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Right ventricular myocardial work: proof-of-concept for non-invasive assessment of right ventricular function

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Aims Right ventricular myocardial work (RVMW) is a novel method for non-invasive assessment of right ventricular (RV) function utilizing RV pressure–strain loops. This study aimed to explore the relationship between RVMW and invasive indices of right heart catheterization (RHC) in a cohort of patients with heart failure with reduced left ventricular ejection fraction (HFrEF), and to compare values of RVMW with those of a group of patients without cardiovascular disease.

Methods and results Non-invasive analysis of RVMW was performed in 22 HFrEF patients [median age 63 (59–67) years] who underwent echocardiography and invasive RHC within 48 h. Conventional RV functional measurements, RV global constructive work (RVGCW), RV global work index (RVGWI), RV global wasted work (RVGWW), and RV global work efficiency (RVGWE) were analysed and compared with invasively measured stroke volume and stroke volume index. Non-invasive analysis of RVMW was also performed in 22 patients without cardiovascular disease to allow for comparison between groups. None of the conventional echocardiographic parameters of RV systolic function were significantly correlated with stroke volume or stroke volume index. In contrast, one of the novel indices derived non-invasively by pressure–strain loops, RVGCW, demonstrated a moderate correlation with invasively measured stroke volume and stroke volume index ($r = 0.63$, $P = 0.002$ and $r = 0.59$, $P = 0.004$, respectively). RVGWI, RVGCW, and RVGWE were significantly lower in patients with HFrEF compared to a healthy cohort, while values of RVGWW were significantly higher.

Conclusion RVGCW is a novel parameter that provides an integrative analysis of RV systolic function and correlates more closely with invasively measured stroke volume and stroke volume index than other standard echocardiographic parameters.

Keywords right ventricle • non-invasive myocardial work • heart failure with reduced ejection fraction • cardiac index • stroke volume

Introduction

Heart failure (HF) is a clinical syndrome characterized by typical symptoms (i.e. dyspnoea, oedema, and fatigue) caused by a structural and/or functional cardiac abnormality resulting in a reduced cardiac output and/or elevated filling pressures.[1] With an estimated global prevalence of ∼38 million individuals,[2] HF is a leading cause of hospitalization and morbidity.[3]

While many echocardiographic parameters provide important prognostic information for patients with HF and reduced left

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ventricular (LV) ejection fraction (HFrEF) (i.e. LV ejection fraction (EF), LV global longitudinal strain),[4] the value of indices evaluating the function of the right ventricle have become increasingly recognized.[5] Right ventricular (RV) speckle tracking echocardiography-derived longitudinal strain is angle-independent and less load-dependent than other conventional parameters of RV systolic function [such as RV fractional area change (FAC) or tricuspid annular plane systolic excursion (TAPSE)][6] and has been demonstrated to have an important role in the prediction of outcomes for individuals with HFrEF.[7]

Despite demonstrating superiority over conventional two-dimensional echocardiography parameters for the evaluation of RV systolic function,[5,8] RV longitudinal strain is a more afterload-dependent parameter than LV global longitudinal strain, due to the thinner walls and lower ventricular elastance of the right ventricle.[9] Furthermore, RV longitudinal strain does not integrate RV dyssynchrony or post-systolic shortening into its quantitative output, components of RV function that have been demonstrated to correlate with invasively derived cardiac index.[10]

Recently, LV myocardial work, a non-invasive estimate of the LV pressure–volume loop, was proposed as method to provide a comprehensive evaluation of LV systolic function, accounting for both afterload and LV dyssynchrony. LV myocardial work is calculated from LV pressure–strain loop analysis, incorporating speckle tracking echocardiography-derived LV global longitudinal strain and non-invasive brachial cuff blood pressure measurements.[11] However, no such technique has been applied for the estimation of RV function, neither for individuals with HFrEF nor for any other patient group. Therefore, the present study aimed to explore the relationship between the non-invasive estimation of RV myocardial work (RVMW) and invasive indices of right heart catheterization (RHC) in a cohort of patients with HFrEF, utilizing software dedicated for myocardial work analysis of the left ventricle. An additional aim was to compare the values of RVMW in a cohort with HFrEF with those of a group of patients without cardiovascular disease.

Methods

Study population

From the departmental electronic records of the Leiden University Medical Center (Leiden, The Netherlands), all patients with HFrEF who underwent RHC during the period of January 2006–July 2020 were selected. Those who had an echocardiogram performed within 48 h of RHC were included for further evaluation (*Figure 1*). Patients with active endocarditis, severe tricuspid regurgitation (TR), and congenital heart disease were excluded. Additionally, a healthy population consisting of individuals without cardiovascular disease who underwent echocardiography during the same period as the HF patients were selected for derivation of the normal reference values for RVMW indices.[12] Patient demographics and clinical data were collected from the departmental electronic medical record (EPD-vision; Leiden University Medical Center, Leiden, The Netherlands). As this study involved the retrospective analysis of clinically acquired data, the institutional review board of the Leiden University Medical Center waived the need for written patient informed consent. The data that supports the findings of this study are available on reasonable request to the corresponding author.

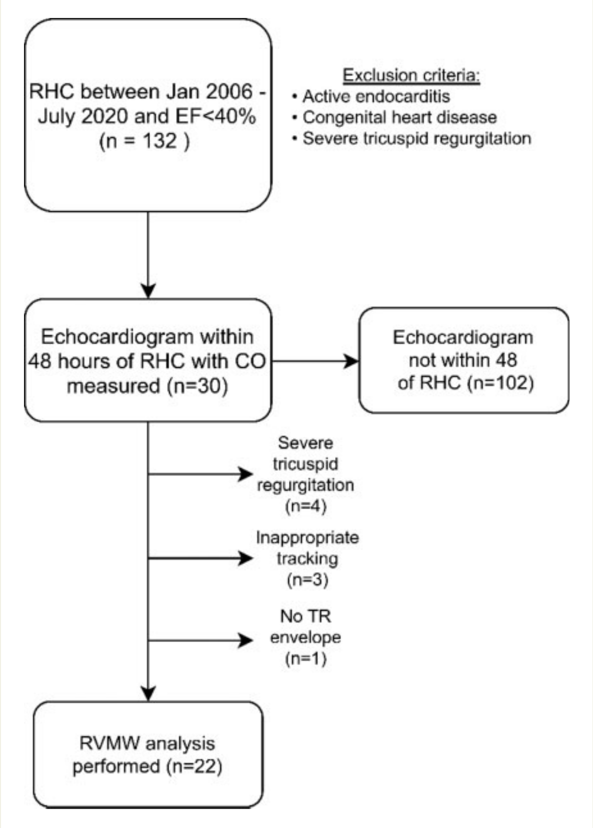

Figure 1 Study flow chart. EF, ejection fraction; RHC, right heart catheterization; RVMW, right ventricular myocardial work; TR, tricuspid regurgitation.

