The noninvasive echocardiographic assessment of right ventricular myocardial work in a healthy population

Jian Wu
Department of Echocardiography, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China
Xinyi Huang
Department of Echocardiography, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China
Kunhui Huang
Department of Echocardiography, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China
Qiumei Gao
Department of Echocardiography, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China
Yuan Tian
Department of Echocardiography, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China
Biqin Lin
Department of Ultrasonography, Xiamen Humanity Hospital, Fujian Medical University, Xiamen, China
Yiruo Tang
Department of Echocardiography, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China
Xu Chen
Department of Echocardiography, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China
Maolong Su (sumaolong@xmu.edu.cn)
Department of Echocardiography, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, Xiamen, China

---

Research Article

Keywords: echocardiography, right ventricular function, myocardial work, Normal population

Posted Date: May 13th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-1633505/v1

Abstract

Background: Right ventricular (RV) myocardial work (RVMW) is the latest indicator to assess RV function. Nevertheless, the physiological determinants of RVMW have not been studied and reference ranges for normal RVMW indices remain to be established.

Methods: A total of 263 healthy volunteers (median age 34 years, 38% men) were prospectively enrolled. RVMW indices were analysed by RV pressure-strain loop (RVPSL) in a specific software.

Results: The lowest values for RV global work index (RVGWI) were 133 mmHg% and 206 mmHg%, RV global constructive work (RVGCW) were 165 mmHg% and 241 mmHg%, and RV global work efficiency (RVGWE) were 78% and 83% in men and women, respectively. The highest values for RV global wasted work (RVGWW) in men and women were 67 mmHg% and 79 mmHg%, respectively. RVGWI and RVGCW were significantly lower in men than in women. RVGWW significantly increased according to age in men and women. RVGWE significantly decreased with age in women. Multivariable analysis revealed RVGWI, RVGCW and RVGWE increased along with increasing pulmonary artery systolic pressure (PASP).

Conclusions: Normal reference values of RVMW were obtained by echocardiography. Quantitative data on RVMW could be essential in clinical work and clinical experiments.

1. Background

The importance of the right ventricle was neglected compared to the left ventricle in clinical work and research on cardiovascular disease for decades. However, with increasing evidence that right ventricular dysfunction is closely related to the treatment and prognosis of the disease, the right ventricle has received increasing attention from clinical and scientific researchers.[1] The most frequently used methods to analyse right ventricular (RV) function are measuring the tricuspid annular plane systolic excursion (TAPSE), RV fractional area change (RV FAC), and myocardial tissue Doppler velocities (S').[2, 3] [4]However, TAPSE, RV FAC, and S' do not consider RV afterload. Due to afterload has a great effect on the thin-walled right ventricle, ignoring the influence of afterload will make the parameters above unable to evaluate the RV function accurately.[5] Recently, RV longitudinal strain, as a superior method to evaluate RV function, is still an afterload dependent parameter.[6, 7]

RV myocardial work (RVMW) is a novel indicator to quantitatively analyse RV function.[8] RVMW indices are acquired by integrating the RV global longitudinal strain (RV GLS), pulmonary artery pressures, and tricuspid and pulmonic valvular events by a specific software. Thus, RVMW could theoretically evaluate RV function more precisely than conventional two-dimensional parameters. This study aimed 1) to obtain normal reference values for the RVMW in a large cohort healthy population; 2) to evaluate the effects of age and gender on RVMW parameters; and 3) to explore the relationships between RVMW indices and other baseline parameters.

2. Methods

2.1. Study population

A group of 372 healthy Asian volunteers was prospectively recruited from April 2021 to July 2021. The inclusion criteria were as follows: age ≥ 18 years, normal results on physical examination, normal electrocardiogram, normal results on two-dimensional echocardiography (2DE), and no history of cardiovascular or respiratory diseases. The Institutional Ethics Committee approved the protocol, and all subjects provided informed consent before undergoing examinations.

2.2. Echocardiographic Acquisition

Transthoracic echocardiography was acquired using a Vivid E95 scanner (GE Vingmed Ultrasound, Norway) following recommended protocols.[9, 10] 2DE images were acquired by M5Sc probe and four-dimensional echocardiography 4DE) RV images were acquired by 4Vc probe. Acquisitions of the tricuspid regurgitation (TR) jets by colour Doppler were obtained from the apical four-chamber views. All electrocardiogram-triggered echocardiography images were obtained over 3 to 5 consecutive cardiac cycles during breath-hold. Datasets were stored digitally and analysed offline.

