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Prognostic Implications of Increased Right Ventricular Wall Tension in Secondary Tricuspid Regurgitation

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Secondary tricuspid regurgitation (TR) imposes a chronic volume overload on the right ventricle (RV) which can increase RV wall tension (RVWT). The aim of this study was to investigate the prognostic implications of increased RVWT in patients with significant secondary TR. A total of 1,142 patients with moderate-to-severe secondary TR were included. Based on the simplified Laplace-Young's law, RVWT was defined as the product between pulmonary artery systolic pressure (PASP) and RV base-to-apex length. The association between RVWT and risk of all-cause death was identified with spline curve analysis and patients were divided according to the cut-off of RVWT beyond which the hazard ratio (HR) and 95% confidence interval for all-cause mortality were above 1. Four hundred sixty-five (41%) patients had RVWT >3,300 mm Hg x mm and formed the group with increased RVWT. Patients with increased RVWT were more likely male, had more frequent heart failure symptoms and presented with more co-morbidities, larger RV and left ventricular (LV) dimensions, worse LV function, more severe secondary TR and higher PASP compared with patients with nonincreased RVWT. During a median follow-up of 51 (17 to 86) months, 586 (51%) patients died. The cumulative 5-year survival rate was significantly worse in patients with increased RVWT as compared with patients with nonincreased RVWT (38% vs 63% p <0.001). After correcting for potential confounders, increased RVWT retained an independent association with all-cause mortality (HR 1.555; 95% CI 1.268 to 1.907; p <0.001). In conclusion, increased RVWT is independently associated with worse prognosis and its evaluation may improve risk stratification in patients with significant secondary TR. **© 2020 The Author(s). Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/)** **(Am J Cardiol 2020;136:131−139)**

Secondary tricuspid regurgitation (TR) affects approximately 1.6 million patients in the United States.[1] This common condition is caused by tricuspid annular (TA) dilation either due to right ventricular (RV)[2] or right atrial dilation leading to leaflet tethering and/or malcoaptation.[3] Recently, both the awareness of the negative impact of secondary TR on functional capacity and long-term mortality[4−6] and the possibility to treat patients at high surgical risk with transcatheter interventions[7] have increased interest in the pathophysiology and imaging of secondary TR. Secondary TR imposes a chronic volume overload on the RV which is often combined with pressure overload.[8,9] These two conditions induce RV adaptation which in the first phase mainly consists of RV hypertrophy at the cost of an increase in RV filling pressure.[10] The increase in RV end-diastolic pressure is accompanied by an increase in RV wall tension (RVWT) which can have a detrimental effect on the RV.[11,12] According to Laplace-Young's law, RVWT is directly proportional to the pressure acting on the RV wall and to the RV dimensions.[13−15] RVWT can be estimated from standard echocardiography and has been shown to correlate well with heart failure symptoms and prognosis in small cohorts of patients with pulmonary hypertension.[14,15] The potential utility of RVWT for risk-stratification of patients with RV chronic volume overload has never been evaluated. Accordingly, the aim of the current study was to investigate the prognostic implications of increased RVWT in a large cohort of patients with moderate or severe secondary TR.

Methods

Patients diagnosed with moderate or severe secondary TR at the Leiden University Medical Centre (Leiden, the Netherlands) between June 1995 and September 2016 were identified. Patients with primary TR (valve prolapse, endocarditis, rheumatic heart disease, or tumor), congenital heart

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See page 138 for disclosure information.

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disease, or who underwent tricuspid valve interventions after the diagnosis of significant secondary TR, were excluded. In addition, patients with incomplete data to assess secondary TR severity and/or RVWT (i.e., RV base-to-apex length and/or pulmonary artery systolic pressure [PASP]) were excluded. Demographic and clinical data were collected from the departmental Cardiology Information System (EPD-VisionVR; Leiden University Medical Centre, Leiden, the Netherlands) when significant secondary TR was first diagnosed on echocardiography and were analyzed retrospectively. The institutional review board of the Leiden University Medical Centre approved this retrospective analysis of clinically acquired data and waived the need for patient written informed consent. Clinical characteristics included symptoms of left- and right-sided heart failure, cardiovascular risk factors, co-morbidities, medical therapy, and cardiac devices. Data on the New York Heart Association (NYHA) functional class were collected.[16] Kidney function was estimated with the calculation of glomerular filtration rate according to the Modification of Diet in Renal Disease formula.[17]