Right heart catheterization

All procedures were performed in the catheterization laboratory by an experienced interventional cardiologist. A standard 7.5 Fr triple lumen Swan Ganz catheter (Edwards Lifesciences, Irvine, CA, USA) was inserted via an 8 Fr introducer sheath through the right femoral or right internal jugular vein at the operator's discretion and advanced to the left or right pulmonary artery under fluoroscopic guidance. Right atrial (RA) pressure, systolic and diastolic RV pressure, systolic, diastolic, and mean pulmonary artery pressure (mPAP), and pulmonary capillary wedge pressure (PCWP) were obtained at end-expiration. Cardiac output was obtained by thermodilution, as the average of three measurements. Stroke volume index and cardiac index were calculated by indexing stroke volume and cardiac output to body surface area, respectively (estimated using the Dubois formula). RV stroke work was calculated according to methods previously described.[13]

Echocardiographic data acquisition and standard measurements

Comprehensive transthoracic echocardiography was performed utilizing a Vivid 7 or E9 ultrasound system (General Electric Vingmed Ultrasound, Milwaukee, WI, USA) with patients at rest in the left lateral decubitus position. Electrocardiogram-triggered echocardiographic data were acquired with 3.5 MHz or M5S transducers. Data were stored digitally in a cine-loop format for offline analysis with EchoPAC software (EchoPAC 204, General Electric Vingmed Ultrasound). LVEF was calculated using the biplane Simpson method, while LV mass was calculated using the standard linear two-dimensional approach.[14] TAPSE was measured on M-mode recordings of the lateral tricuspid annulus in an RV-focused apical view, while peak systolic myocardial velocity of the RV lateral annulus (RV S′) was measured using tissue Doppler imaging, according to guideline recommendations.[14] RV end-systolic and end-diastolic areas were acquired in an RV-focused apical view, with RV FAC calculated as: RV FAC = [(RV end-diastolic area - RV end-systolic area)/RV end-diastolic area] × 100%.[14] Systolic pulmonary artery pressure (PASP) was estimated from the TR jet peak velocity applying the modified Bernoulli equation and adding mean RA pressure. Estimated mean RA pressure was derived from the inferior vena cava diameter and its collapsibility.[15] Pulmonary artery mean pressure (PAMP) was obtained by the formula: mean RV-RA gradient + mean RA pressure. The mean RV-RA gradient was calculated by tracing the TR velocity-time integral.[16] Pulmonary artery diastolic pressure (PADP) was calculated as: PADP = 1.5 × [PAMP - (PASP/3)].[15] All other standard measurements were performed according to the American Society of Echocardiography guidelines.[14]

Quantification of RVMW

The novel indices of RVMW were analysed utilizing proprietary software originally developed for the assessment of LV myocardial work by two-dimensional speckle tracking echocardiography (EchoPAC Version 204). This software has been validated for a variety of different patient subgroups for the measurement of LV myocardial work.[11,17] The non-invasive evaluation of LV myocardial work was first developed by Russell *et al.*[11] as a tool for the estimation of LV myocardial oxygen consumption. In this non-invasive model, an estimate of the area of the myocardial force-segment length loop was approximated by non-invasive brachial cuff blood pressure recordings (as a substitute for myocardial force) and global longitudinal strain by speckle-tracking echocardiography (as a substitute for segment length), and was validated with pressure–volume loops derived invasively with micromanometer-tipped catheters. Similar principles may be applied to the right ventricle, allowing for the approximation of RV myocardial force-segment length loops with pressure–strain loops. Pulmonary pressures may be used to derive an estimate of myocardial force, while strain derived by speckle tracking echocardiography can be used to estimate changes in segment length.

An RV-focused apical four-chamber view was used to evaluate RV global longitudinal strain, with the region of interest including both the RV free wall and interventricular septum.[18] Analysis of RV global rather than free wall strain was performed because the left ventricle, via the septum, is estimated to contribute up to 20–40% to overall RV stroke volume and pulmonary flow.[19,20] Measurements of RV strain and pulmonary systolic and diastolic pressures were then synchronized by cardiac cycle timings (determined by pulmonic and tricuspid valve events) to produce non-invasively derived pressure–strain loops for the right ventricle (*Figure 2*). The event timings of the pulmonic valve were determined by pulsed-wave interrogation in the basal parasternal short-axis view, while tricuspid valve event timings were derived from direct visualization in the RV-focused apical four-chamber view. Whenever both valve timings were adequately visualized in the parasternal short-axis view at the level of the aortic valve, this was used preferentially.

Four parameters of RVMW were derived:

(1) RV global work index (RVGWI, mmHg%): the area within the global RV pressure–strain loop, calculated from tricuspid valve closure to opening.
(2) RV global constructive work (RVGCW, mmHg%): defined as the work contributing to the shortening of the cardiac myocytes during systole and the lengthening during isovolumic relaxation.
(3) RV global wasted work (RVGWW, mmHg%): defined as the work contributing to the lengthening of the cardiac myocytes during systole and the shortening during isovolumic relaxation.
(4) RV global work efficiency (RVGWE, %): defined as RVGCW divided by the sum of RVGCW and RVGWW.

