Unmasking right ventricular dysfunction in chronic rheumatic mitral regurgitation

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Abstract

Aims: Right ventricular (RV) systolic function is an important predictor of mortality but has been poorly studied in chronic rheumatic mitral regurgitation (CRMR). We studied RV systolic function using speckle-tracking echocardiography (STE) in patients with CRMR.

Methods: Seventy-seven patients with CRMR and 40 healthy controls were enrolled in a cross-sectional study at Chris Hani Baragwanath Hospital between January and October 2014. RV peak systolic strain (PSS) and left ventricular (LV) global longitudinal strain (GLS) were measured using Philips Qlab 9 STE software.

Results: RVPSS was lower in CRMR patients compared to the controls (–16.8 ± 4.5 vs –19.2 ± 3.4%, $p = 0.003$) with no difference in conventional RV systolic function parameters ($p = 0.39$). RVPSS was lower in severe CRMR compared to moderate CRMR patients (–14.3 ± 4.23 vs –18 ± 4.18%, $p < 0.0001$). CRMR patients with LV systolic dysfunction had a greater reduction in RVPSS and LVGLS compared to those with preserved LV systolic function ($p = 0.001$). LVGLS and significant tricuspid regurgitation (TR) were independent predictors of RVPSS ($p < 0.001$).

Conclusion: In CRMR patients, RVPSS was a more sensitive marker for detecting earlier RV systolic dysfunction than traditional RV functional parameters.

Keywords: right ventricle, rheumatic mitral insufficiency, speckle-tracking echocardiography

Submitted 15/12/18, accepted 16/4/19
Published online 24/5/19
Cardiovasc J Afr 2019; **30**: 216–221 www.cvja.co.za

DOI: 10.5830/CVJA-2019-020

Systolic dysfunction of the right ventricle (RV) is a known predictor of mortality after acute myocardial infarction or coronary artery bypass grafting, and in heart failure and primary pulmonary hypertension (PHT).[1-4] In addition to left ventricular (LV) parameters, RV systolic function provides adjunctive information in the decision-making process regarding surgical intervention in mitral regurgitation (MR).[5,6]

Pre-operative RV function is an important determinant of intra-operative and postoperative outcomes in MR and therefore has prognostic implications.[5,7] Additionally, RV dysfunction may have important implications in terms of predicting greater haemodynamic impairment of the LV and secondary PHT due to MR.[8,9] Furthermore, it has been suggested that there may be direct involvement of the RV by the rheumatic process, resulting in necrosis of the myocytes, fibrosis and calcification of the myocardium, with resultant RV dysfunction.[10]

Recently, newer imaging techniques such as speckle-tracking-derived RV strain have emerged, which offer several advantages over traditional echocardiographic parameters for assessing overt and subclinical RV systolic dysfunction.[6,10,11,12,13] There are no studies that have assessed RV function in chronic rheumatic mitral regurgitation (CRMR). We therefore aimed to (1) study RV systolic function using speckle-tracking echocardiography (STE) in patients with CRMR; and (2) determine the predictors of RV free-wall peak systolic strain (PSS) in CRMR.

Methods

We conducted a cross-sectional study at the Chris Hani Baragwanath Academic Hospital. Patients were enrolled between January and October 2014. All patients were screened and patients deemed to have moderate or severe CRMR were referred for possible inclusion in the study. A total of 91 patients with presumed CRMR underwent clinical evaluation, resting electrocardiogram and detailed echocardiographic assessment according to a pre-determined protocol.

The inclusion criteria were patients aged 18 years or older with echocardiographic features of moderate or severe CRMR. Patients were excluded if they had significant aortic valve disease, concurrent mitral stenosis with a valve area of less than 2 cm^2, documented ischaemic heart disease, pre-existing non-valvular cardiomyopathy, prior cardiac surgery, congenital or pericardial disease, pregnancy, severe systemic disorders such as renal failure, uncontrolled hypertension (systolic blood pressure > 140 mmHg and diastolic blood pressure > 90 mmHg), were on medication or had severe anaemia (haemoglobin < 10 g/dl). Fourteen patients were excluded due to the following: atrial fibrillation, anaemia, renal dysfunction and inadequate image quality.