2.3. Echocardiographic Measurements

Echocardiographic images were analysed using EchoPAC v204 (GE Vingmed Ultrasound). RV end-diastolic and end-systolic volume, and RV ejection fraction were obtained by the software package (4D Auto RVQ). RVMW indices were analysed with a software package (AFI) designed for the quantitative analysis of the left ventricular (LV) myocardial work (LVMW) by speckle tracking echocardiography. The prognostic validation of LVMW was performed in several studies.[11–13]

PASP was computed as: PASP = $4vTR^2$ + mean right atrial (RA) pressure.[14] Mean RA pressure was estimated based on the diameter and collapsibility of the inferior vena cava.[3] The mean RV-RA gradient was estimated by tracing TR velocity-time integral (Fig. 1A).[15] Pulmonary artery mean pressure (PAMP) equals mean RV-RA gradient plus mean RA pressure. According to the theoretical formula, pulmonary artery diastolic pressure (PADP) was calculated as: PADP = 1.5 [PAMP - (PASP/3)].[3]

In the RV-focused apical four-chamber view, RV GLS was evaluated by tracing the interventricular septum and RV free wall.[10] The event timings of the tricuspid and pulmonic valve were derived from direct visualization in the parasternal short-axis views. Measurements of RV GLS, PASP, and PADP were then synchronized by tricuspid and pulmonic valve event timings to noninvasively produce RV pressure–strain loop (RVPSL) (Fig. 1B, 1C, and 1D).

RVMW indices acquired by RVPSL included the following four parameters:

1) RV global work index (RVGWI): the area of RVPSL, which presents the total RVMW during tricuspid valve closure and tricuspid valve opening.

2) RV global constructive work (RVGWE): constructive work during shortening in systole and lengthening during isovolumic relaxation (IVR).

3) RV global wasted work (RVGWW): wasted work during lengthening in systole and shortening during IVR.

4) RV global work efficiency (RVGWE): RVGCW / (RVGCW + RVGWW).

All the standard measurements were made according to the widely accepted guidelines.[4]

2.4. Statistical analysis

The normality of variables was assessed with the Kolmogorov–Smirnov test. Normally distributed continuous variables are expressed as mean ± SD, and those that were not normally distributed were expressed as median (first quartile, third quartile). The highest (97.5th percentile) and lowest (2.5th percentile) expected values for RVMW indices were calculated from a bootstrap of 1000 samples.

Normally distributed data were compared using two-tailed independent Student's *t tests* or one-way ANOVA. Nonnormally distributed data were compared using the Mann–Whitney U test or Kruskal–Wallis test. The Spearman correlation coefficient was used to assess correlations between variables. Univariable and multivariable linear regression analyses were performed to test the correlations between RVMW indices and baseline parameters.

The intra- and interobserver variability of the RVMW indices were estimated in 20 random subjects by Bland–Altman analysis. One observer analysed the same echocardiographic images at two different times and two independent blinded observers analysed the same echocardiographic images.

All data were analysed using SPSS 26.0 (SPSS Inc., IBM Corp). When $P < 0.05$, the difference between variables was considered significant.

3. Results

3.1. clinical characteristics

Seventeen subjects were excluded from enrolment due to poor 2DE or RV 4DE images. Ninety-two subjects were excluded due to the TR Doppler envelope could not being obtained or TR Doppler envelopes being of poor tracking quality. Thus, in our study population, the feasibility of RVMW assessment was 70.7%. The clinical and echocardiographic characteristics of the enrolled subjects are displayed in Table 1.

3.2. RVMW parameters

Table 2 summarizes the RVMW parameters from the population. The lowest expected value for RVGWI was 133 mmHg% in men and 206 mmHg% in women, 165 mmHg% and 241 mmHg% for RVGCW, and 78% and 83% for RVGWE, respectively. The highest expected values of RVMW indices were 67 mmHg% in men and 79 mmHg% in women for RVGWW. RVGWI and RVGCW were significantly lower in men than in women, while the RVGWW and RVGWE showed no significant differences between genders.

3.3. Age and sex differences in RVMW parameters

Table 3 and Figure 2 shows the age and sex differences in RVMW indices. RVGWW increased with age in men and women (R^2 = 0.04, P = 0.034 and R^2 = 0.11, P < 0.0001, respectively). RVGWE decreased with age in women (R^2 = 0.04, P = 0.003) along with increasing PASP (R^2 = 0.16, P = 0.001). RVGWI and RVGCW were higher in women than those in men in the <30 years, 30-40 years, and 40-50 years subgroups (all P < 0.01). RVGCW were higher in men in the ≥50 years subgroup than those in the <30 years, 30-40 years, and 40-50 years subgroups (P = 0.005, P = 0.028 and P = 0.017, respectively). RVGCW were lower in women in the <30 years group than those in the 40-50 years, and ≥50 years subgroups (P < 0.0001 and P = 0.021, respectively).