Transthoracic echocardiographic data were acquired with patients at rest using available ultrasound systems (Vivid 7, E9 and E95 systems; GE-Vingmed) equipped with 3.5 MHz or M5S transducers. All images were digitally stored for offline analysis with commercially available software (EchoPAC version 113.0.3, 202, and 203; GE-Vingmed). The parasternal, apical, and subcostal views were used to acquire echocardiographic data according to current recommendations.[18–21] Presence of significant (moderate and severe) aortic stenosis, mitral regurgitation, and mitral stenosis were defined according to current guidelines.[18,19] RV linear dimensions were acquired at end-diastole on an RV-focused apical view or alternatively from an apical 4-chamber view and included: TA diameter, RV basal and midventricular diameter and RV base-to-apex length.[21] RV base-to-apex length was measured as the distance from the plane of the TA to the RV apex (Figure 1). RV systolic function was quantified based on TA plane systolic excursion (TAPSE) measured on M-mode recordings of the lateral tricuspid annulus.[21] RV fractional area change (FAC) was calculated using the following formula: (end-diastolic area − end-systolic area)/end-diastolic area x 100.[21] TR grade was assessed by a multiparametric approach including qualitative, semiquantitative, and quantitative parameters measured on bi-dimensional, color, continuous-, and pulsed-wave Doppler data as recommended.[18,19] The simplified Bernoulli equation was used to estimate PASP from the TR jet peak velocity and adding 3, 8, or 15 mm Hg based on inferior vena cava diameter and collapsibility during normal inspiration[21] (Figure 1). A value of PASP ≥36 mm Hg was used to define increased pulmonary pressures.[22] Based on Laplace-Young's law,[13] RVWT was derived as follows: PASP x RV base-to-apex length (Figure 1). In this formula PASP represents the pressure acting on the RV free wall during systole. As previously suggested,[15] RV base-to-apex length was preferred over other RV diameters because the systolic motion of the RV occurs mainly along its length, and therefore the RV motion vector is more parallel to the RV base-to-apex axis than to the other RV diameters. RV free wall thickness was not included in the formula due to its high intra- and inter-observer variability[23] and its significant dependency on image quality and plane,[21] which could significantly confound the estimation of RVWT.

All patients were followed up for the occurrence of all-cause mortality. Survival data were retrieved from the departmental Cardiology Information System and the Social Security Death Index and were collected for all patients.

The adherence to a normal distribution for continuous variables was visually assessed comparing a histogram of the sample data to a normal probability curve. Continuous variables are presented as mean ± standard deviation if they had a Gaussian distribution and as median and interquartile range if not normally distributed. Categorical variables are presented as absolute frequencies and percentages. To assess the hazard ratio (HR) change for all-cause

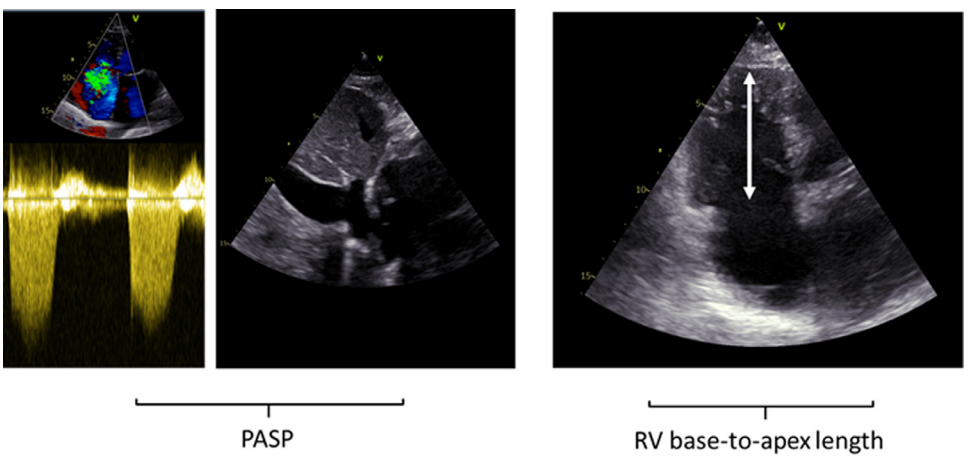

Figure 1. Derivation of Right Ventricular Wall Tension from Standard Echocardiography. PASP = pulmonary artery systolic pressure; RV = right ventricular.

