (11%) had prior myocardial infarction. One-hundred and twenty-six (66%) patients were found to have PH at RHC, 37 (19%) of whom presented with a precapillary form.[2] Among the 37 pre-capillary PH patients, 14 (38%) patients were on PH follow-up and 8 of them (57%) were using PH-specific therapies; 23 patients (62%) had a novel diagnosis of pre-capillary PH.

Echocardiographic parameters of RV diastolic function are summarized in Table 2; except for E/e', isovolumetric relaxation time and deceleration time of the E wave, which were consistent with altered RV diastolic function, mean values were within normal limits according to guidelines. RVD3 and TRPG were both available for 159 patients, therefore RVWT analyses has been performed in this subpopulation.

Haemodynamic comparison

RVWT was associated with invasive assessment of RVEDP, with a R index equal to 0.343 (R^2: 0.117, $p < 0.001$), as depicted in Fig. 1. Contrarily, correlation between validated

Table 1. Demographic, haemodynamic and echocardiographic characteristics of the study population ($n = 190$).

Baseline features	
Age (years)	61.85 ± 13.72
Male sex	103 (53.9%)
NYHA I–II	144 (75.80%)
COPD	10 (5.26%)
PH	126 (66%)
Precapillary PH	37 (29%)
Prior myocardial infarction	21 (11.06%)
RHC parameters	
Cardiac output by thermodilution (l/min)	5.35 ± 1.87
mPAP (mmHg; $n = 190$)	31.21 ± 12.35
PVR (WU; $n = 184$)	2.68 ± 2.22
PAWP (mmHg; $n = 190$)	17.70 ± 7.67
RVSWI (g/m/beat; $n = 178$)	8.27 ± 4.75
Echocardiographic left heart parameters	
EF (%; $n = 190$)	50.29 ± 16.21
LVEDD (mm; $n = 185$)	50.46 ± 9.79
LVEDV (ml; $n = 161$)	111.36 ± 79.08
Lateral mitral S' wave (cm/s; $n = 184$)	7.27 ± 2.66
Mean mitral E/A ($n = 135$)	1.37 ± 1.79
Mean mitral E/E' ($n = 169$)	13.85 ± 10.94
Left atrial volume index (ml/mq; $n = 93$)	51.95 ± 22.34
Mild or moderate mitral regurgitation	180 (94.8%)
Echocardiographic right heart parameters	
RV FAC (%; $n = 150$)	41.43 ± 10.45
TAPSE (mm; $n = 183$)	20.31 ± 5.59
TRPG (mmHg; $n = 184$)	35.17 ± 17.64
TAPSE/TRPG (mm/mmHg; $n = 183$)	0.72 ± 0.41
RVD3 (mm; $n = 159$)	65.32 ± 8.95
Tricuspid S' wave (cm/s; $n = 179$)	10.70 ± 2.96
Mild or moderate tricuspid regurgitation	176 (92.6%)

Note: Values in brackets indicate the unit of measurement and number of patients for each variable.
NYHA: New York Heart Association; COPD: chronic obstructive pulmonary disease; PH: pulmonary hypertension; mPAP: mean pulmonary artery pressure; PVR: pulmonary vascular resistance; PAWP: pulmonary artery wedge pressure; RVSWI: right ventricle stroke work index; EF: ejection fraction; LVEDD: left ventricle end-diastolic diameter; LVEDV: left ventricle end-diastolic volume; RV FAC: right ventricle fractional area change; TAPSE: tricuspid annulus plane systolic excursion; TRPG: tricuspid regurgitation peak gradient.

echocardiographic methods to estimate RVEDP was not statistically significant, except for tricuspid E wave velocity ($p = 0.002$), as shown in Table 3. After Fisher's R-to-Z transformation, the correlation between RVWT and RVEDP was significantly higher than the correlation between canonical parameters and RVEDP (all $p < 0.01$), except for tricuspid E wave velocity ($p = 0.198$). RVWT significantly correlated with several indexes of RV uncoupling, such as pulmonary vascular resistance (PVR), PA pulsatory

pressure, PA compliance, right ventricular stroke work index (RVSWI) and the ratio between cardiac index (CI) and mean right atrial pressure (mRAP) (all $p < 0.001$), as shown in Fig. 2 and Table 4.