3.4. RVMW indices and other baseline parameters relationship

Univariable analysis and multivariable analysis for RVMW indices are shown in Table 4. As excepted, RVGWE significantly decreased according to age on univariable analysis, and the opposite occurred for the other RVMW indices. Multivariable analysis showed: 1) RVGWI and RVGCW were lower in men than in women (P < 0.0001 and P < 0.0001, respectively); 2) RVGWI, RVGCW and RVGWE increased with PASP (P < 0.0001, P < 0.0001, and P = 0.027, respectively); 3) RVGWW increased with age, body mass index (BMI), and PASP (P = 0.001, P = 0.014, and P = 0.019, respectively).

3.5. Interobserver and intraobserver variability

The intra- and interobserver variability of the RVMW indices are summarized in Table 5, Figure 3, and Figure 4, which indicated high intra- and interobserver reproducibility.

4. Discussion

To our knowledge, this is the first to use echocardiography to quantitatively analyse RVMW in a large cohort of healthy population. RVMW, derived from RVPSL, was first introduced as the latest method to assess RV function by Butcher et al.[8]. In their study, RVMW indices had significant differences between patients with reduced LV ejection fraction and the healthy control group. Meanwhile, all RVMW indices were demonstrated significantly correlated with RV GLS. Moreover, RVGCW revealed a moderate correlation with invasive RV stroke volume. Recently, Russell et al.[11] revealed myocardial glucose metabolism, which was computed by 18F-fluorodeoxyglucose (FDG) positron emission tomography (PET), strongly correlated with noninvasive LVMW. Bokhari et al.[16] have demonstrated that RV myocardial glucose metabolism is associated with pulmonary pressure by 18F- FDG PET. Those discoveries reveal that afterload-enrolled noninvasive RVMW could be more reliable than conventional methods in evaluating RV function.

Our study establishes normal reference values for RVMW indices in healthy Asian adults, and examines the influence of baseline parameters on the reference ranges. Our data suggest that the RVMW index is independent of sex. In our study, RVGWI and RVGCW were lower in men than in women, while no differences were found in RVGWW and RVGWE between genders. Moreover, multivariable analysis for RVGWI and RVGCW were lower in men than in women and the opposite occurred for RVGWW. Specifically, when considering both age and gender, RVGWI and RVGCW were all higher in women than in men in <50 years subgroups. These findings may be due to the RV myocardial systolic function is greater in women than in men.[17] Studies have pointed out that estrogen in women has beneficial effects on the heart, such as regulating inflammation, myocardial hypertrophy, myocardial fibrosis, cardiovascular function and so on.[18, 19] After menopause, estrogen in women is significantly reduced, and the protective effect on the heart is weakened.

There are some differences in RVMW indices according to age. Univariable analysis showed that RVGWI, RVGCW, and RVGWW significantly increased and RVGWE significantly decreased according to age. When gender is considered, only RVGWW increased with age in men and women. Multivariable analysis revealed that only RVGWW significantly increased according to age. RVGWE decreased with age in women along with increasing PASP. RVGCW were higher in men in the ≥50 years subgroup than those in the other age subgroups. RVGCW were lower in women in the <30 years group than those in the 40-50 years, and ≥50 years subgroups. In total, the results above may reflect the physiological processes of aging, such as progressive myocardial fibrosis and cardiomyocyte regulation.[20]

Finally, multivariable analysis showed all RVMW indices did not correlate with BMI, body surface area (BSA), or heart rate, except for RVGWW significantly increased according to BMI. Multivariable analysis revealed RVGWI, RVGCW and RVGWE increased along with increasing PASP, and RVGWW increased according to PADP. This result may be explained that increasing pulmonary artery pressure presents increasing RV afterload, and may boost RVMW to higher levels of energy. Thus, in pulmonary hypertension (PH), RVMW may be at higher energy consumption levels to compensate for increased afterload, which is reflected in higher RVMW indices. Therefore, RVMW could play a vital role in assessing the effectiveness of treatment of patients with PH.