mortality across a range of RVWT values a spline curve analysis was performed. The cut-off value for RVWT associated with excess mortality was used to define increased and nonincreased RVWT groups. Differences between patients with increased versus nonincreased RVWT were analyzed using the unpaired Student t-test for normally distributed continuous variables, the Mann-Whitney *U* test for non-normally distributed continuous variables, and the Pearson χ^2 for categorical variables. The 1-, 5-, and 10-year cumulative survival rates were estimated with Kaplan-Meier curves, and differences between groups (increased RVWT vs nonincreased RVWT) were analyzed using the Mantel-Cox log-rank test. A multivariable Cox proportional hazards regression analysis was performed to assess the demographic, clinical and echocardiographic features that were independently associated with all-cause mortality. Moreover, a multivariable spline model was used to further characterize the relation between the risk of all-cause mortality and RVWT. Potential confounders with a significant p value ($p < 0.05$) in the univariable analysis were included in the multivariable Cox regression analysis and spline model. Hazard ratio (HR) and 95% confidence intervals (CIs) were calculated. The additional prognostic value of RVWT, when added to a Cox regression basal model, was evaluated with the calculation of χ^2 change. P values <0.05 were considered significant. All data were analyzed with SPSS for Windows, version 25 (SPSS Inc, IBM Corp) and in R environment 4.0.1 (R Foundation for Statistical Computing) using the "Stats," "Survival," "rms,' and "Greg" packages.

Results

Overall, 1,142 patients were included in the study (Supplementary Figure 1S); the median age was 72 (interquartile range, 63 to 78) years, 50% were male, 79% had moderate secondary TR and 21% had severe secondary TR. For RVWT, the HR for all-cause mortality crossed 1 (neutral effect) at the value of 3300 mm Hg x mm (Figure 2). Based on the spline curve analysis, values of RVWT >3300 mm Hg x mm identified increased RVWT, whereas values ≤3300 mm Hg x mm identified nonincreased RVWT. According to this cut-off (3300 mmHg x mm), 465 (41%) patients of the study population had increased RVWT. The clinical characteristics of the overall population and for patients with increased and nonincreased RVWT are presented in Table 1. Approximately half of the patients were known to have atrial fibrillation (54% permanent or persistent and 46% paroxysmal). A total of 460 (44%) patients were in NYHA class III or IV, peripheral oedema was observed in 246 (23%) patients, and 640 (58%) patients were using diuretics at the time of diagnosis of significant secondary TR. In a per-group analysis, patients with increased versus nonincreased RVWT were of similar age. Patients with increased RVWT were more likely to be male, had higher body mass index and prevalence of comorbidities and cardiovascular risk factors; and were more likely to present with heart failure symptoms and to receive diuretics compared with those with nonincreased RVWT.

The echocardiographic characteristics of the overall population and of patients with increased versus nonincreased RVWT are presented in Table 2. Overall, the mean LVEF was moderately reduced, 24% of the patients had concomitant significant aortic stenosis, 27% had significant mitral regurgitation and <1% had significant mitral stenosis. Mean RV dimensions were increased, the TAPSE was decreased and PASP was increased (≥36 mm Hg) in 764 (67%) patients. In per-group analysis, patients with increased and nonincreased RVWT had similar TAPSE.