RVWT was significantly higher in patients diagnosed with PH (2747 mmHg × mm vs 1422 mmHg × mm, $p < 0.001$), as were TRPG (41.37 mmHg vs 23.26 mmHg, $p < 0.001$) and RVD3 (66.95 mm vs 62.02 mm, $p < 0.001$). Moreover, RVWT showed a slightly higher correlation with mean pulmonary artery pressure than TRPG and RVD3 alone (R: 0.74, 0.72 and 0.26, respectively, all $p < 0.001$).

Follow-up and survival

Among the 190 patients who were included in the study, 31 (16%) were lost at follow-up, and 159 patients were included in the analysis. Mean follow-up was five years and three months; death was observed in 47 (30%) patients. Among the 27 patients (14%) who were enrolled for PH follow-up, 5 (19%) died at follow-up.

The 159 patients available for analysis were divided into two groups by the cut-off value of 1945 mmHg × mm, defined by low (RVWT < 1945 mmHg × mm) or high RVWT (RVWT > 1945 mmHg × mm), as calculated by

Table 2. Validated echocardiographic parameters for evaluation of right ventricular diastolic function ($n = 190$).

E (m/s)	0.43 ± 0.157
A (m/s)	0.43 ± 0.130
E/A	0.97 ± 0.42
E DcT (s)	0.75 ± 0.34
IVRT (ms)	84.86 ± 34.25
E' (cm/s)	9.19 ± 3.45
A' (cm/s)	12.24 ± 4.08
E'/A'	0.8267 ± 0.6259
E/E'	5.17 ± 2.52

Note: Values are expressed as mean ± standard deviation.
E DcT: E wave deceleration time; IVRT: isovolumetric relaxation time.

Table 3. Correlation between echocardiographic parameters of right ventricular diastolic function and right ventricular end-diastolic pressure.

Characteristics	R–R^2	p Values
E (m/s)	0.25–0.06	0.002
A (m/s)	0.08–0.01	0.388
E/A	0.08–0.01	0.399
E DcT (s)	0.01– < 0.01	0.921
IVRT (ms)	0.06– < 0.01	0.499
E' (cm/s)	0.08– < 0.01	0.307
A' (cm/s)	0.13–0.02	0.131
E'/A'	0.12–0.02	0.159
E/E'	0.03– < 0.01	0.714