The final sample included 77 patients. Forty age- and gender-matched controls were also included in the study. All healthy volunteers with no known diseases and adequate echocardiographic windows were recruited from the community following an advertisement for the study. A tolerance of five years was allowed for age matching. The study was approved by the University of the Witwatersrand Ethics Committee (M140114).

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Transthoracic echocardiography was performed on all patients in the left lateral position by experienced sonographers using a S5-1 transducer on a Philips iE33 system (Amsterdam, the Netherlands). The images were obtained according to a standardised protocol. The data were transferred and analysed offline using the Xcelera workstation (Philips).

All linear chamber measurements were performed according to the American Society of Echocardiography (ASE) chamber guidelines.[14] Measurements relating to LV diastolic function were performed in accordance with the ASE guidelines on diastolic function and included pulse-wave Doppler at the mitral tips and tissue Doppler of both medial and lateral mitral annuli.[15] Measurements relating to the RV were based on the ASE guidelines on the RV.[16] All LV volumes were indexed to body surface area. We used a LV ejection fraction (EF) cut-off of < 60% to define decreased LV systolic function in MR.[17]

MR was considered of rheumatic aetiology when the morphology of the valve satisfied the proposed World Heart Federation criteria for the diagnosis of chronic rheumatic heart disease (RHD).[18] MR severity was assessed with an integrated approach using qualitative, semi-quantitative and quantitative methods as per ASE valvular regurgitation guidelines.[19]

Two-dimensional echocardiography images were obtained at end-expiration from LV long-axis apical four-, three- and two-chamber (A4C, A3C and A2C) views with frame rates of 60–80 frames per second.[20] Three consecutive cardiac cycles were recorded and averaged.[21] LV endocardial surface was traced manually in the three views by a point-and-click approach.[20,22] The speckle-tracking points were modified to allow for adequate speckle-tracking of the LV wall.[20,22] The LV was divided into 17 segments. Peak LV longitudinal systolic strain was calculated for long-axis A4C, A3C and A2C views, and global LV systolic strain was calculated by averaging the three apical views.[20,22]

RV free-wall PSS was derived from a modified A4C RV focused view.[10] Once three points, namely the RV apex, medial and lateral tricuspid annulus, were defined, the software automatically traced the endocardial and epicardial border.[10] Philips QLAB version 9.0 software allowed off-line semi-automated analysis of speckle-based strain. This results in the division of the RV into six standard segments in the A4C view.[10,23,24] The region of interest, once created, can be manually adjusted as needed to allow for adequate speckle-tracking.[6] The RV free-wall PSS was obtained by averaging three lateral segments (the basal, mid and apical RV wall).[25] The interventricular septum was excluded from analysis.[23,24] The longitudinal ε curves for each segment and a mean curve of all segments was generated by the software. These curves were used to derive peak negative RV free-wall PSS.

Statistical analysis

This was performed with Statistica (version 12.5, series 0414 for Windows). Continuous variables are expressed as mean ± SD or median (IQR). The Student's *t*-test or Mann–Whitney *U*-test were used to compare continuous variables. Categorical variables were evaluated with the chi-squared and Fisher's exact tests when necessary. A *p*-value of < 0.05 was recognised as statistically significant.

Univariate and multivariate linear regression analysis was used to identify possible independent determinants of RV free-wall PSS. The independent variables with $p \leq 0.05$ on univariate analyses were tested in multivariate models. Pearson's correlation coefficient was used to assess the co-linearity between variables. These models were further analysed using the forward and backward multiple linear regression methods.

The intra- and inter-observer variabilities were assessed for RV free-wall PSS and LVGLS. Measurements were done in 20 randomly selected subjects. Inter- and intra-observer reproducibility was assessed by calculating coefficients of variation. A *p*-value < 0.05 was considered statistically significant.

Results

There was no statistically significant difference in age, gender, systolic blood pressure, diastolic blood pressure, body mass index and heart rate between the patients with MR and the controls ($p > 0.05$) (Table 1). Hypertension, HIV and a combination of the two co-morbidities were identified in 41.5, 12.9 and 15.5% of patients, respectively. Forty-two per cent of the patients were in New York Heart Association functional class 1, the remainder were in class 2 (49%) and 3 (9%).