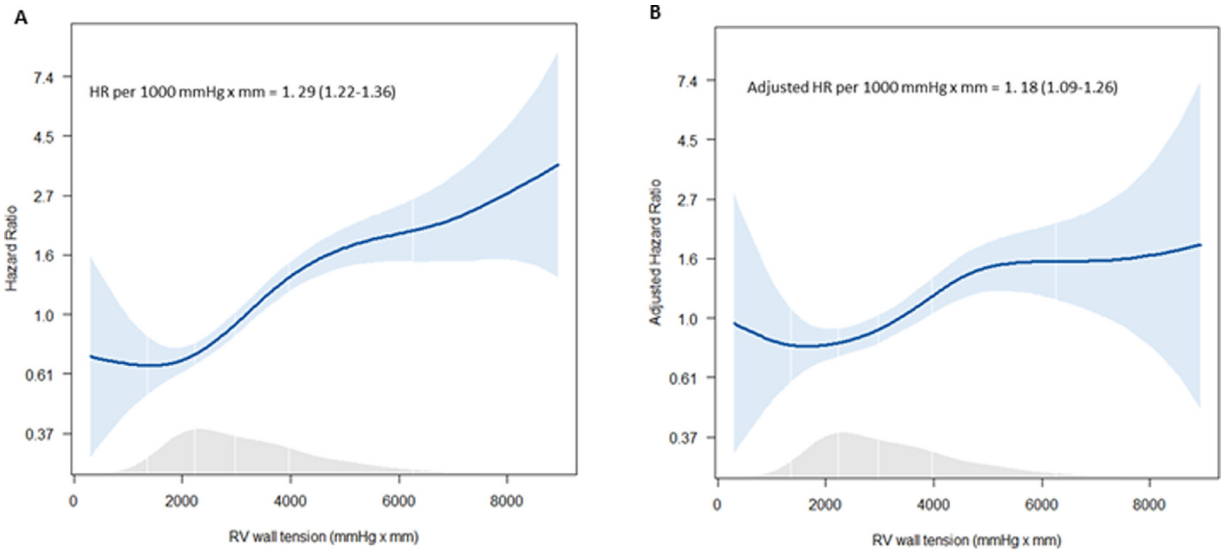

Figure 2. Spline Curves for RV Wall Tension vs All-Cause Mortality. Panel A shows the changes in hazard ratio for all-cause mortality across right ventricular wall tension (RVWT) at the time of significant secondary tricuspid regurgitation diagnosis. Panel B shows the same relation adjusted for the potential confounders identified based on the univariable Cox regression analysis (including: age, gender, coronary artery disease, diabetes mellitus, chronic obstructive pulmonary disease, NYHA class, peripheral oedema, diuretic use, renal function, left ventricular systolic function, left atrial volume, moderate-to-severe mitral regurgitation, moderate-to-severe aortic stenosis, RV systolic function, tricuspid annular diameter, cardiac implantable device, vena contracta width). The density plots in grey show the distribution of the population according to RVWT. RV = right ventricular.

Table 1
Characteristics of the study population

Variable	Overall (n = 1,142)	Non-increased RV wall tension [RV systolic pressure x RV length ≤3300] (n = 677)	Increased RV wall tension [RV systolic pressure x RV length >3300] (n = 465)	p Value
Age (years)	72 (63-78)	72 (63-79)	71 (63-78)	0.259
Men	575 (50%)	295 (44%)	380 (60%)	<0.001
Body mass index (kg/m^2)	26 ± 4	25 ± 4	26 ± 4	0.043
Hypertension	846 (81%)	499 (80%)	447 (82%)	0.497
Hypercholesterolemia*	494 (48%)	274 (44%)	220 (52%)	0.011
Diabetes mellitus	209 (20%)	80 (13%)	129 (31%)	<0.001
Coronary artery disease	455 (40%)	237 (36%)	218 (47%)	<0.001
Chronic obstructive pulmonary disease	152 (15%)	81 (13%)	71 (17%)	0.107
eGFR (ml/min/1.73 m^2)	65 ± 29	69 ± 28	59 ± 29	<0.001
Current or former smoker	314 (30%)	176 (28%)	138 (33%)	0.128
Atrial fibrillation	536 (50%)	323 (51%)	213 (49%)	0.441
NYHA class III-IV	460 (44%)	215 (36%)	245 (57%)	<0.001
Peripheral oedema	246 (23%)	102 (16%)	144 (32%)	<0.001
Diuretic use	640 (58%)	331 (51%)	309 (69%)	<0.001
Pacemaker/ICD	412 (36%)	234 (35%)	178 (39%)	0.196

* Defined according to total cholesterol ≥190 mg/dL or previous pharmacological treatment.
Values are presented as mean ± SD, median (IQR) or n (%). Percentages are calculated based on data availability.
eGFR = estimated glomerular filtration rate; ICD = implantable cardiac defibrillator; NYHA = New York Heart Association; RV = right ventricular.

Table 2
Echocardiographic features in patients with increased vs non-increased RV wall tension

Variable	Overall (n = 1142)	Non-increased RV wall tension [RV systolic pressure x RV length ≤3300] (n = 677)	Increased RV wall tension [RV systolic pressure x RV length >3300] (n = 465)	p Value
LV EDD (mm)	48 ± 11	46 ± 10	52 ± 12	<0.001
LV ESD (mm)	39 ± 13	36 ± 12	42 ± 14	<0.001
LV EDV (ml)	112 (80-166)	99 (74-137)	141 (92-207)	<0.001
LV EF (%)	44 ± 16	47 ± 15	41 ± 16	<0.001
LA maximum volume (ml)	93 (59-127)	80 (55-118)	105 (72-137)	<0.001
LAVI (ml/m^2)	50 (34-69)	46 (30-65)	57 (40-72)	<0.001
Significant AS	258 (24%)	138 (21%)	120 (27%)	0.021
Significant MR	301 (27%)	135 (22%)	151 (33%)	<0.001
Significant MS	8 (0.7%)	4 (0.6%)	4 (0.9%)	0.592
RV basal diameter (mm)	45 ± 8	44 ± 8	47 ± 9	<0.001
RV mid diameter (mm)	35 ± 9	33 ± 8	38 ± 9	<0.001
RV base-to-apex length (mm)	72 ± 12	68 ± 12	78 ± 11	<0.001
RV EDA (cm^2)	25 ± 12	23 ± 9	29 ± 15	<0.001
RA area (cm^2)	28 ± 11	27 ± 11	29 ± 10	<0.001
FAC (%)	34 ± 13	37 ± 13	31 ± 12	<0.001
TAPSE (mm)	15 ± 5	16 ± 5	15 ± 5	0.057
PASP (mm Hg)	44 ± 16	35 ± 8	58 ± 14	<0.001
Moderate TR	900 (79%)	549 (81%)	351 (76%)	0.023
Severe TR	242 (21%)	128 (19%)	114 (24%)	
TA diameter (mm)	42 ± 8	41 ± 8	44 ± 8	<0.001
Vena contracta (mm)	11 ± 4	11 ± 4	11 ± 4	0.460
EROA (mm^2)	68 (43-105)	70 (44-110)	62 (42-101)	0.012
RVol (ml/beat)	65 (39-104)	59 (37-99)	72 (43-112)	0.001