To date, LVMW has been studied in the areas of hypertension, heart failure, cardiac resynchronization therapy, cardiac amyloidosis, nonobstructive hypertrophic Cardiomyopathy, dilated cardiomyopathy, diabetes mellitus, and so on.[21] [22-25] In contrast to LVMW, RVMW is rarely used in clinical and scientific research. As previous studies demonstrated, as the most used measurements of RV function, TAPSE, RV FAC, and S' are load-dependent.[4, 7] Although, some studies verified RV GLS is less load-dependent.[7, 26, 27] Due to the RV thin walls and low RV elastance, afterload impact of RV GLS still cannot be ignored.[6] Therefore, RVMW, integrating RV GLS, pulmonary pressures, and tricuspid and pulmonic valvular events, could provide a more comprehensive and precise estimation of RV function. In the future, RVMW can also be applied to assessing RV function in a variety of diseases.

Clinical implications

As a noninvasive and convenient technique, RVMW derived by echocardiography enable it to provide a scientific theoretical basis and practical significance for assessing RV function. Notably, the data showed excellent agreement and repeatability in assessing RVMW indices, which raises the possibility that these new advanced echocardiographic parameters could be used in clinical practice such as PH, heart failure, RV dyssynchrony, and so on.

Study limitations

Acquiring and quantifying RVMW datasets using a single provider platform may affect the applicability of these reference values to data obtained from other provider platforms. In addition, commercial software required to measure RVMW is specifically designed to measure LVMW. Therefore, the calculation of RVMW is not as accurate as LVMW due to the complex and irregular shape of the right ventricle.[28, 29] Non-invasive RVPSL may need to be validated with invasively derived RVPSL in the future. Meanwhile, for ethical reasons, cardiac magnetic resonance or right heart catheterization was not used to verify the validity of RVMW. Also, as the TR Doppler envelope may not be acquired or the imaging of the TR Doppler envelope is obscure in some normal population, we might have had selection bias. Furthermore, although all subjects were asymptomatic on regular exams, we cannot rule out the possibility of subclinical cardiovascular or respiratory disease, particularly in the elderly. Finally, it remains unknown whether our results can be generalized to non-Asia subjects.

5. Conclusions

This is the first comprehensive study using echocardiography to obtain reference values for the RVMW in a large cohort of normal population. Age, gender, and pulmonary artery pressure should be considered to identify RVMW indices. The availability of RVMW reference values could strengthen the value of echocardiography in evaluating RV function.

Abbreviations

RV: right ventricular; RVMW: RV myocardial work; RVGWI: RV global work index; RVGCW: RV global constructive work; RVGWE: RV global work efficiency; RVGWW: RV global work waste; PASP: pulmonary artery systolic pressure; TAPSE: tricuspid annular plane systolic excursion; RV FAC: RV fractional area change; S’: myocardial tissue Doppler velocities; RV GLS: RV global longitudinal strain; 2DE: two-dimensional echocardiography; TR: tricuspid regurgitation; LV: left ventricular; LVMW: LV myocardial work; RA: right atrial; PAMP: pulmonary artery mean pressure; PADP: pulmonary artery diastolic pressure; RVPSL: RV pressure–strain loop; IVR: isovolumic relaxation; BMI: body mass index; FDG: fluorodeoxyglucose; PET: positron emission tomography; BSA: body surface area; PH: pulmonary hypertension

Declarations

Ethics approval and consent to participate

The protocol was approved by the Institutional Ethics Committee of Xiamen Cardiovascular Hospital of Xiamen University, and all subjects provided written informed consent before undergoing examinations.

Consent for publication

Consent for publication was obtained from all the participates.

Availability of data and material

The data and material underlying this article will be shared on reasonable request to the corresponding authors.

Competing interests

The authors declare that they have no competing interests.

Funding

This study was supported by the Xiamen's Key Project of Medical and HealthSciences (No. 3502Z20209147) and the Science and Technology Planning Project of Xiamen (No. 3502Z20214ZD2183 and grant No. 3502Z20214ZD1166).

Authors' contributions:

Maolong Su and Xu Chen conceived the study design, provided project oversight, and performed the final approval of the version to be submitted. Jian Wu and Xinyi Huang took ultrasound images, interpreted the data, and wrote the manuscript. Kunhui Huang, Qiumei Gao, and Biqin Lin took ultrasound images and revised the article carefully. Yuan Tian provided the method for the study and substantively revised the article. Yiruo Tang revised the article for significant intellectual content. All authors read and approved the final manuscript.

Acknowledgements

Not applicable.