Among the CRMR patients, moderate MR was present in 51 (66%) and severe MR in 26 (34%) subjects. As expected, compared to controls, linear and volumetric measures of the LV revealed a greater degree of LV dilatation, and LV mass as well as left atrial volumes were increased. LVEF was significantly lower in CRMR patients compared to the controls. In addition, analysis of LV diastolic parameters revealed that compared to the controls, E′ of both annuli was lower and E/E′ was higher (Table 2).

Pulmonary artery systolic pressure (PASP) was significantly higher in the MR group compared to the controls (35.1 ± 16.9 vs 22.1 ± 5.6 mmHg, $p < 0.0001$). Grade ≥ 2+ tricuspid regurgitation (TR) was present in 30% of the patients with CRMR. No difference was noted between RV basal size, right atrial volume indexed, tricuspid annular plane systolic excursion (TAPSE) and RVS′ between the CRMR and control groups. However RV free-wall PSS was significantly lower in the CRMR patients compared to the controls (Table 2, Fig. 1).

Patients with severe CRMR had higher PASP and a greater degree of RV hypertrophy compared to those with moderate MR (Table 3). RV free-wall PSS was significantly lower in severe MR compared to patients with moderate MR, whereas no difference was detected between these groups for both TAPSE and tricuspid S′. A similar trend of depressed RVPSS with unchanged TAPSE and RVS′ was noted when comparing patients with LV dysfunction with those with preserved LVEF (Table 4).

Table 1. Baseline clinical characteristics of the study population

Variable	*CRMR patients (n = 77)*	*Controls (n = 40)*	p-*value*
Age (years)	44 ± 13.6	42 ± 13.4	0.4
Gender (M:F)	13:64	8:32	0.6
Body surface area (m²)	1.7 ± 0.2	1.8 ± 0.2	0.01
Body mass index (kg/m²)	27.1 ± 5.9	28.4 ± 6.2	0.3
Systolic blood pressure (mmHg)	124.2 ± 11.4	124 ± 17.5	0.94
Diastolic blood pressure (mmHg)	77 ± 9.1	75.7 ± 12.6	0.52
Heart rate (beats/min)	77.1 ± 12.6	76.3 ± 14.1	0.75

Data are presented as mean ± SD or %.
CRMR: chronic rheumatic mitral regurgitation.

Table 2. Echocardiographic parameters of the study population

Variable	*CRMR patients (n = 77)*	*Controls (n = 40)*	p-*value*
LV parameters			
EDD (mm)	54.8 ± 9.4	42.5 ± 4.8	< 0.0001
ESD (mm)	41.4 ± 9.4	27.1 ± 4.2	< 0.0001
LVPWD (mm)	8.5 ± 1.5	9.2 ± 1.9	0.03
EDVi (ml/m²)†	93.2 ± 30.1	47.9 ± 13.5	< 0.0001
ESVi (ml/m²)†	40.0 ± 22.2	17.8 ± 6.4	< 0.0001
LAVi (ml/m²)†	64.1 ± 39.9	21.9 ± 4.9	< 0.0001
EF (%)	58.5 ± 12.9	62.8 ± 11.2	0.07
LVMi (kg/m²)†	102.7 ± 36.3	65.6 ± 20.3	< 0.0001
E wave (cm/s)	133.8 ± 48.1	77.0 ± 17.6	< 0.0001
A wave (cm/s)	98.4 ± 33.5	59.6 ± 13.0	< 0.0001
E′ medial (cm/s)	7.3 ± 2.3	8.8 ± 2.8	0.002
E′ lateral (cm/s)	10.1 ± 4.0	13.4 ± 3.6	< 0.0001
E/E′ medial (cm/s)	20.1 ± 10.7	9.4 ± 3.0	< 0.0001
E/E′ lateral (cm/s)	15.4 ± 8.8	5.9 ± 1.6	< 0.0001
S′ medial (cm/s)	6.3 ± 1.3	7.1 ± 1.6	0.004
S′ lateral (cm/s)	7.3 ± 2.5	8.2 ± 2.6	0.07
LV GLS (%)	–16.1 ± 5.3	–17.9 ± 2.1	0.04
RV parameters			
RV base (mm)	32.1 ± 6.9	30.8 ± 4.7	0.28
RVS′ (cm/s)	11.5 (9.7–13.8)	11.6 (10.5–13.4)	0.29
TAPSE (cm)	2.1 ± 0.4	2.2 ± 3.2	0.78
RAVi (ml/m²)†	23.1 ± 12.9	18.6 ± 5.4	0.03
TR (grade ≥ 2+ TR) (%)	30%	–	–
PASP (mmHg)	35.1 ± 16.9	22.1 ± 5.6	< 0.0001
RV free-wall PSS (%)	–16.8 ± 4.5	–19.2 ± 3.4	0.003