Statistical analysis

All statistical analyses were performed using SPSS version 25.0 (SPSS Inc., IBM Corp). Categorical variables are expressed as numbers and percentages. Adherence to a normal distribution was verified using the Kolmogorov–Smirnov test and visual assessment of histograms. Normally distributed continuous variables are presented as mean ± standard deviation while variables that are non-normally distributed are presented as median and interquartile range. Categorical variables were compared using the χ^2 test. Continuous variables were compared using the Student's *t*-test if normally distributed, while the Mann–Whitney *U* test was utilized for non-normally distributed variables. Spearman correlation was used to investigate the relationship between invasively derived stroke volume and stroke volume index, and the parameters of RV systolic function (including the novel indices of RVMW). Ten random individuals were selected for evaluation of intraobserver and interobserver agreement using intraclass correlation coefficients (ICCs) and Bland–Altman analysis. Intraobserver measurements were performed offline after a 4-week interval. The second observer was blinded to the measurements of the first observer for interobserver measurements. All tests were two-sided and *P*-values <0.05 were considered statistically significant.

Results

Clinical characteristics

Twenty-six patients with HFrEF fulfilled the inclusion criteria. Four patients were excluded from RVMW analysis due to inappropriate tracking or the absence of a measurable TR envelope (feasibility, 85%). An additional 22 individuals without cardiovascular disease were selected for comparison of the non-invasively derived parameters of RVMW with HFrEF patients. Patients with HFrEF were older (62.5 vs. 53.5 years, $P = 0.037$) and more frequently male (77% vs. 32%, $P = 0.004$) compared to the individuals without cardiovascular disease. Of the HFrEF patients, 73% were in New York Heart Association Class III or IV and 50% had ischaemic cardiomyopathy. Additional patient demographic and clinical data are presented in *Table 1*.

Conventional echocardiographic parameters

Patients with HFrEF had a lower LVEF [18.4% (±6.8) vs. 59.9% (±4.6), $P < 0.001$], LV global longitudinal strain [-3.5% (±1.7) vs. -20.5% (±2.1), $P < 0.001$], and RV global longitudinal strain [-9.6% (±4.7) vs. -21.8% (±3.0), $P < 0.001$] when compared to the individuals without cardiovascular disease. In addition, estimated PASP, LV mass index, RV end-diastolic area, RV basal diameter, RV mid-diameter, and indexed RA volume were significantly higher in the HFrEF group, while stroke volume index derived from echocardiography was significantly lower compared to individuals without cardiovascular disease (*Table 2*).

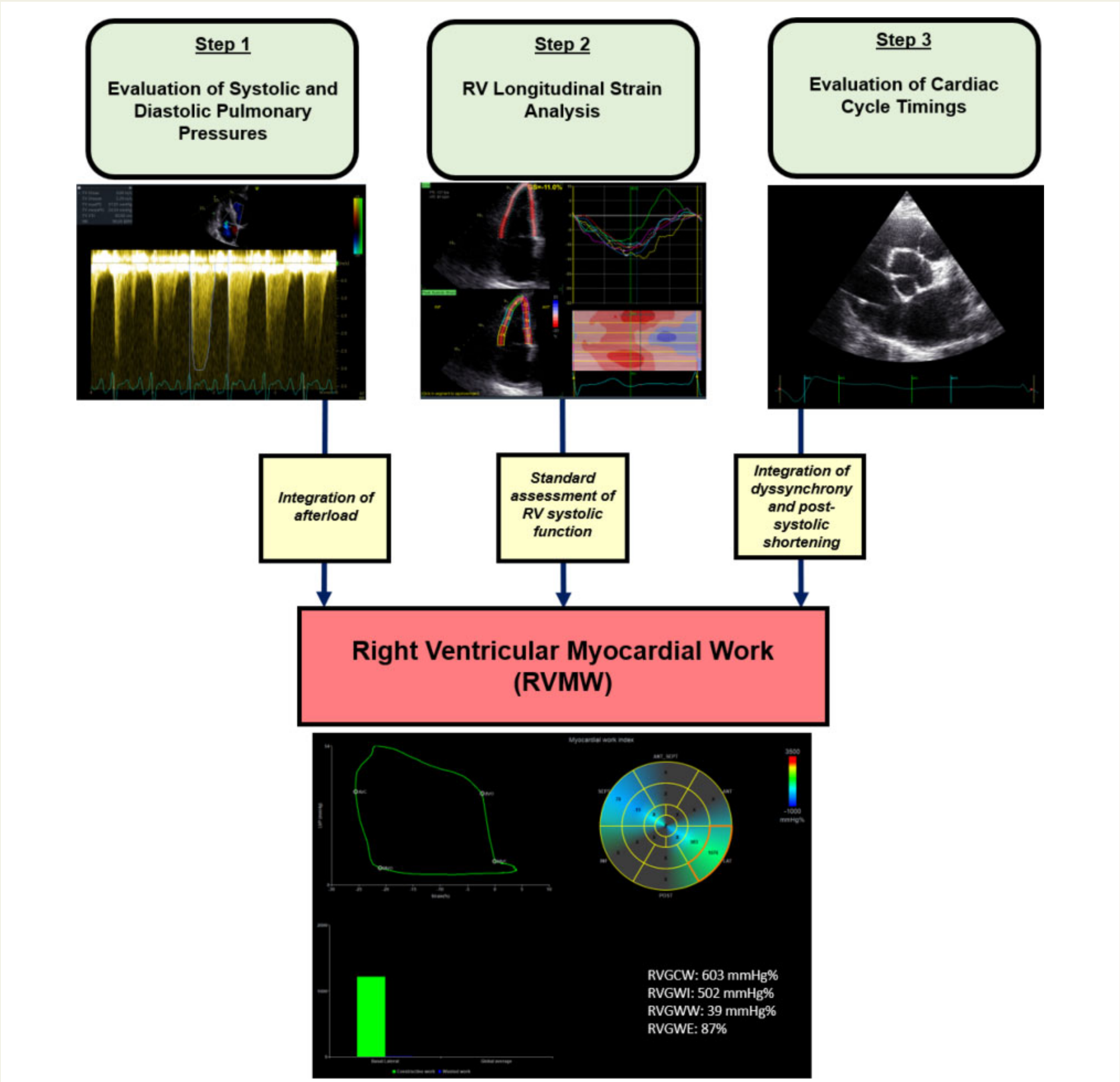

Figure 2 Method for the calculation of RVMW. RVMW provides an integrative analysis of RV function, incorporating speckle tracking echocardiography-derived RV strain, pulmonary pressures, and cardiac cycle timings. Cardiac cycle timings are determined by pulmonic and tricuspid valve opening and closure events, identified through either direct visualization of two-dimensional images or by pulsed-wave Doppler interrogation. Integration of event timings allows for the quantitative evaluation of RV dyssynchrony and post-systolic contraction. Indices of RVMW are calculated based on non-invasively derived pressure–strain loops for the right ventricle. RV, right ventricular; RVGCW, right ventricular global constructive work; RVGWE, right ventricular global work efficiency; RVGWI, right ventricular global work index; RVGWW, Right ventricular global wasted work; RVMW, right ventricular myocardial work.