E DcT: E wave deceleration time; IVRT: isovolumetric relaxation time.
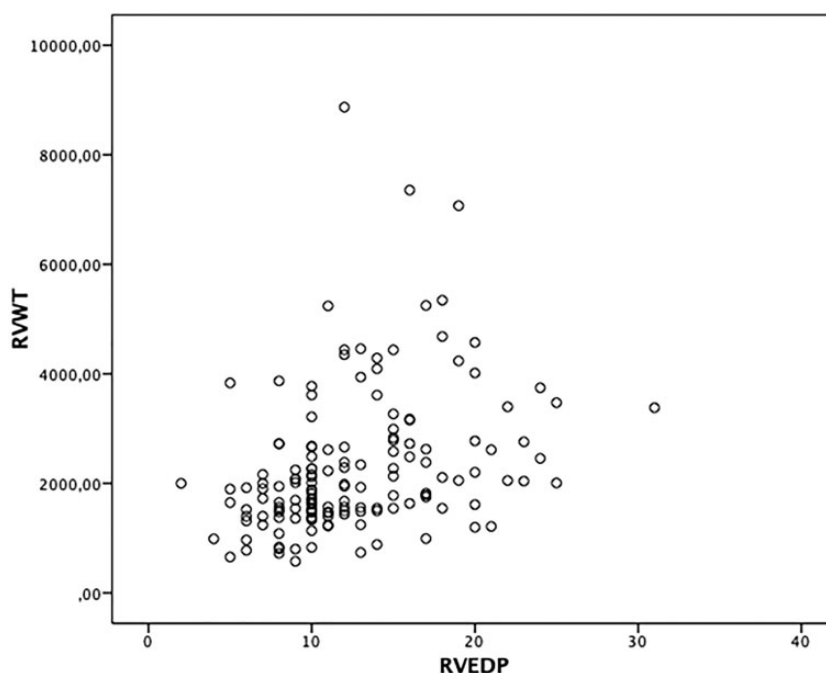
Fig. 1. Relationship between right ventricular end-diastolic pressure and right ventricular wall tension ($n = 159$).
RVWT: right ventricular wall tension; RVEDP: right ventricular end-diastolic pressure.
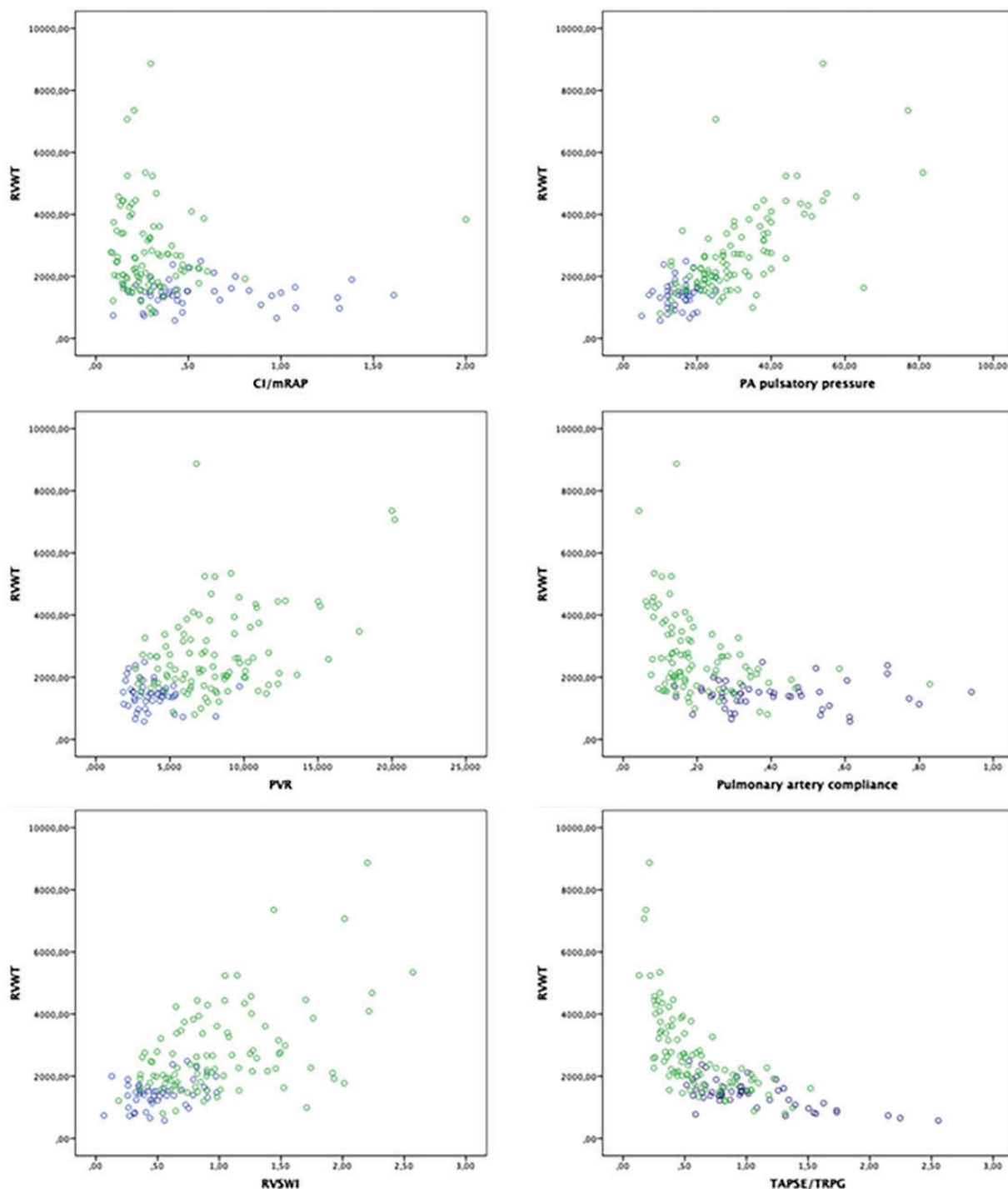
Fig. 2. Relationship between right ventricular wall tension (RVWT) and cardiac index over mean right atrial pressure (CI/mRAP) (*top left panel*), pulmonary artery (PA) pulsatory pressure (*top right panel*), pulmonary vascular resistance (PVR) (*middle left panel*), pulmonary artery compliance (*middle right panel*), right ventricle stroke work index (RVSWI) (*bottom left panel*) and tricuspid annular plane systolic excursion over tricuspid regurgitation peak gradient (TAPSE/TRPG) (*bottom right panel*). The blue dots indicate patients without pulmonary hypertension (PH); the green dots denote patients with PH.