References

1. Konstam MA, Kiernan MS, Bernstein D, Bozkurt B, Jacob M, Kapur NK, et al. **Evaluation and Management of Right-Sided Heart Failure: A Scientific Statement From the American Heart Association**. Circulation 2018, **137**(20):e578-e622.
2. Aloia E, Cameli M, D'Ascenzi F, Sciaccaluga C, Mondillo S. **TAPSE: An old but useful tool in different diseases**. Int J Cardiol 2016, **225**:177–183.
3. Rudski LG, Lai WW, Afilalo J, Hua L, Handschumacher MD, Chandrasekaran K, et al. **Guidelines for the echocardiographic assessment of the right heart in adults: a report from the American Society of Echocardiography endorsed by the European Association of Echocardiography, a registered branch**

of the European Society of Cardiology, and the Canadian Society of Echocardiography**. J Am Soc Echocardiogr 2010, **23**(7):685–713; quiz 786 – 688.

4. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, et al. **Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging**. J Am Soc Echocardiogr 2015, **28**(1):1–39 e14.
5. Crystal GJ, Pagel PS. **Right Ventricular Perfusion: Physiology and Clinical Implications**. Anesthesiology 2018, **128**(1):202–218.
6. Walker LA, Buttrick PM. **The right ventricle: biologic insights and response to disease: updated**. Curr Cardiol Rev 2013, **9**(1):73–81.
7. Tadic M, Pieske-Kraigher E, Cuspidi C, Morris DA, Burkhardt F, Baudisch A, et al. **Right ventricular strain in heart failure: Clinical perspective**. Arch Cardiovasc Dis 2017, **110**(10):562–571.
8. Butcher SC, Fortuni F, Montero-Cabezas JM, Abou R, El Mahdiui M, van der Bijl P, et al. **Right ventricular myocardial work: proof-of-concept for non-invasive assessment of right ventricular function**. Eur Heart J Cardiovasc Imaging 2021, **22**(2):142–152.
9. Cosyns B, Garbi M, Separovic J, Pasquet A, Lancellotti P. Education Committee of the European Association of Cardiovascular Imaging A: **Update of the echocardiography core syllabus of the European Association of Cardiovascular Imaging (EACVI)**. Eur Heart J Cardiovasc Imaging 2013, **14**(9):837–839.
10. Badano LP, Kolias TJ, Muraru D, Abraham TP, Aurigemma G, Edvardsen T, et al. **Standardization of left atrial, right ventricular, and right atrial deformation imaging using two-dimensional speckle tracking echocardiography: a consensus document of the EACVI/ASE/Industry Task Force to standardize deformation imaging**. Eur Heart J Cardiovasc Imaging 2018, **19**(6):591–600.
11. Russell K, Eriksen M, Aaberge L, Wilhelmsen N, Skulstad H, Remme EW, et al. **A novel clinical method for quantification of regional left ventricular pressure-strain loop area: a non-invasive index of myocardial work**. Eur Heart J 2012, **33**(6):724–733.
12. Edwards NFA, Scalia GM, Shiino K, Sabapathy S, Anderson B, Chamberlain R, et al. **Global Myocardial Work Is Superior to Global Longitudinal Strain to Predict Significant Coronary Artery Disease in Patients With Normal Left Ventricular Function and Wall Motion**. J Am Soc Echocardiogr 2019, **32**(8):947–957.
13. Hubert A, Le Rolle V, Leclercq C, Galli E, Samset E, Casset C, et al. **Estimation of myocardial work from pressure-strain loops analysis: an experimental evaluation**. Eur Heart J Cardiovasc Imaging 2018, **19**(12):1372–1379.
14. Vazquez de Prada JA, Ruano J, Martin-Duran R, Larman M, Zueco J, Ortiz de Murua JA, et al. **Noninvasive determination of pulmonary arterial systolic pressure by continuous wave Doppler**. Int J Cardiol 1987, **16**(2):177–184.
15. Aduen JF, Castello R, Lozano MM, Hepler GN, Keller CA, Alvarez F, et al. **An alternative echocardiographic method to estimate mean pulmonary artery pressure: diagnostic and clinical**

implications. J Am Soc Echocardiogr 2009, **22**(7):814–819.