Data are presented as mean ± SD or %. †Values are indexed to BSA. CRMR, chronic rheumatic mitral regurgitation; EDVi, end-diastolic volume indexed; ESVi, end-systolic volume indexed; IVSD, interventricular septal diameter; LAVi, left atrial volume indexed; EDD, end-diastolic diameter; EF, ejection fraction; ESD, end-systolic diameter; GLS, global longitudinal strain; LV, left ventricle; LVMi, left ventricular mass indexed; NYHA, New York Heart Association; PASP, pulmonary artery systolic pressure; PWD, posterior wall diameter; PSS, peak systolic strain; RAVi, right atrial volume indexed; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

Table 3. RV systolic function parameters according to severity of MR

Variable	*Moderate CRMR (n = 51)*	*Severe CRMR (n = 26)*	p-*value*
RV wall thickness (mm)	5.9 ± 1.6	7.2 ± 2.3	0.006
PASP (mmHg)	31.0 ± 12.3	43.9 ± 21.3	0.001
RVS′ (cm/s)	11.6 (9.9–14.6)	11.4 (9.4–13.4)	0.29
TAPSE (cm)	2.1 ± 0.38	2.0 ± 0.4	0.28
RV free-wall PSS (%)	–17.7 ± 4.2	–15 ± 4.7	0.01

Data are presented as median (IQR), mean ± SD. CRMR, chronic rheumatic mitral regurgitation; PASP, pulmonary artery systolic pressure; PSS, peak systolic strain; RV, right ventricle; TAPSE, tricuspid annular plane systolic excursion.

There was a positive correlation between RV free-wall PSS and LVGLS in patients with CRMR ($r = 0.3$, $p < 0.001$). The majority of patients (45%) had preserved RV free-wall PSS and LVGLS, 26% had decreased LVGLS and RV free-wall PSS, 18% had diminished LVGLS and preserved RV free-wall PSS, and a minority (11%) had preserved LVGLS with decreased RV free-wall PSS (Fig. 2).

By univariate linear regression analysis, severe MR, grade ≥ 2+ TR, PASP, LVEF, LV end-diastolic diameter, lateral S′ and LVGLS showed a significant association with RV free-wall PSS, with LVGLS having the strongest correlation (Table 5). By multivariate linear regression analysis after adjusting for age and gender, LVGLS and grade ≥ 2+ TR emerged as the most important predictors of RVPSS (Table 5).

RV free-wall PSS measurements were feasible in 76 patients. In one patient, RV free-wall PSS was not feasible due to poor imaging of the lateral wall, however, LVGLS could be quantified. The intra-observer coefficient of variation for RV free-wall PSS was 7% with a mean difference ± SD of 0.4 ± 2.7 ($p = 0.5$), and for LVGLS it was 2.4% with a mean difference ± SD of 1.1 ± 2.7 ($p = 0.09$). The inter-observer variability coefficient was 7.6% for RV free-wall PSS with a mean difference ± SD of 0.5 ± 3.8 ($p = 0.5$) and for LVGLS it was 9.8% with a mean difference ± SD of 0.25 ± 2.4 ($p = 0.6$).