Parameters of RVMW by two-dimensional speckle tracking echocardiography

Table 2 compares the values of RVMW indices between HFrEF patients and individuals without cardiovascular disease. As expected, RVGWI [241.4 mmHg% (±124.6) vs. 381.2 mmHg% (±103.6), $P < 0.001$], RVGCW [344.0 mmHg% (±125.9) vs. 414.2 mmHg% (±103.4), $P = 0.050$], and RVGWE [73.5% (66.4–86.5) vs. 95.5% (93.4–96.6), $P < 0.001$] were significantly lower, while RVGWW [70.0 mmHg% (42.8–134.1) vs. 14.8 mmHg% (9.3–20.6), $P < 0.001$] was significantly higher in the HFrEF group when compared to individuals without cardiovascular disease. Examples of RVMW measurements are demonstrated in *Figure 4*. Correlations of parameters of

Table 1 **Patient characteristics of HFrEF and no CVD groups**

Variables	HFrEF (*n* = 22)	No CVD (*n* = 22)	*P*-value
Age (years)	62.5 (59.0–67.3)	53.5 (35.0–65.5)	0.037
Male gender	17 (77%)	15 (68%)	0.004
Obesity (BMI > 30kg/m^2)	3 (14%)	2 (9%)	0.634
CKD (eGFR < 60 mL/min/1.73 m^2)	12 (55%)		
Diabetes	7 (32%)		
COPD	2 (9%)		
Hypertension	6 (27%)		
Dyslipidaemia	8 (36%)		
Indication for RHC			
LVAD workup	16 (73%)		
Evaluation of cardiomyopathy	6 (27%)		
Aetiology of heart failure			
Ischaemic	11 (50%)		
Non-ischaemic	11 (50%)		
NYHA class			
III or IV	16 (73%)		
Medication			
ARB/ACEi/ARNi	18 (82%)		
MRA	18 (82%)		
Diuretics	22 (100%)		
Beta-blocker	17 (77%)		
Oral anticoagulation	17 (77%)		

Data are presented as median (25th–75th percentile) if not normally distributed.
ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; ARNi, angiotensin receptor-neprilysin inhibitors; BMI, body mass index; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; HFrEF, heart failure with reduced ejection fraction; LVAD, left ventricular assist device; MRA, mineralocorticoid receptor antagonist; NYHA, New York Heart Association; RHC, right heart catheterization.

RVMW with standard parameters of RV systolic function are presented in Supplementary data online, *Table S1*.

RHC parameters

For the 22 patients with HFrEF who underwent invasive RHC, median stroke volume [52.9 (42.8–64.1) mL], stroke volume index [26.4 (22.1–31.3) mL/m^2], and mean cardiac index were reduced (2.1 ± 0.63 L/min/m^2), while median mPAP [34.7 (18.7–47.0) mmHg], PCWP [20.5 (12.0–34.0) mmHg], and RA pressure [10 (4–17) mmHg] were increased. Additional RHC data are summarized in *Table 3*.

Relationship between RHC parameters and parameters of RV systolic function

The correlations between stroke volume and stroke volume index measured on RHC and the various echocardiographic parameters of RV systolic function were evaluated in the cohort of HFrEF patients. None of the standard echocardiographic parameters of RV systolic function were significantly correlated with stroke volume or stroke volume index, including FAC (r = -0.23, P = 0.33 and r = -0.13, P = 0.57, respectively), RV global longitudinal strain (r = -0.11, P = 0.63 and r = -0.27, P = 0.23, respectively), RV free wall longitudinal strain (r = -0.07, P = 0.75 and r = -0.22, P = 0.32, respectively), TAPSE (r = 0.25, P = 0.27 and r = 0.27, P = 0.22, respectively), and echocardiography-derived stroke volume (r = 0.25, P = 0.27 and r = 0.29, P = 0.19, respectively) (*Figure 3*). The echocardiographically derived parameters of LVEF, LV global longitudinal strain, RVGWI, RVGWW, RVGWE, and PASP did not significantly correlate with invasively derived stroke volume or stroke volume index. However, one of the novel indices derived non-invasively by pressure–strain loops, RVGCW, demonstrated a significant correlation with invasively measured stroke volume and stroke volume index (r = 0.59, P = 0.004 and r = 0.63, P = 0.002, respectively). Additionally, RVGCW was also correlated with cardiac index (r = 0.42, P = 0.049) measured during RHC.

Intraobserver and interobserver variability

The ICC for intraobserver variability was 0.915 for RVGCW (P < 0.001), 0.959 for RVGWI (P < 0.001), and 0.967 for RVGWE (P < 0.001), demonstrating excellent reliability (*Table 4*). The ICC for intraobserver variability for RVGWW indicated good reliability at 0.868 (P < 0.001). The ICC for interobserver variability for RVGWW was 0.938 (P < 0.001), demonstrating excellent reliability, while the interobserver variability was 0.858 for RVGCW (P = 0.001), 0.802 for RVGWI (P = 0.001), and 0.826 for RVGWE (P < 0.001) indicating good reliability. Bland–Altman analysis for assessing the intraobserver and interobserver variability of the four novel parameters of RVMW is shown in *Figure 5*.