16. Bokhari S, Raina A, Rosenweig EB, Schulze PC, Bokhari J, Einstein AJ, et al. **PET imaging may provide a novel biomarker and understanding of right ventricular dysfunction in patients with idiopathic pulmonary arterial hypertension**. Circ Cardiovasc Imaging 2011, **4**(6):641–647.
17. Petersen SE, Aung N, Sanghvi MM, Zemrak F, Fung K, Paiva JM, et al. **Reference ranges for cardiac structure and function using cardiovascular magnetic resonance (CMR) in Caucasians from the UK Biobank population cohort**. J Cardiovasc Magn Reson 2017, **19**(1):18.
18. Deroo BJ, Korach KS. **Estrogen receptors and human disease**. J Clin Invest 2006, **116**(3):561–570.
19. Voloshenyuk TG, Gardner JD. **Estrogen improves TIMP-MMP balance and collagen distribution in volume-overloaded hearts of ovariectomized females**. Am J Physiol Regul Integr Comp Physiol 2010, **299**(2):R683-693.
20. Karamitsos TD, Arvanitaki A, Karvounis H, Neubauer S, Ferreira VM. **Myocardial Tissue Characterization and Fibrosis by Imaging**. JACC Cardiovasc Imaging 2020, **13**(5):1221–1234.
21. Chan J, Edwards NFA, Khandheria BK, Shiino K, Sabapathy S, Anderson B, et al. **A new approach to assess myocardial work by non-invasive left ventricular pressure-strain relations in hypertension and dilated cardiomyopathy**. Eur Heart J Cardiovasc Imaging 2019, **20**(1):31–39.
22. Wang CL, Chan YH, Wu VC, Lee HF, Hsiao FC, Chu PH. **Incremental prognostic value of global myocardial work over ejection fraction and global longitudinal strain in patients with heart failure and reduced ejection fraction**. Eur Heart J Cardiovasc Imaging 2021, **22**(3):348–356.
23. Vecera J, Penicka M, Eriksen M, Russell K, Bartunek J, Vanderheyden M, et al. **Wasted septal work in left ventricular dyssynchrony: a novel principle to predict response to cardiac resynchronization therapy**. Eur Heart J Cardiovasc Imaging 2016, **17**(6):624–632.
24. Clemmensen TS, Eiskjaer H, Ladefoged B, Mikkelsen F, Sorensen J, Granstam SO, et al. **Prognostic implications of left ventricular myocardial work indices in cardiac amyloidosis**. Eur Heart J Cardiovasc Imaging 2021, **22**(6):695–704.
25. Huang D, Cui C, Zheng Q, Li Y, Liu Y, Hu Y, et al. **Quantitative Analysis of Myocardial Work by Non-invasive Left Ventricular Pressure-Strain Loop in Patients With Type 2 Diabetes Mellitus**. Front Cardiovasc Med 2021, **8**:733339.
26. Wright L, Negishi K, Dwyer N, Wahi S, Marwick TH. **Afterload Dependence of Right Ventricular Myocardial Strain**. J Am Soc Echocardiogr 2017, **30**(7):676–684 e671.
27. Missant C, Rex S, Claus P, Mertens L, Wouters PF. **Load-sensitivity of regional tissue deformation in the right ventricle: isovolumic versus ejection-phase indices of contractility**. Heart 2008, **94**(4):e15.
28. Redington AN, Gray HH, Hodson ME, Rigby ML, Oldershaw PJ. **Characterisation of the normal right ventricular pressure-volume relation by biplane angiography and simultaneous micromanometer pressure measurements**. Br Heart J 1988, **59**(1):23–30.
29. Sheehan F, Redington A. **The right ventricle: anatomy, physiology and clinical imaging**. Heart 2008, **94**(11):1510–1515.