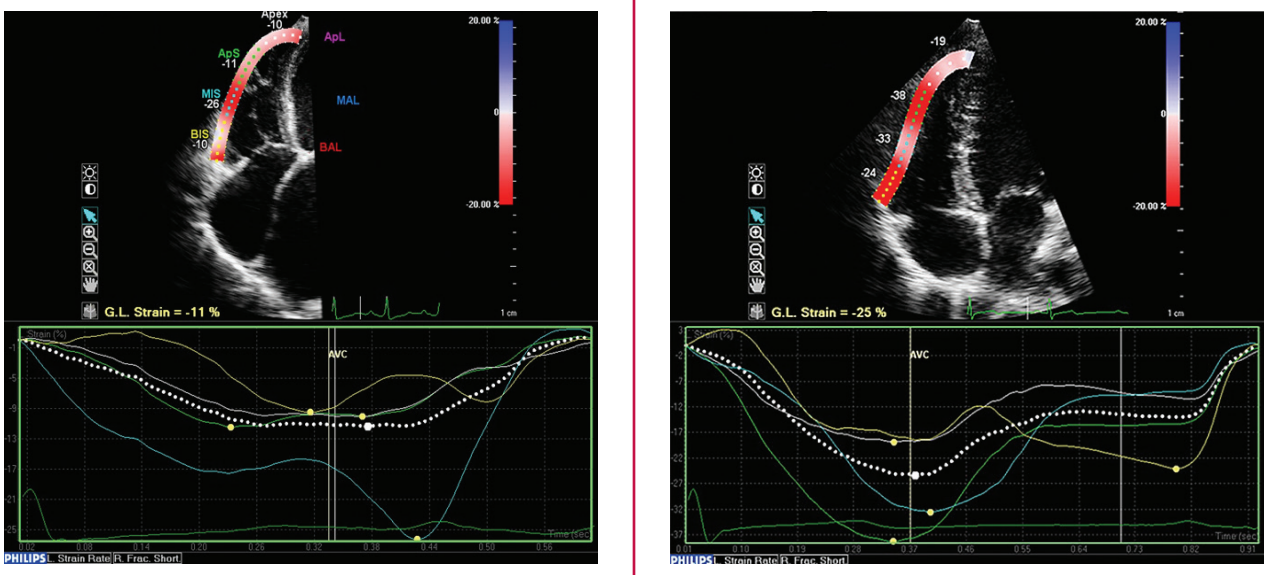

Fig. 1. Reduced RV free-wall peak systolic strain (PSS) in a chronic rheumatic mitral regurgitation patient (left) compared to normal RV free-wall PSS in a control subject (right).

Table 4. Comparison of RV systolic function parameters in CRMR according to LV systolic function

Variable	*LVEF < 60% (n = 32)*	*LVEF ≥ 60% (n = 45)*	p-*value*
RVS′ (cm/s)	11.3 (9.7–13.0)	12.0 (9.6–14.7)	0.27
TAPSE (cm)	1.9 ± 0.30	2.1 ± 0.41	0.07
LVGLS (%)	–13.1 ± 5.6	–18.2 ± 3.9	< 0.001
RVPSS (%)	–14.6 ± 4.1	–18.2 ± 4.2	0.0003
PASP (mmHg)	39.9 ± 21.5	31.6 ± 11.5	0.03

Data are presented as median (IQR), mean ± SD or %. EDD, end-diastolic diameter; GLS, global longitudinal strain; LV, left ventricle; PASP, pulmonary artery systolic pressure; PSS, peak systolic strain; RV, right ventricle; RVH, right ventricular hypertrophy; TAPSE, tricuspid annular plane systolic excursion.

Discussion

The pertinent findings of this study are firstly, that RV free-wall PSS is a sensitive marker of subclinical RV dysfunction in CRMR patients, as evidenced by depressed RV free-wall PSS when conventional clinical measures of RV function were normal. This trend was observed with CRMR patients compared to controls, moderate compared to severe MR and between those with normal LVEF and those with depressed LVEF. Secondly, LVGLS and significant TR were the most important determinant of RV free-wall PSS.

RV functional impairment and decreased LVEF are powerful predictors of cardiovascular and overall survival in degenerative MR.[6] The main determinants of RV function in MR are RV load, myocardial function, neuro-hormonal abnormalities and ventricular interaction.[5,26]

Only RV free-wall PSS was measured in this study as the interventricular septum contributes minimally to RV function.[27] RVPSS is known to have prognostic and predictive value in various cardiovascular disease states.[1,27] In this study RV systolic