Table 2 Echocardiographic characteristics of HFrEF vs. no CVD patient groups

Variables	HFrEF (*n* = 22)	No CVD (*n* = 22)	*P*-value
RVGWI (mmHg%)	241.4 ± 124.6	381.2 ± 103.6	<0.001
RVGCW (mmHg%)	344.0 ± 125.9	414.2 ± 103.4	0.017
RVGWW (mmHg%)	70.0 (42.8–134.1)	14.8 (9.3–20.6)	<0.001
RVGWE (%)	73.5 (66.4–86.5)	95.5 (93.4–96.6)	<0.001
LVEF (%)	18.4 ± 6.8	59.9 ± 4.6	<0.001
LV GLS (%)	-3.5 ± 1.7	-20.5 ± 2.1	<0.001
LV mass index (g/m^2)	187.3 ± 54.5	90.2 ± 20.9	<0.001
TAPSE (mm)	14.8 ± 3.7	24.0 ± 3.7	<0.001
RV GLS (%)	-9.6 ± 4.7	-21.8 ± 3.0	<0.001
RV FWLS (%)	-13.3 ± 6.6	-25.3 ± 4.2	<0.001
PASP (mmHg)	41.5 ± 12.6	22.6 ±3.8	<0.001
Echocardiography-derived stroke volume index (mL/m^2)	27 (22–43)	41 (38–46)	0.009
RV S′ (cm/s)	6.8 ± 1.7	10.2 ± 1.7	<0.001
RV FAC (%)	30.9 ± 12.5	49.0 ± 9.3	<0.001
RV EDA (cm^2)	24.4 ± 8.6	19.6 ± 4.5	0.029
RV basal diameter (mm)	49.2 ± 12.4	36.1 ± 5.4	<0.001
RV mid-diameter (mm)	33.5 ± 9.0	27.7 ± 5.0	0.014
TA diameter (mm)	33.5 ± 6.5	26.8 ± 5.3	0.001
RAVI (mL/m^2)	33.6 (23.4–56.3)	22.2 (17.8–27.6)	0.002

Data are presented as mean ± SD if normally distributed or median (25th–75th percentile) if not normally distributed.

CVD, cardiovascular disease; EDA, end-diastolic area; FAC, fractional area change; HFrEF, heart failure with reduced ejection fraction; LV, left ventricular; LVEF, left ventricular ejection fraction; LV GLS, left ventricular global longitudinal strain; PASP, pulmonary artery systolic pressure; RAP, right atrial pressure; RV FWLS, right ventricle free wall longitudinal strain; RV GLS, right ventricle global longitudinal strain; RV S′, right ventricular S prime; RVGCW, right ventricular global constructive work; RVGWE, right ventricular global work efficiency; RVGWI, right ventricular global work index; RVGWW, right ventricular global wasted work; TA, tricuspid annular; TAPSE, tricuspid annular plane systolic excursion.

Discussion

The present study is a proof-of-concept of the feasibility of RVMW indices measurements in HFrEF and its correlation with invasively measured stroke volume and stroke volume index. Compared to a healthy cohort, RVGWI, RVGCW, and RVGWE were demonstrated to be significantly lower in patients with HFrEF, while values of RVGWW were significantly higher. Non-invasively measured RVGCW was the only echocardiographic parameter that showed an association with invasively measured stroke volume and stroke volume index in patients with HFrEF. RVMW indices may enhance the non-invasive understanding of the pathophysiology of patients with HFrEF and improve the non-invasive characterization of their response to therapies.

RVMW in HFrEF vs. patients without cardiovascular disease

Several small studies evaluating LV myocardial work in individuals with HFrEF have demonstrated reduced values of LV global work index, constructive work, and work efficiency when compared to those of healthy controls.[21,22] Furthermore, values of LV wasted work were observed to be higher in those with HFrEF. These differences appeared to be secondary to a combination of increased wasted work due to LV dyssynchrony and a reduction in LV global longitudinal strain.[22] However, non-invasive measurements of RVMW indices have not been published before. The present study shows for the first time the feasibility of the measurement of RVMW indices and compares them between HFrEF patients and individuals without structural heart disease. In patients with HFrEF, a reduction in RVGWI, RVGCW, and RVGWE was observed when compared to a healthy population. Similar to the LV, the lower values of RVGCW, RVGWI, and RVGWE observed in those with HFrEF can be explained by the presence of RV dyssynchrony and increased wasted work. In contrast to the left ventricle, the higher levels of wasted work observed for the right ventricle were likely due to a combination of post-systolic shortening secondary to pulmonary hypertension and septal dyssynchrony due to ventricular interdependence.

Superiority of RVMW over standard parameters of RV systolic function

Theoretically, the calculation of the indices of RVMW through the estimation of non-invasive pressure–strain loops provides a more comprehensive estimation of RV function when compared to standard echocardiographic measures. In contrast with RV longitudinal strain, TAPSE and RV FAC, the parameters of RVMW integrate contractility, RV dyssynchrony and pulmonary pressures into their quantitation. In addition to providing a more comprehensive assessment of RV function, RVMW is not subject to the technical limitations of other standard parameters of RV systolic function. TAPSE is angle-dependent, load-dependent, and varies according to the degree of cardiac translation,[6,14] while RV FAC is limited by increased load-dependency and only fair interobserver reproducibility.[14]