Tables

Table 3 is available in the Supplementary Files section

Table 1 Clinical and echocardiographic characteristics of the study population

Parameters	Total (n=263)	Men (n=100)	Women (n=163)	*p*-value*
Age (years)	34 (29, 45)	34 (29, 43)	35 (29, 45)	0.454
Height (cm)	163 (158, 170)	172 (169, 175)	159 (156, 163)	<0.0001
Weight (kg)	58 (52, 67)	68 (62, 75)	54 (50, 59)	<0.0001
BMI (kg/m²)	22.2 (20.1, 24.2)	23.0 (21.8, 25.1)	21.2 (19.2, 23.5)	<0.0001
BSA (m²)	1.6 (1.5, 1.8)	1.8 (1.7, 1.9)	1.5 (1.5, 1.6)	<0.0001
SBP (mmHg)	119 (108, 129)	126 (117, 131)	114 (104, 125)	<0.0001
DBP (mmHg)	72 ± 10	74 ± 10	70 ± 10	0.010
Heart rate (bpm)	66 (61, 74)	64 (58, 72)	68 (63, 75)	0.001
PASP (mmHg)	22 (19, 25)	21 (19, 25)	22 (20, 25)	0.115
PAMP (mmHg)	16 (14, 18)	16 (14, 18)	17 (15, 18)	0.008
PADP (mmHg)	14 (12, 15)	13 (11, 15)	14 (12, 15)	0.001
RV EDV (ml)	91 (83, 104)	108 (97, 121)	87 (78, 92)	<0.0001
RV ESV (ml)	38 (34, 45)	49 (42, 55)	35 (31, 38)	<0.0001
RV ejection fraction (%)	58 (56, 60)	55 (54, 56)	60 (58, 61)	<0.0001
TAPSE (mm)	21 (19, 24)	22 (19, 24)	20 (18, 23)	0.127
RV FAC (%)	47 ± 6	44 ± 4	49 ±5	<0.0001

BMI, body mass index; BSA, body surface area; DBP, diastolic blood pressure; EDV, end-diastolic volume; ESV, end-systolic volume; FAC, fractional area change; RV, right ventricular; PADP, pulmonary artery diastolic pressure; PAMP, pulmonary artery mean pressure; PASP, systolic pulmonary artery pressure; SBP, systolic blood pressure; TAPSE, tricuspid annular plane systolic excursion. **P*-value refers to gender differences.

Table 2 Parameters of right ventricular myocardial work

	Total, mean ± SD or median (IQR)	Total, 95% limits of normality ± SE[a,b]	Men, mean ± SD or median (IQR)	Men, 95% limits of normality ± SE[a,b]	Women, mean ± SD or median (IQR)	Women, 95% limits of normality ± SE[a,b]	*p*-value*
RVGWI (mmHg%)	306 (249, 351)	186 ± 5.0[b]	270 (219, 326)	133 ± 15.4[b]	323 (275, 375)	206 ± 8.1[b]	< 0.0001
RVGCW (mmHg%)	354 (297, 408)	225 ± 5.9[b]	319 (269, 375)	165 ± 18.2[b]	372 (321, 433)	241 ± 12.6[b]	< 0.0001
RVGWW (mmHg%)	21 (11, 33)	66 ± 3.3[a]	22 (14, 32)	67 ± 6.6[a]	20 (11, 35)	79 ± 5.6[a]	0.607
RVGWE (%)	93 (90, 96)	83 ± 0.5[b]	92 (89, 95)	78 ± 1.8[b]	94 (90, 96)	83 ± 0.7[b]	0.057

IQR, interquartile range; RV, right ventricular; RVGCW, RV global constructive work; RVGWE, RV global work efficiency; RVGWI, RV global work index; RVGWW, RV global work waste; SD, standard deviation; SE, standard error.

[a]Highest expected value.

[b]Lowest expected value.

**P*-value refers to gender differences.

Table 4 Univariable and multivariable analysis for 2DE MW parameters

	Univariable analysis		Multivariable analysis	
	Coefficient	*p*-value	Standardized β-coefficient	*p*-value
RVGWI (mmHg%)				
Age (years)	0.125	0.043		
Men (=1)	-0.331	<0.0001	-0.242	<0.0001
BMI (kg/m²)	-0.153	0.013		
BSA (m²)	-0.300	<0.0001		
Heart rate (bpm)	0.099	0.109		
PASP (mmHg)	0.716	<0.0001	0.752	<0.0001
PADP (mmHg)	0.478	<0.0001		
RVGCW (mmHg%)				
Age (years)	0.187	0.002		
Men (=1)	-0.331	<0.0001	-0.197	<0.0001
BMI (kg/m²)	-0.122	0.048		
BSA (m²)	-0.308	<0.0001		
Heart rate (bpm)	0.081	0.188		
PASP (mmHg)	0.771	<0.0001	0.735	<0.0001
PADP (mmHg)	0.560	<0.0001		
RVGWW (mmHg%)				
Age (years)	0.305	<0.0001	0.215	0.001
Men (=1)	0.035	0.575		
BMI (kg/m²)	0.207	0.001	0.212	0.014
BSA (m²)	0.030	0.633		
Heart rate (bpm)	-0.080	0.193		
PASP (mmHg)	0.219	<0.0001		
PADP (mmHg)	0.234	<0.0001	0.184	0.019
RVGWE (%)				
Age (years)	-0.126	0.041		

Men (=1)	-0.111	0.074		
BMI (kg/m²)	-0.222	<0.0001		
BSA (m²)	-0.183	0.003		
Heart rate (bpm)	0.127	0.039		
PASP (mmHg)	0.089	0.150	0.184	0.027
PADP (mmHg)	0.021	0.737		

BMI, body mass index; BSA, body surface area; PADP, pulmonary artery diastolic pressure; PASP, pulmonary systolic artery pressure; RV, right ventricular; RVGCW, RV global constructive work; RVGWE, RV global work efficiency; RVGWI, RV global work index; RVGWW, RV global wasted work.