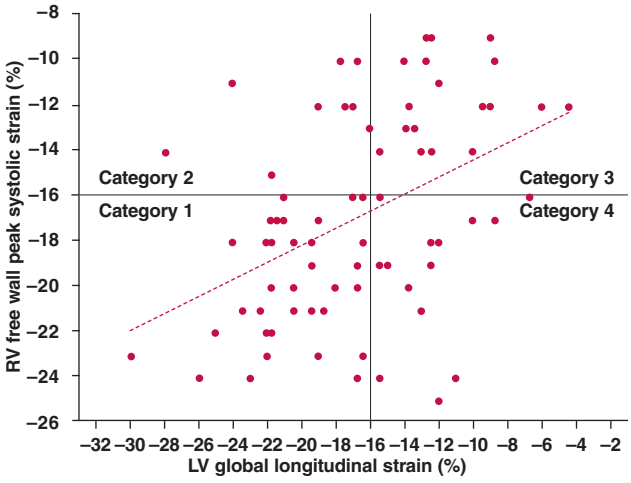

Fig. 2. Correlation between RV free-wall peak systolic strain (PSS) and LV global longitudinal strain (LVGLS) in chronic rheumatic mitral regurgitation (R^2 = 0.1984, p < 0.001). Category 1, normal LVGLS and normal RV free-wall PSS; category 2, normal LVGLS and decreased RV free-wall PSS; category 3, decreased LVGLS and decreased RV free-wall PSS; category 4, decreased LVGLS and normal RV free-wall PSS.

Table 5. Predictors of RV free-wall PSS in chronic rheumatic mitral regurgitation: uni- and multivariate linear regression analysis

Univariate models	R-*value*	*Adjusted* R^2	p-*value*
Age (years)	0.06	0.004	0.56
Gender (M)	0.14	0.008	0.20
LVEF (%)	0.33	0.09	0.003
LVEDD (mm)	0.29	0.07	0.009
Lateral S′ (cm/s)	0.24	0.04	0.03
PASP (mmHg)	0.31	0.08	0.006
Severe MR	0.29	0.07	0.008
LVGLS (%)	0.44	0.18	< 0.001
Grade ≥ 2+ TR	0.42	0.16	0.0001
Multivariate model $R = 0.56$, $p < 0.0001$			
LVGLS (%)	0.40	0.07	0.0004
Grade ≥ 2+ TR	0.37	0.07	0.001
Multivariate model $R = 0.58$, $p < 0.0001$			
LVGLS (%)	0.35	0.08	0.0009
Grade ≥ 2+ TR	0.38	0.46	0.005
PASP (mmHg)	–0.0007	0.44	0.99
Multivariate model $R = 0.57$, $p < 0.0001$			
LVGLS (%)	0.39	0.08	0.0006
Grade ≥ 2+ TR	0.29	0.24	0.01
Severe MR	0.12	0.26	0.27
Multivariate model $R = 0.56$, $p < 0.0001$			
LVGLS (%)	0.30	0.34	0.008
Grade ≥ 2+ TR	0.36	0.08	0.001
LVEF (%)	–0.08	0.31	0.45
Multivariate model $R = 0.55$, $p < 0.0001$			
LVGLS (%)	0.33	0.29	0.004
Grade ≥ 2+ TR	0.36	0.07	0.002
Lateral S′ (cm/s)	–0.04	0.38	0.69
Multivariate model $R = 0.5$, $p < 0.001$			
LVGLS (%)	0.34	0.16	0.002
Grade ≥ 2+ TR	0.36	0.05	0.001
LVEDD (mm)	0.13	0.14	0.26

EDD, end-diastolic diameter; EF, ejection fraction; GLS, global longitudinal strain; LV, left ventricle; MR, mitral regurgitation; PASP, pulmonary artery systolic pressure; TR, tricuspid regurgitation.

dysfunction was more prevalent by STE than with commonly used conventional markers of systolic function such as TAPSE and RVS′. STE-derived RVPSS has been shown to be feasible and reproducible for clinical use.[1,11,12] In this study RV free-wall PSS was feasible and reproducible in assessing RV function in CRMR. STE has been shown to be advantageous over conventional echocardiographic parameters used to measure RV systolic function in a variety of cardiovascular disorders such as heart failure, pulmonary hypertension and pre-operative and postoperative RV function assessment.[6,11,12,13,28]

This finding can be explained by technical aspects, as speckle-tracking is angle independent and less influenced by heart motion compared to TAPSE and RVS′.[1] Additionally, TAPSE and S′ only measure regional RV function, whereas RV free-wall PSS is able to provide more global assessment of RV function.[1] Furthermore, Focardi *et al.* recently showed that among all RV systolic function parameters, RVPSS had the best correlation with RVEF measured by cardiac magnetic resonance imaging.[29] Therefore, although STE is limited by image quality and load

dependence, unlike traditional echocardiographic parameters, it is able to detect subclinical longitudinal RV dysfunction.