Youden's index in conjunction with ROC analysis. Kaplan Meier analysis for overall survival showed a global *p*-value of 0.036 (OR: 1.67; Fig. 2). In patients with high RVWT, stratifying survival analysis by PH aetiology (pre vs post-capillary) did not result significant ($p = 0.801$). Conversely, stratification of the study population by low or preserved tricuspid annulus plane systolic excursion (TAPSE), RV fractional area change or RV S' according

Table 4. Correlation between right ventricular wall tension and invasive haemodynamic parameters of right ventricular function ($n = 159$).

Characteristics	R–R^2	p Value
mPAP	0.742–0.550	<0.001
PA pulsatory pressure	0.740–0.547	<0.001
RV differential pressure	0.794–0.630	<0.001
mRAP	0.326–0.106	<0.001
CI/mRAP	0.209–0.044	0.012
RVSWI	0.326–0.106	<0.001
PA compliance	0.449–0.202	<0.001
PVR	0.531–0.282	<0.001
RV basal diameter	0.326–0.106	<0.001
RV medium diameter	0.403–0.162	<0.001
Right atrium area	0.204–0.042	0.013
RV FAC	0.382–0.146	<0.001
RV end-diastolic area	0.347–0.120	<0.001

PA: pulmonary artery; RV: right ventricle; mRAP: mean right atrium pressure; CI: cardiac index; PVR: pulmonary vascular resistance; RVSWI: right ventricle stroke work index; RV FAC: right ventricle fractional area change.

to guidelines' cut-offs was not associated with survival (log-rank p-values 0.536, 0.383 and 0.076, respectively) (Fig. 3). TAPSE/TRPG was not significantly able to predict survival using the proposed cut-off of 0.36 mm/mmHg ($p = 0.181$)[18]; a similar result was observed by stratifying our population according to the TRPG cut-off of 30 mmHg ($p = 0.107$).