Values are presented as mean ± SD, median (IQR) or n (%). Percentages are calculated based on data availability.
AS = aortic stenosis; EDA = end-diastolic area; EDD = end-diastolic diameter; EDV = end-diastolic volume; EF = ejection fraction; EROA = effective regurgitant orifice area; ESD = end-systolic diameter; FAC = fractional area change; LAVI = left atrial volume index; LV = left ventricle; MR = mitral regurgitation; PASP = pulmonary artery systolic pressure; RA = right atrium; RV = right ventricle; RVol = regurgitant volume; TA = tricuspid annulus: TAPSE = tricuspid annular plane excursion; TR = tricuspid regurgitation.

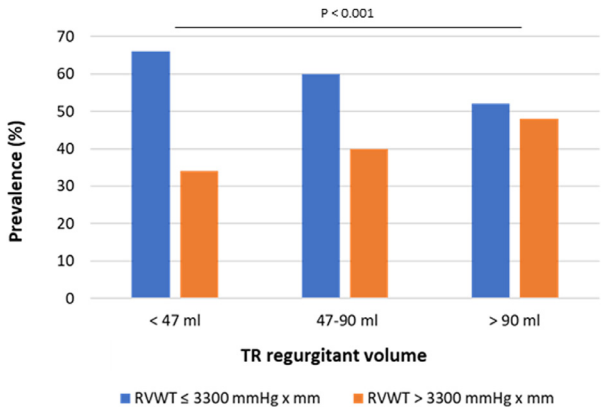

Figure 3. Association between RV wall tension and secondary TR severity. The figure shows the increase in the prevalence of patients with increased RV wall tension (orange boxes) with worsening of TR (tertiles of regurgitant volume − x-axis). RVWT = right ventricular wall tension; TR = tricuspid regurgitation.

Patients with increased RVWT had larger left ventricular (LV) dimensions, lower LVEF, a higher prevalence of concomitant significant aortic stenosis or mitral regurgitation, larger RV dimensions, lower FAC, higher pulmonary artery pressures, and were more likely to present with severe secondary TR as compared with patients without increased RVWT. As shown in Figure 3, the prevalence of increased RVWT significantly increased across tertiles of secondary TR regurgitant volume (34% for a regurgitant volume <47 ml, 40% for a regurgitant volume 47 to 91 ml, and 48% for a regurgitant volume >91 ml; p <0.001).

During a median follow-up of 51 (17 to 86) months, 586 (51%) patients died. Overall, the cumulative survival rates were 72% at 1 year, 53% at 5 years, and 39% at 10 years. The Kaplan-Meier curves showed significantly lower survival rates in patients with increased RVWT compared with patients without increased RVWT (log-rank χ^2: 77.02, p <0.001; see Figure 4). The 1-, 5-, and 10-year cumulative survival rates were significantly worse in patients with increased RVWT in comparison with nonincreased RVWT (81% vs 59% at 1 year, p <0.001; 63% vs 38% at 5 years, p <0.001; and 47% vs 28% at 10 years, p <0.001). Univariable Cox regression analysis showed that age, male gender, diabetes mellitus, known coronary artery disease, chronic obstructive pulmonary disease, renal function, NYHA class III-IV, diuretics, peripheral oedema, cardiac implantable electronic devices, LVEF, LA volume, concomitant significant mitral regurgitation or aortic stenosis, RV dimensions, RV systolic function (either evaluated with TAPSE or FAC), increased PASP, individual parameters reflecting TR severity, and increased RVWT were associated with all-cause mortality (Supplementary Table 1S). In the multivariable Cox regression analysis, after correcting for potential confounders, increased RVWT was independently associated with an increased risk of all-cause mortality (HR 1.555; 95% CI 1.268 to 1.907, p <0.001; see Table 3) together with age, diabetes mellitus, renal function, NYHA class III-IV, diuretic use, and TAPSE. The multivariable spline model adjusted for potential confounders confirmed the independent association between the RVWT and mortality risk (Figure 2). Importantly, as shown in Table 3, RVWT when added to the basal model (both as continuous and dichotomous variable) yielded a greater increase in the predictivity of the model (i.e., χ^2 value) compared with PASP.