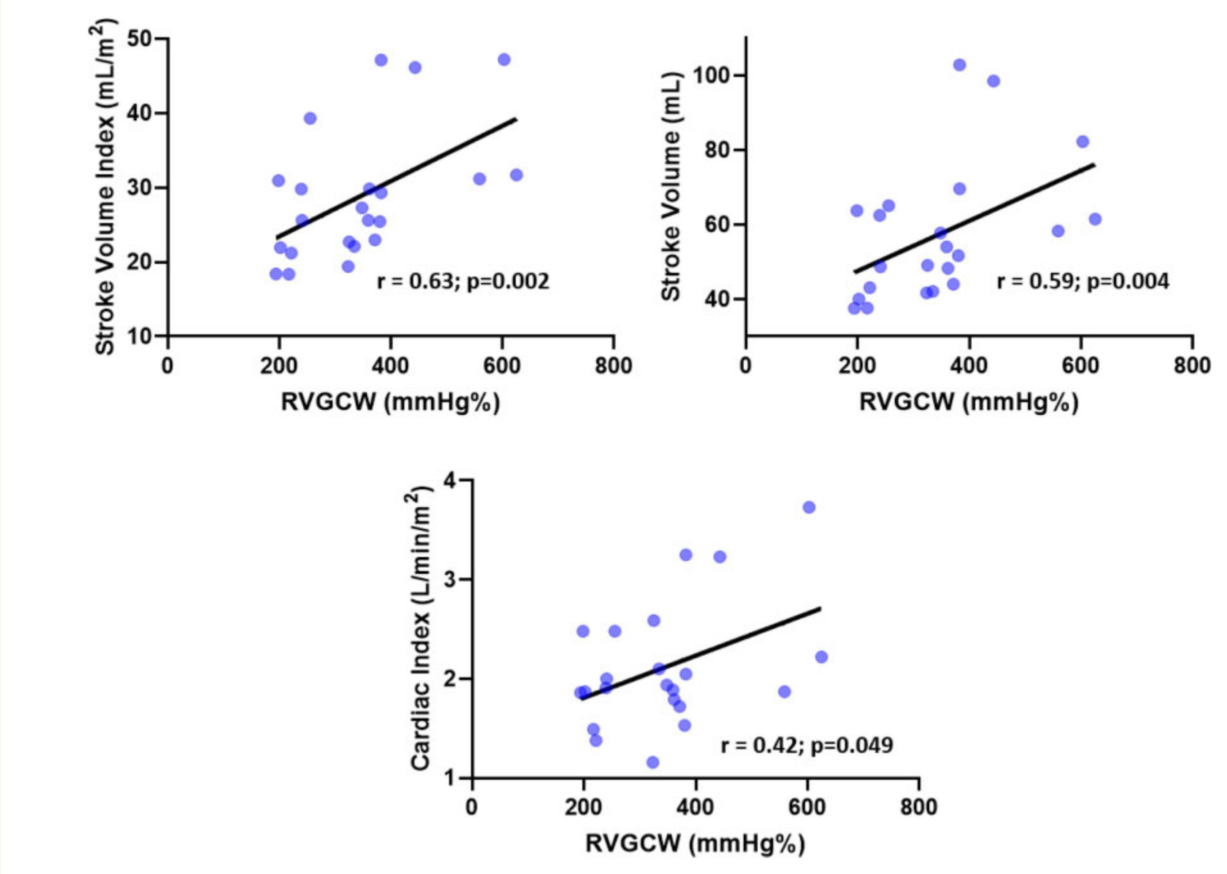

Figure 3 Correlation of RVGCW with invasive parameters of RV systolic function. Significant correlations between RVGCW and invasively derived stroke volume index, stroke volume, and cardiac index are evident. RV, right ventricular; RVGCW, right ventricular global constructive work.

Table 3 HFrEF patient right heart catheterization characteristics

Variables	*n* = 22
Right atrial pressure (mmHg)	10 (4–17)
sPAP (mmHg)	48.0 ± 19.1
dPAP (mmHg)	26 (12.5–35.5)
mPAP (mmHg)	34.7 (18.7–47.0)
Stroke volume (mL)	52.9 (42.8–64.1)
Stroke volume index (mL/m²)	26.4 (22.1–31.3)
Cardiac index (L/min/m²)	2.1 ± 0.63
RV stroke work (mmHg × mL)	25.8 (14.8–37.3)
PCWP (mmHg)	20.5 (12.0–34.0)

Data are presented as mean ± SD if normally distributed or median (25th–75th percentile) if not normally distributed.

dPAP, diastolic pulmonary artery pressure; HFrEF, heart failure with reduced ejection fraction; mPAP, mean pulmonary artery pressure; PCWP, pulmonary capillary wedge pressure; RV, right ventricular; sPAP, systolic pulmonary artery pressure.

Both experimental and clinical studies have demonstrated that RV longitudinal strain measured by speckle tracking echocardiography is afterload dependent, although less than other standard measures of RV systolic function.[23,24] Therefore, by accounting for afterload, RVMW provides an insight into RV-pulmonary arterial coupling, potentially delivering a more precise estimate of RV systolic function. For example, *Figure 4B* demonstrates the parameters of RVMW for a patient with HFrEF and an RV global longitudinal strain of -13.2%, while *Figure 4C* displays the same measurements for an individual with HFrEF and an RV global longitudinal strain of -5.8%. If examining only the difference in RV global longitudinal strain, one would conclude that the patient in *Figure 4B* has better RV systolic function. However, in this case, much of the difference is secondary to differences in afterload, with invasively measured stroke volume index demonstrating comparable RV systolic function, despite the significant discrepancy in RV global longitudinal strain. Likewise, as RVMW accounts also for pulmonic pressures, estimates of RVGCW were comparable between patients despite the disparity in RV global longitudinal strain. In another example, a comparison can be made between the patients in *Figure 4A and B*: both had similar RV global longitudinal strain, yet the patient in *Figure 4A* was generating an equivalent value of RV global longitudinal strain despite a significantly higher afterload. The increased pulmonic pressures were accounted for in RVMW analysis, reflected by the higher values of RVGCW and RVGWI for the individual in *Figure 4A*. As expected, this patient also had a higher stroke volume index when compared to the patient in *Figure 4B*.