Discussion

PH prognosis strictly depends on the interplay between pulmonary circulation and the RV. The coupling between RV afterload, i.e. pulmonary circulation, and RV global function is defined by the ratio between RV end-systolic elastance and PA elastance (Ees/Ea), as previously described. During the first phases of PH, the RV maintains a pseudo-physiological coupling at the cost of altered metabolism and increased RVEDP, thus leading to raised RVWT while patients are still asymptomatic and coupling is preserved.[6–9] The aim of this study was to identify a novel echocardiographic parameter which could estimate initial RV stress in a population without evident RV dysfunction and normal systolic contractility: we found that RVWT was the only echocardiographic parameter, apart from tricuspid E wave velocity, which is associated with a raising RVEDP, which is the first step in the natural history of RV failure. Moreover, we observed a significant relationship between this new parameter and a large number of invasive indexes of RV mal-adaptation to afterload (CI/mRAP, RVSWI) and altered pulmonary elastance (PA compliance, PA pulsatory pressure).[19]

To our knowledge, this is the first study aiming to find an index able to estimate RV wall stress; few methods have been proposed to estimate left ventricular wall tension,[20] but none had been assessed for the RV so far.

In our study, an increase in RVWT reflected into a significant increase of all-cause mortality: RVWT showed a significant prognostic impact with a cut-off of 1945 mmHg × mm, while traditional parameters of systolic RV function could not significantly predict prognosis. This might be due to the characteristics of our population, consisting of patients without PH or at an early/intermediate phase of the disease, when the RV still performs normally or near normally, and therefore canonical parameters of impaired systolic function might not be significantly altered, while the RV silently starts to strain against growing PVR. We would also like to stress the fact that TRPG could not significantly stratify prognosis with a cut-off value of 30 mmHg; however, only 26 patients with TRPG < 30 mmHg underwent RHC and a net, albeit non-significant, separation can be seen between the two curves of TRPG ($p = 0.107$, Fig. 3). This, however, stresses the concept that RVWT might have a significant impact on PH prognosis, which might be more meaningful than TRPG alone, denoting an effective and silent RV derangement.

Several limits must be addressed. First, in the absence of a 'gold standard' method to estimate RVWT, we had to rely on indirect hemodynamic indexes of early RV diastolic (and systolic) dysfunction, such as RVEDP. Furthermore, using RVD3 as the only diameter in the formula for RVWT calculation is an oversimplification of the complex RV anatomy; nevertheless, as previously explained, since RV contraction occurs mainly on the longitudinal axis, RV length, which runs parallel to this axis, was chosen to find RVWT. Moreover, a significant association was consistently found between the other RV diameters and RVWT in several sub-analyses not presented in this paper. Another limitation of the present study is the inability to trace back the specific cause of death; however, it may be inferred that an excess of all-cause mortality in this population could be largely driven by cardiovascular death due to the relatively high prevalence of PH (66%).