Discussion

In this large cohort of patients with significant secondary TR, 41% showed increased RVWT at the time of diagnosis. Patients with increased RVWT presented more frequently with heart failure symptoms, had more co-morbidities, worse LV function, higher PASP, more severe TR, and larger RV dimensions compared with patients with non-increased RVWT. Increased RVWT was associated with poorer outcomes in patients with significant secondary TR independently of clinical, echocardiographic and biochemical parameters. Moreover, RVWT had incremental prognostic value over conventional echocardiographic parameters.

Secondary TR can be related to several pathological conditions which can be grouped into 4 etiological categories[24]: left-sided valvular heart disease, LV systolic and/or diastolic dysfunction, pulmonary hypertension, and atrial fibrillation. These conditions and secondary TR itself determine RV remodeling, which consists of RV hypertrophy and eventually RV dilation and dysfunction[25] that leads to further TA dilation, leaflet tethering and secondary TR, creating a vicious circle of increased volume overload of the RV, further RV dysfunction and worsening of secondary TR.[26] The mechanism associating the volume overload to RV remodeling and dysfunction, may be partly explained by RVWT. This parameter reflects both RV preload and afterload and may represent the driving force of RV dilation and maladaptation to RV chronic pressure and volume overload. Increased RVWT diminishes RV coronary perfusion pressure during the entire cardiac cycle, contributing to myocardial damage that can lead to RV dysfunction over time.[11] In our cohort, increased RVWT was associated with more co-morbidities, LV dysfunction, higher PASP, and greater tricuspid regurgitant volume, reflecting more severe secondary TR. Interventions aiming at reducing RVWT and potentially also secondary TR may halt and reverse RV remodeling. Optimization of medical therapy targeting co-morbidities and LV dysfunction may reduce RVWT. Sacubitril/valsartan in patients with heart failure and reduced LVEF has been demonstrated to reduce LV volumes, improve LV systolic/diastolic function and decrease secondary mitral regurgitation more than valsartan alone,[27,28] potentially leading to a decrease in pulmonary pressures and to a reduction in RVWT and secondary TR. Continuous positive airway pressure treatment in patients with obstructive sleep apnoea[29] and optimization of bronchodilator and supplemental oxygen therapy in patients with chronic obstructive pulmonary disease[30] can decrease pulmonary pressures and therefore improve RVWT. Optimization of preload in patients with chronic kidney disease can also have a beneficial effect on RVWT. Furthermore, interventions on the tricuspid valve have the ability to decrease the chronic volume overload of the RV[7] and hypothetically they could also reduce RVWT. Dedicated prospective studies would be needed to investigate the potential effects of