The decreased RV free-wall PSS with preserved traditional markers of RV systolic function in this study implies subclinical RV dysfunction. The mechanism of reduced RV strain in this study may be related to the elevated PASP, as the RV is known to be extremely sensitive to afterload.[26,28] Even small increases in pulmonary vascular resistance can markedly decrease RV contractile function. Prior studies have noted a similar relationship between RV systolic performance and pulmonary hypertension in degenerative MR.[5,6]

Le Torneau *et al*. have shown in their study that, even though increased RV afterload secondary to PHT was an important cause of RV dysfunction in MR, LV dysfunction also contributed significantly to RV dysfunction, due to their interdependent relationship.[5] In this study PASP was only modestly elevated but the markers of LV remodelling and systolic function such as LVGLS, LVEDD and S′ velocity were markedly abnormal. Therefore, in agreement with Le Torneau *et al*.,[5] LV remodelling and LV dysfunction, in addition to the modest elevation in PASP, may be important causes of RV functional impairment in CRMR.

This is supported by the finding of reduced RV free-wall PSS in patients with LVEF < 60% and reduced LVGLS. Additionally, most patients had abnormal RV free-wall PSS in the presence of abnormal LVGLS, and those with normal RV free-wall PSS also had normal LVGLS. However, conventional RV systolic function parameters were still preserved even in the presence of LV systolic dysfunction. Hence, once abnormalities in LV systolic function are noted in MR, systematic RV function assessment must be done with not only traditional parameters but also STE, in order to detect subclinical RV dysfunction and reduce mortality associated with biventricular functional impairment.[5]

Severe MR was associated with worse RV function and was found to be a determinant of RVPSS in a study by Le Torneau *et al*.[5] Volume overload as a result of chronic MR results in LV remodelling, as noted in our study, and this in turn results in abnormalities of RV and LV interaction. RV free-wall PSS was lower in patients with severe MR compared to moderate MR. This association can be explained by greater chronic volume overload of the LV and left atrium, accompanied by increased PASP secondary to backward transmission of increased LV pressure, as well as remodelling of the pulmonary vasculature in severe compared to moderate MR.[30] However, a lack of difference in traditional RV systolic function parameters between the moderate and severe MR groups was present, and therefore quantitative RV function assessment in CRMR mandates evaluation by both conventional indices and RV longitudinal strain.

TR was an independent predictor of RV free-wall PSS. Significant TR is likely a reflection of deteriorating RV function secondary to left-sided disease. The increase in RV preload initially results in increased RV free-wall PSS due to increased myocardial lengthening in diastole and shortening in systole. Once RV myocardial contractile dysfunction ensues, however, RV systolic strain declines, as RV reaches the descending limb of the Frank–Starling curve.

Finally, the decline in RV free-wall PSS may be partially attributed to primary RV dysfunction. The intrinsic myocardial functional abnormality may be a result of longstanding activation of neuro-hormonal pathways and increased afterload secondary to chronic mitral regurgitation.[8,26] We further speculate that there may be direct involvement of the RV myocardium by the rheumatic process.

This study had two limitations: first, lack of reference standard for RV functional assessment such as additional imaging in the form of cardiac MRI and three-dimensional echocardiography, and second, we did not routinely perform right and left heart catheterisation to assess PASP, pulmonary vascular resistance and coronary anatomy.

Conclusion

In CRMR patients, RV free-wall PSS was a more sensitive marker for detecting earlier RV systolic dysfunction than traditional RV functional parameters. LVGLS and TR were important determinants of RV free-wall PSS in CRMR.

The first author was the recipient of the Carnegie PhD Fellowship award (Carnegie Corporation grant no. b8749.r01).

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