Despite its limitations, this method may be the first step in the research of predictors of early RV stress in a population where the diagnosis must be as premature as possible. We strongly believe that a deeper analysis of RV stress could have a huge impact in this field of research, be it either with magnetic resonance imaging or by invasive haemodynamic assessment, which could plot a pressure/volume loop to derive Ees/Ea.[21] Our method, however, is simple, bed-side disposable and cheap, and it could identify patients who may require further analyses and strict follow-up, due to the fact that the patient's RV may be facing a subtle, but risky, increase of wall tension.
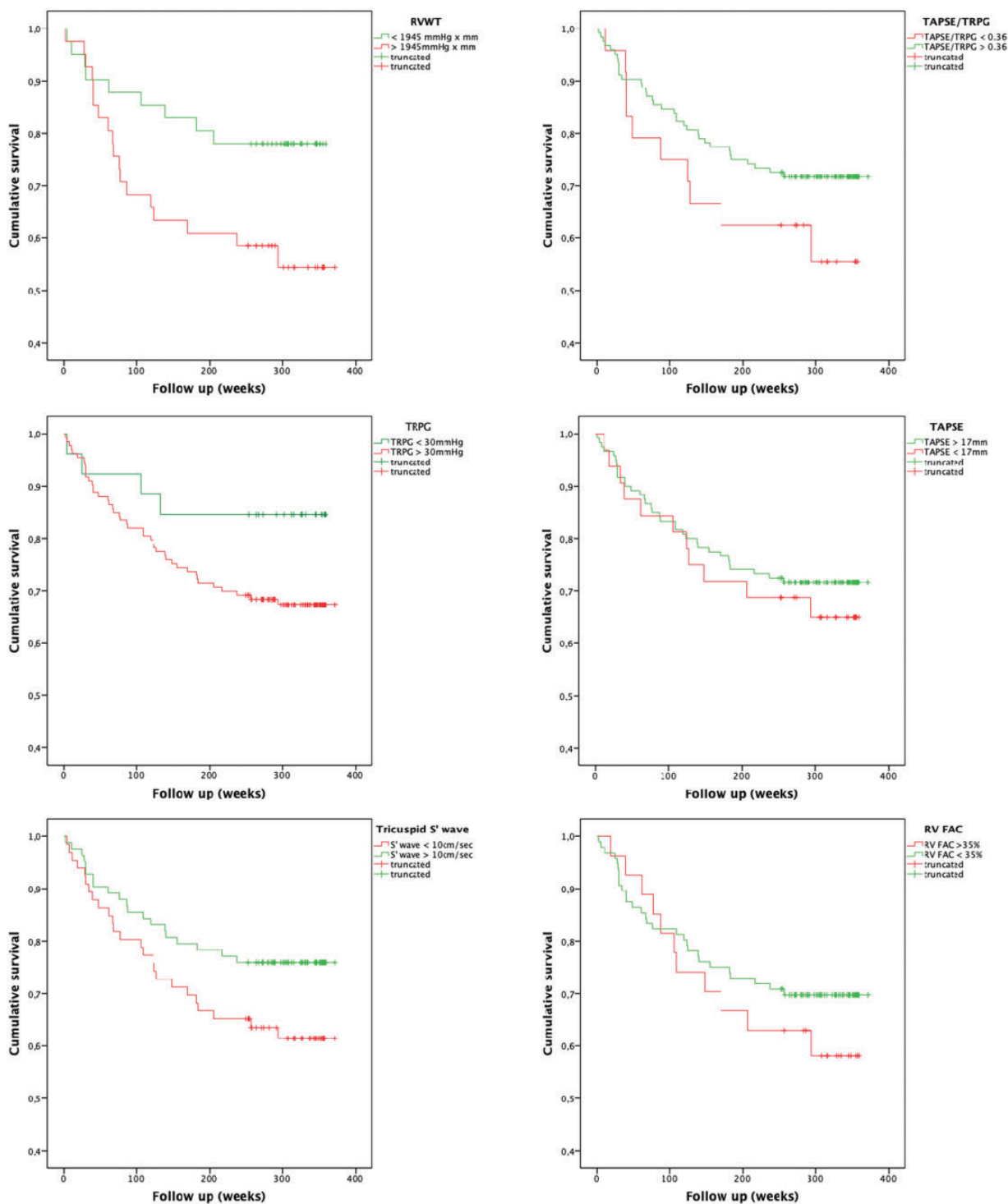
Fig. 3. Kaplan–Meier curves describing cumulative survival for all-cause mortality according to right ventricular wall tension (RVWT) (*top left panel*), tricuspid annular plane systolic excursion over tricuspid regurgitation peak gradient (TAPSE/TRPG) (*top right panel*), TRPG (*middle left panel*), TAPSE (*middle right panel*), tricuspid S' wave *(bottom left panel)* and right ventricle fractional area change (RV FAC) (*bottom right panel*).

Conclusions

In conclusion, we identified a novel bedside echocardiographic predictor of altered RV haemodynamics, which is precociously altered in patients without overt RV failure and is associated to all-cause mortality at a long-term follow-up. Further studies are needed to confirm its role in PH patients, primarily with a prospective and not a retrospective analysis. We strongly hope that in the near future, new and more precise methods to identify silent RV failure will be conceived.