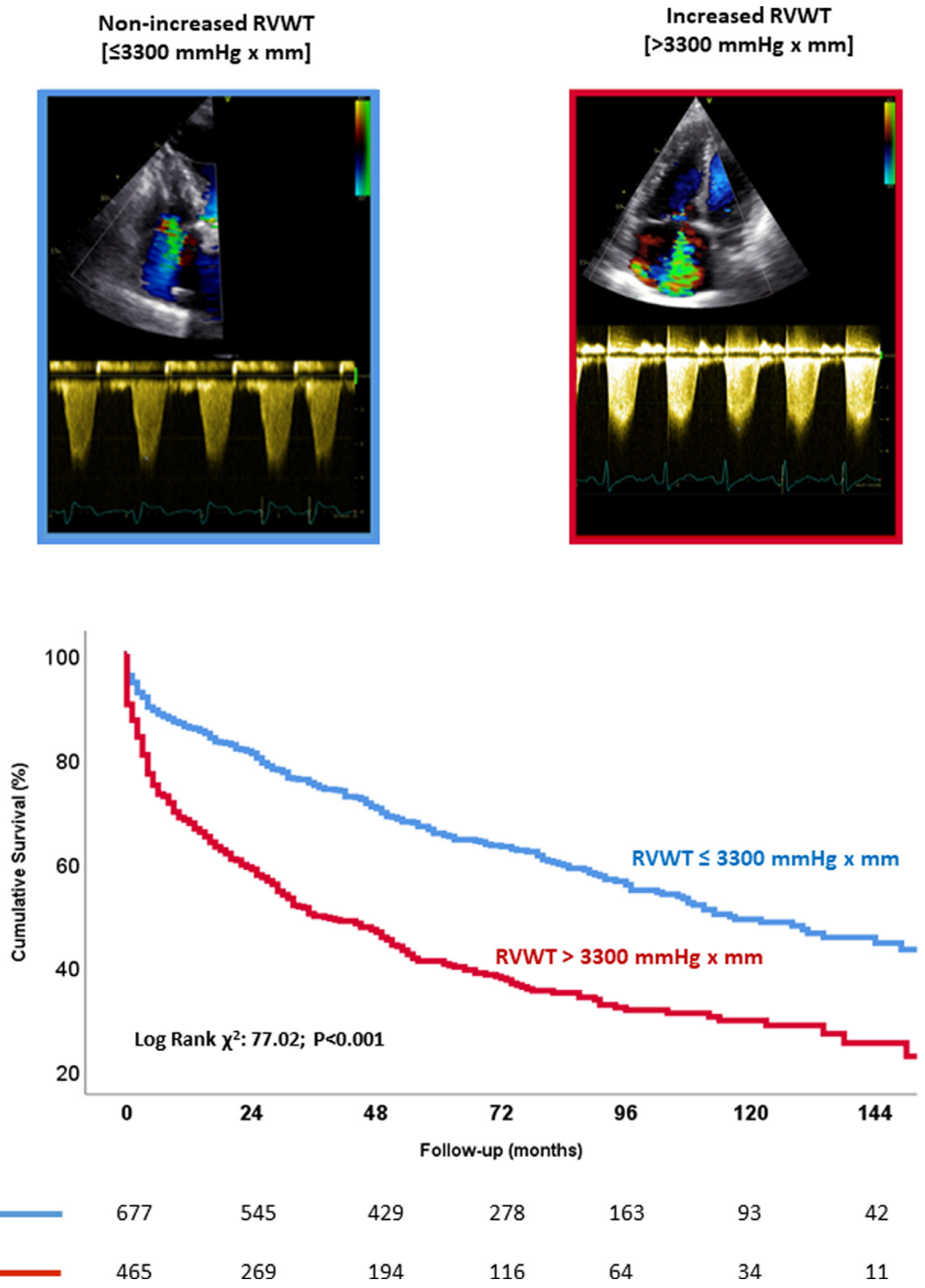

Figure 4. Prognostic implications of increased RVWT in patients with secondary TR. Increased RVWT (red box and line) was associated with worse prognosis compared to non-increased RVWT (light-blue box and line). RVWT = right ventricular wall tension; TR = tricuspid regurgitation.

the abovementioned therapies on RVWT in the context of significant TR.

Based on current guidelines, tricuspid valve surgery is indicated in patients with severe secondary TR undergoing left-sided valve surgery (class IC) and may be considered in patients with a previous left-sided valve operation who have developed symptomatic secondary TR with progressive RV dilation in the absence of RV or LV dysfunction (class IIaC).[19] Taking into account the RVWT (driving force of RV remodeling) instead of late markers of RV remodeling such as RV dilation and/or dysfunction may help to improve risk-stratification of patients with secondary TR. In the current study, increased RVWT was independently associated with a 56% increase in the risk of all-cause mortality. Interestingly, in the multivariable analysis RVWT was the only echocardiographic parameter aside from PASP and TAPSE that showed an association with the primary outcome. Furthermore, when added to the basal

Table 3
Multivariable Cox proportional hazard models for all-cause mortality

Variable	Multivariable basal model		Basal model + PASP		Basal model + RVWT	
	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value
Patient demographics and co-morbidities						
Age	1.028 (1.019-1.038)	<0.001	1.028 (1.019-1.038)	<0.001	1.029 (1.019-1.039)	<0.001
Male gender	1.237 (0.997-1.534)	0.054	1.238 (0.997-1.539)	0.054	1.166 (0.937-1.450)	0.168
Diabetes mellitus	1.351 (1.071-1.706)	0.011	1.302 (1.030-1.645)	0.027	1.280 (1.013-1.618)	0.039
Coronary artery disease	1.212 (0.984-1.495)	0.071	1.195 (0.969-1.474)	0.097	1.206 (0.978-1.486)	0.080
COPD	1.877 (0.925-1.523)	0.177	1.213 (0.945-1.556)	0.129	1.189 (0.927-1.525)	0.173
eGFR	0.992 (0.987-0.996)	<0.001	0.992 (0.988-0.997)	0.001	0.993 (0.988-0.997)	0.002
NYHA class III-IV	1.837 (1.497-2.255)	<0.001	1.792 (1.459-2.199)	<0.001	1.810 (1.476-2.219)	<0.001
Diuretics	1.356 (1.066-1.724)	0.013	1.372 (1.079-1.746)	0.010	1.325 (1.042-1.685)	0.022
Peripheral oedema	1.103 (0.874-1.392)	0.408	1.073 (0.850-1.354)	0.553	1.051 (0.833-1.326)	0.678
Pacemaker/ICD	1.144 (0.934-1.401)	0.194	1.142 (0.932-1.399)	0.201	1.000 (0.998-1.002)	0.737
Echocardiographic parameters						
LVEF	0.996 (0.989-1.003)	0.209	0.996 (0.989-1.003)	0.221	0.996 (0.989-1.003)	0.287
LA maximal volume	1.000 (0.998-1.002)	0.899	1.000 (0.998-1.002)	0.721	1.000 (0.998-1.002)	0.737
Significant MR	1.197 (0.968-1.480)	0.098	1.159 (0.937-1.434)	0.175	1.177 (0.952-1.455)	0.133
Significant AS	1.209 (0.974-1.501)	0.086	1.216 (0.980-1.510)	0.076	1.178 (0.948-1.463)	0.139
TA diameter	1.007 (0.993-1.021)	0.336	1.008 (0.994-1.023)	0.265	1.004 (0.990-1.019)	0.587
TAPSE	0.978 (0.956-1.001)	0.056	0.978 (0.956-1.001)	0.060	0.976 (0.954-0.998)	0.036
VC width of TR	1.006 (0.981-1.003)	0.630	1.007 (0.981-1.034)	0.587	1.011 (0.985-1.038)	0.413
PASP≥36 mmHg			1.413 (1.124-1.775)	0.003		
Increased RVWT [> 3304 mmHg x mm]					1.555 (1.268-1.907)	<0.001
Model predictivity with the addition of increased PASP or RVWT compared to the basal model						
Model χ^2	230.985		237.319		248.828	
$\Delta\ \chi^2$ compared with the basal model			9.199	0.002	17.980	<0.001
Model predictivity with the addition of PASP or RVWT (as continuous variable) compared to the basal model						
Model χ^2	230.985		247.018		251.488	
$\Delta\ \chi^2$ compared with the basal model			15.312	<0.001	19.304	<0.001