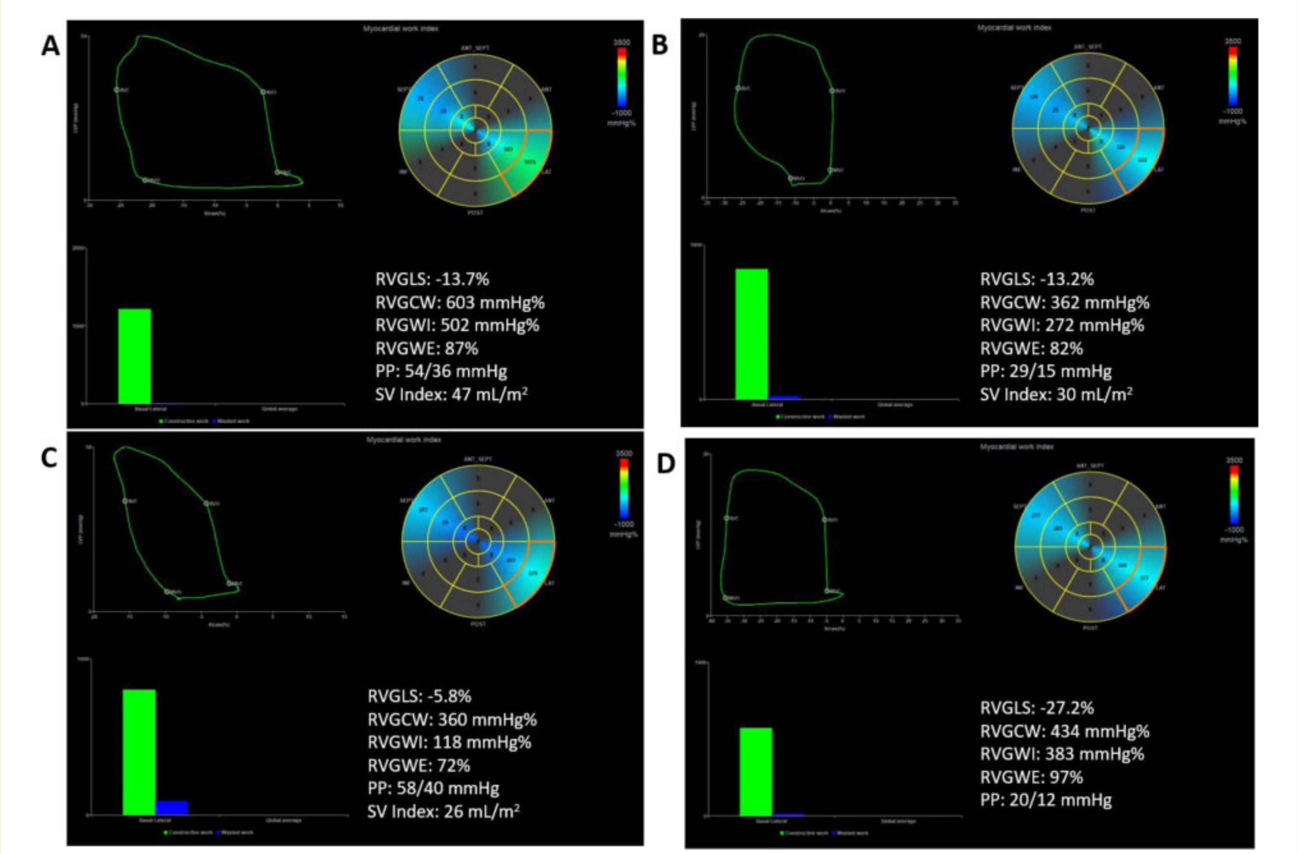

Figure 4 Comparison of RVMW parameters and cardiac index in three patients with HFrEF (*A*–*C*) and in one individual without cardiovascular disease (*D*), demonstrating the important impact of afterload on parameters of RVMW. PP, pulmonary pressures; RVGCW, right ventricular global constructive work; RVGLS, right ventricle global longitudinal strain; RVGWE, right ventricular global work efficiency; RVGWI, right ventricular global work index; RVGWW, right ventricular global wasted work.

Table 4 Intraclass correlation coefficients for intraobserver and interobserver variability for RVMW parameters

Variables	Interobserver variability ($n = 10$)		Intraobserver variability ($n = 10$)	
	Intraclass correlation coefficient	95% confidence interval	Intraclass correlation coefficient	95% confidence interval
RVGWI (mmHg%)	0.802	0.394–0.946	0.959	0.845–0.990
RVGCW (mmHg%)	0.858	0.523–0.963	0.915	0.703–0.978
RVGWW (mmHg%)	0.938	0.729–0.985	0.868	0.580–0.965
RVGWE (%)	0.826	0.380–0.956	0.967	0.880–0.992

RVGCW, right ventricular global constructive work; RVGWW, right ventricular global wasted work; RVGWE, right ventricular global work efficiency; RVGWI, right ventricular global work index; RVMW, right ventricular myocardial work.

RVMW also integrates RV dyssynchrony and post-systolic shortening into its non-invasive estimate of RV function, through the synchronization of pulmonic and tricuspid valvular events with RV longitudinal strain. Any myocardial lengthening occurring during systole and shortening during isovolumic relaxation are recorded as RV wasted work and do not contribute to RV constructive work. Therefore, any inefficient post-systolic shortening does not contribute to estimates of RVGCW, explaining at least in part, the stronger association of RVGCW with stroke volume and stroke volume index compared to conventional parameters of RV systolic function. The impact of RV dyssynchrony on RV function has been demonstrated in a study of 60 consecutive patients with idiopathic pulmonary arterial hypertension, where a significant negative correlation between post-systolic shortening time and invasively measured