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References

1. Humbert M, Sitbon O, Chaouat A, et al. Survival in patients with idiopathic, familial, and anorexigen-associated pulmonary arterial hypertension in the modern management era. *Circulation* 2010; 122: 156–163.
2. Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS Guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by: Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J* 2016; 37: 67–119.
3. Vonk Noordegraaf A and Galiè N. The role of the right ventricle in pulmonary arterial hypertension. *Eur Respir Rev* 2011; 20: 243–253.
4. Forfia PR, Fisher MR, Mathai SC, et al. Tricuspid annular displacement predicts survival in pulmonary hypertension. *Am J Respir Crit Care Med* 2006; 174: 1034–1041.
5. Naeije R and Manes A. The right ventricle in pulmonary arterial hypertension. *Eur Respir Rev* 2014; 23: 476–487.
6. Vonk Noordegraaf A, Westerhof BE and Westerhof N. The relationship between the right ventricle and its load in pulmonary hypertension. *J Am Coll Cardiol* 2017; 69: 236–243.
7. Sunagawa K, Maughan WL, Burkhoff D, et al. Left ventricular interaction with arterial load studied in isolated canine ventricle. *Am J Physiol* 1983; 245: H773–H780.
8. Fourie PR, Coetzee AR and Bolliger CT. Pulmonary artery compliance: its role in right ventricular-arterial coupling. *Cardiovasc Res* 1992; 26: 839–844.
9. Yoshinaga K, Ohira H, Tsujino I, et al. Attenuated right ventricular energetics evaluated using ^{11}C-acetate PET in patients with pulmonary hypertension. *Eur J Nucl Med Mol Imaging* 2014; 41: 1240–1250.
10. Vanderpool RR, Pinsky MR, Naeije R, et al. RV-pulmonary arterial coupling predicts outcome in patients referred for pulmonary hypertension. *Heart* 2015; 101: 37–43.
11. Magnino C, Omedè P, Avenatti E, et al. Inaccuracy of right atrial pressure estimates through inferior vena cava indices. *Am J Cardiol* 2017; 120: 1667–1673.
12. Thenappan T, Prins KW, Pritzker MR, et al. The critical role of pulmonary arterial compliance in pulmonary hypertension. *Ann Am Thorac Soc* 2016; 13: 276–284.
13. Hoeper MM, Bogaard HJ, Condliffe R, et al. Definitions and diagnosis of pulmonary hypertension. *J Am Coll Cardiol* 2013; 62: D42–D50.
14. Kovacs G, Avian A, Pienn M, et al. Reading pulmonary vascular pressure tracings. How to handle the problems of zero leveling and respiratory swings. *Am J Respir Crit Care Med* 2014; 190: 252–257.
15. Rudski LG, Lai WW, Afilalo J, et al. Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch of the European Society of Cardiology, and the Canadian Society of Echocardiography. *J Am Soc Echocardiogr* 2010; 23: 685–713.
16. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification. *Eur J Echocardiogr* 2006; 7: 79–108.
17. Foale R, Nihoyannopoulos P, McKenna W, et al. Echocardiographic measurement of the normal adult right ventricle. *Heart* 1986; 56: 298.
18. Guazzi M, Bandera F, Pelissero G, et al. Tricuspid annular plane systolic excursion and pulmonary arterial systolic pressure relationship in heart failure: an index of right ventricular contractile function and prognosis. *Am J Physiol Heart Circ Physiol* 2013; 305: H1373–H1381.
19. Blyth KG, Syyed R, Chalmers J, et al. Pulmonary arterial pulse pressure and mortality in pulmonary arterial hypertension. *Respir Med* 2007; 101: 2495–2501.
20. Regen DM. Calculation of left ventricular wall stress. *Circ Res* 1990; 67: 245–252.
21. Tello K, Dalmer A, Vanderpool R, et al. Cardiac magnetic resonance imaging-based right ventricular strain analysis for assessment of coupling and diastolic function in pulmonary hypertension. *JACC Cardiovasc Imaging* 2019; 12: 2155–2164.