AS = aortic stenosis; COPD = chronic obstructive pulmonary disease; eGFR = estimated glomerular filtration rate; HR = hazard ratio; ICD = implantable cardioverter defibrillator; LAVI = left atrial volume index; LVEF = left ventricular ejection fraction; MR = mitral regurgitation; NYHA = New York Heart Association; PASP = pulmonary artery systolic pressure; RVWT = right ventricular wall tension; TA = tricuspid annulus; TAPSE = tricuspid annular plane systolic excursion; TR = tricuspid regurgitation; VC = vena contracta.

multivariable model, RVWT yielded a greater increase in the predictivity of the model compared with PASP, suggesting an incremental prognostic value. Based on Laplace-Young's law, RVWT may be easily derived from standard echocardiography and specifically from the measurements of PASP and RV base-to-apex length. Assessment of RVWT may be not only of help in risk-stratification but also in guiding clinical decision-making. In previous studies,[14,15] RVWT correlated well with invasive measurements of RV diastolic function such as RV end-diastolic pressure, biomarkers of atrial stress (i.e., brain natriuretic peptide) and heart failure symptoms. Differently from invasive measurements of RV function, RVWT can be derived non-invasively at the bed-side making this index practical and useful to monitor patient response to therapeutic adjustments in clinical practice.

The limitations of this single-centre study are inherent to its retrospective design. To acquire the large cohort as presented, 21 years for inclusion and different aetiologies of secondary TR were considered. The use of RV base-to-apex-length to estimate RVWT may be an oversimplification of the RV complex geometry. However, compared with the other RV diameters that could be measured on standard echocardiography, RV-base-to-apex length is the one that relates most closely to RV systolic motion. RVWT may be estimated more accurately by combining different imaging modalities such as Doppler echocardiography to estimate the pressure acting across the RV wall and 3-dimensional echocardiography or cardiac magnetic resonance to measure RV dimensions.

In conclusion, in patients with moderate or severe secondary TR, increased RVWT is independently associated with worse prognosis and may be useful to improve risk-stratification and therapy optimization in this clinical setting.

Author Contribution

Federico Fortuni: conceptualization; data curation; formal analysis; investigation; methodology; project administration; resources; validation; visualization; writing - original draft. Marlieke F Dietz: conceptualization; data curation; formal analysis; investigation; methodology; resources; validation; visualization; writing - review & editing. Steele C Butcher: conceptualization; data curation; methodology; resources; validation; visualization; writing - review & editing. Edgard A. Prihadi: conceptualization; data curation; methodology; resources; validation; visualization; writing - review & editing. Pieter van der Bijl: conceptualization; data curation;

methodology; resources; validation; visualization; writing - review & editing. Nina Ajmone Marsan: conceptualization; funding acquisition; methodology; project administration; supervision; validation; writing - review & editing. Victoria Delgado: conceptualization; data curation; funding acquisition; methodology; project administration; resources; supervision; validation; writing - review & editing. Jeroen J. Bax: conceptualization; data curation; funding acquisition; methodology; project administration; resources; supervision; validation; writing - review & editing.

Disclosures

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.09.022.

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