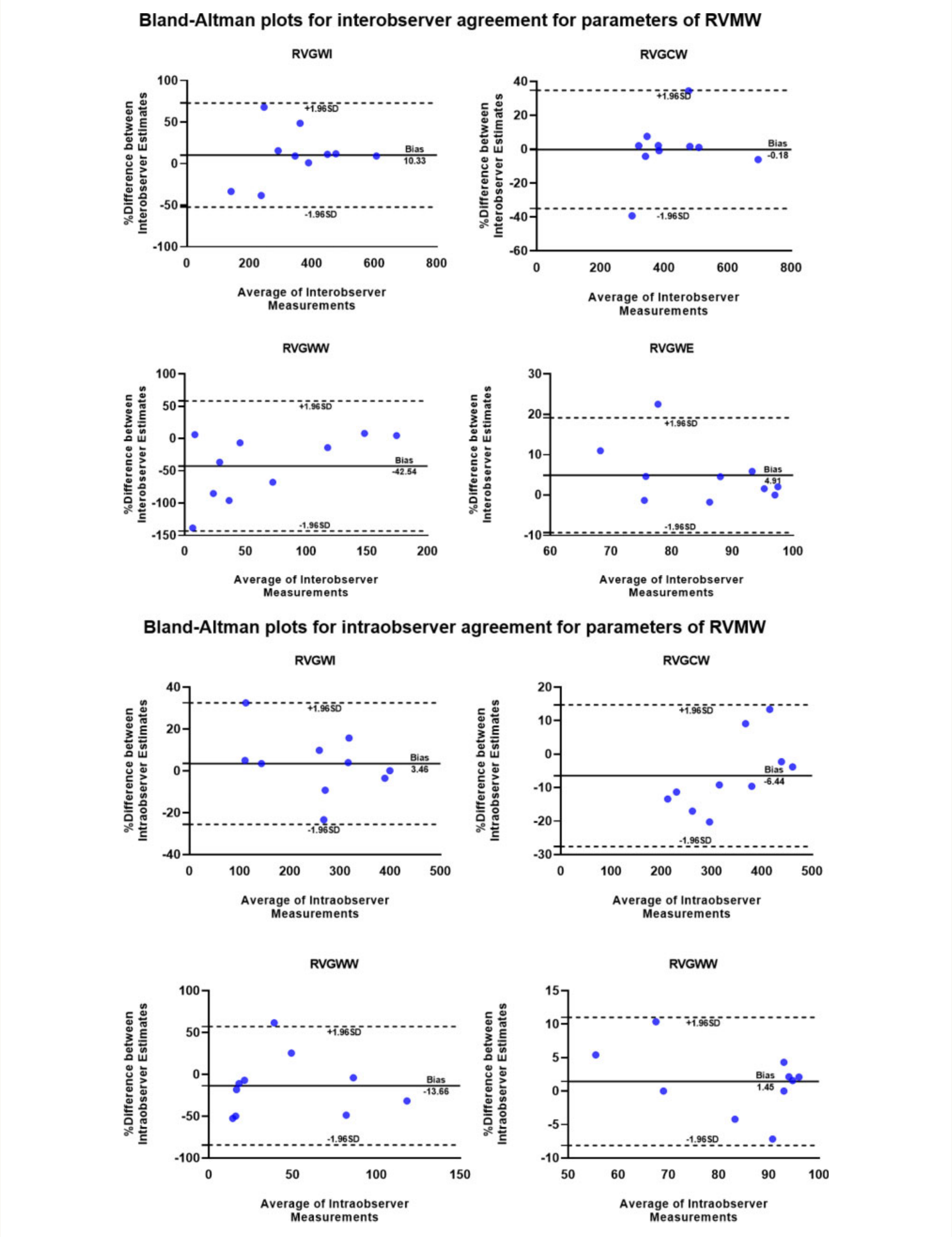

Figure 5 Bland–Altman Plots for interobserver and intraobserver agreement for parameters of right ventricular myocardial work. RVGCW, right ventricular global constructive work; RVGWE, right ventricular global work efficiency; RVGWI, right ventricular global work index; RVGWW, right ventricular global wasted work.

cardiac index was observed.[10] Similarly, in a cohort of patients with pulmonary arterial hypertension, Marcus *et al.*[25] observed that a dyssynchronous left-to-right delay of RV myocardial shortening was correlated with a reduced RV stroke volume, an association best explained by the phenomenon of ventricular interdependence. Conventional echocardiographic and speckle tracking echocardiography-derived parameters do not account for the impact of left-to-right delay and ventricular interdependence on RV stroke volume, possibly explaining the absence of any correlation between these indices and invasively measured stroke volume and stroke volume index. On the other hand, RVMW indices integrate all of these elements of RV dyssynchrony, providing an estimate of the myocardial constructive work that effectively contributes to RV stroke volume.

Clinical implications

In this study, we have demonstrated that parameters of RVMW could provide a non-invasive estimate of stroke volume and stroke volume index in individuals with HFrEF. For serial examinations evaluating treatment response, utilizing speckle tracking echocardiography-derived RV pressure–strain loops could provide a safer alternative than repeating invasive RHC to determine stroke volume or stroke volume index, a procedure with a rate of serious complications of 1.1%.[26] Furthermore, RVMW could be used as a tool to define the prognosis and better characterize a range of RV pathologies by providing a radiation-free, non-invasive estimate of regional RV myocardial energetics and pressure–volume loops. Previously, Russell *et al.*[11] demonstrated that regional myocardial work distribution derived from the area of non-invasive LV pressure–strain loops strongly correlated with myocardial glucose metabolism by 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET). Several studies have demonstrated that the extent of RV glucose uptake on 18F-FDG PET in patients with pulmonary hypertension (including in those with group II pulmonary hypertension) is associated with pressure overload and RV dysfunction[27,28] and may be associated with poor prognosis.[29] This suggests that the non-invasive estimation of RVMW may provide an insight into altered RV energetics in patients with HFrEF, possibly enhancing risk stratification. While speckle tracking echocardiography-derived RV longitudinal strain provides important prognostic information for patients with HFrEF,[5] RVMW could potentially offer incremental predictive benefit through the integration of afterload, quantification of RV dyssynchrony, and estimation of RV myocardial energetics.

Limitations

This study is limited by its single-centre, retrospective design. Furthermore, only a small number of patients were evaluated. Therefore, larger studies will be required to define the normal values of RVMW and to confirm its clinical utility for patients with HFrEF. The generalizability of these results to other RV pathological entities also requires further investigation. In addition, the new echocardiographic measurements were not tested against cardiovascular magnetic resonance or radionuclide ventriculography (considered reference standard for the measurement of RV systolic function). Another important limitation is that the commercial software required for the measurement of RVMW is only provided by a single-vendor and was specifically designed for the assessment of myocardial work of the left ventricle. The derivation of LV pressure–strain loops is based on Laplace's law, which makes simple geometric assumptions, therefore, the irregular and complex geometry of the right ventricle could result in calculated values of myocardial work that are less precise than for those of the left ventricle.[30] In the future, validation of non-invasive RV pressure–strain loops with invasively derived RV pressure–volume loops may be required, as these are different from those of the left ventricle.[30] Finally, the limited number of patients precluded us from investigating the association between RVMW parameters and survival (due to the high probability of type II errors).

Conclusion

RVGCW, a novel parameter of RVMW, was the only non-invasively derived echocardiographic index that correlated with invasively derived stroke volume and stroke volume index in patients with HFrEF. A potential role in aiding clinical decision-making merits further investigation.

Supplementary data

Supplementary data are available at *European Heart Journal - Cardiovascular Imaging* online.

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