Table 5 Intra- and inter-observer variability of RV myocardial work indices

	Intra-observer variability			inter-observer variability		
	Bias	95% CI	ICC	Bias	95% CI	ICC
RVGWI (mmHg%)	1.3	-40.9; 43.4	0.96	-7.7	-41.7; 26.4	0.96
RVGCW (mmHg%)	-4.9	-48.5; 38.8	0.97	-2.6	-44.1; 38.9	0.94
RVGWW (mmHg%)	-2.4	-11.8; 7.0	0.91	0.1	-13.7; 13.9	0.89
RVGWE (%)	-0.6	-2.0; 3.1	0.92	-0.1	-4.1; 3.9	0.89

CI, confidence interval; ICC, intraclass correlation coefficient; RV, right ventricular; RVGCW, RV global constructive work; RVGWE, RV global work efficiency; RVGWI, RV global work index; RVGWW, RV global wasted work.

Figures

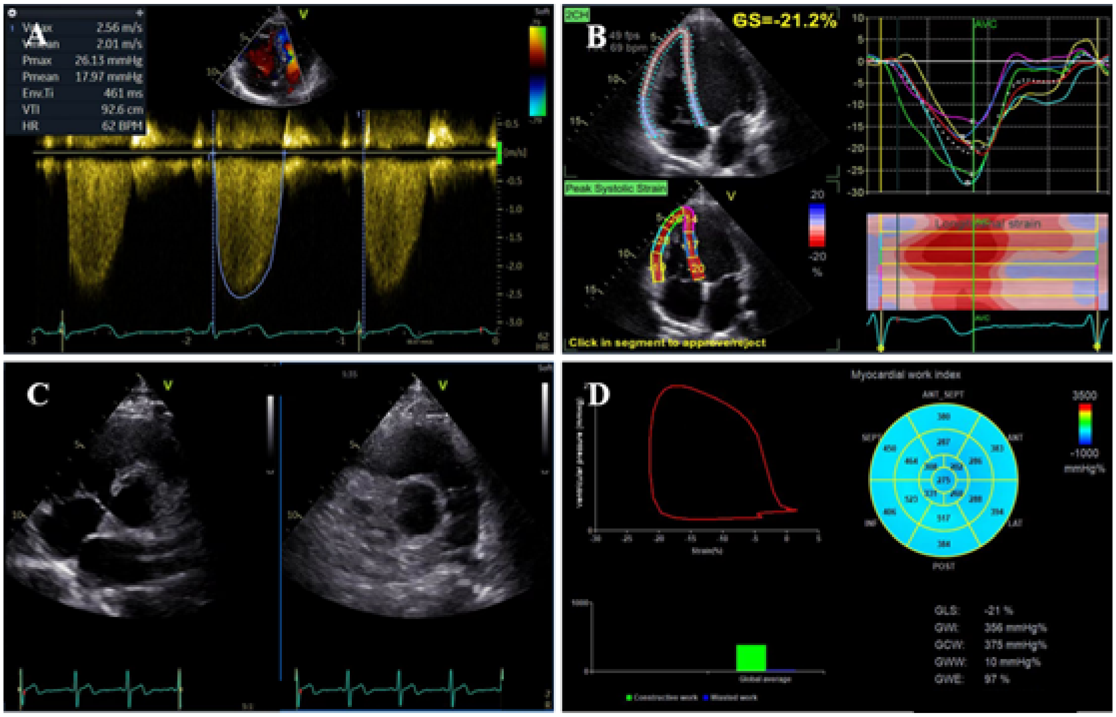

Figure 1

(A) Tracing the tricuspid regurgitation velocity-time integral; (B) Analysis of speckle tracking echocardiography-derived right ventricular global longitudinal strain; (C) Evaluation of the event timings of the tricuspid valve and pulmonic valve in the parasternal short-axis views; (D) Measurement of right ventricular myocardial work by incorporating pulmonary pressures, right ventricular strain, and cardiac cycle timings.

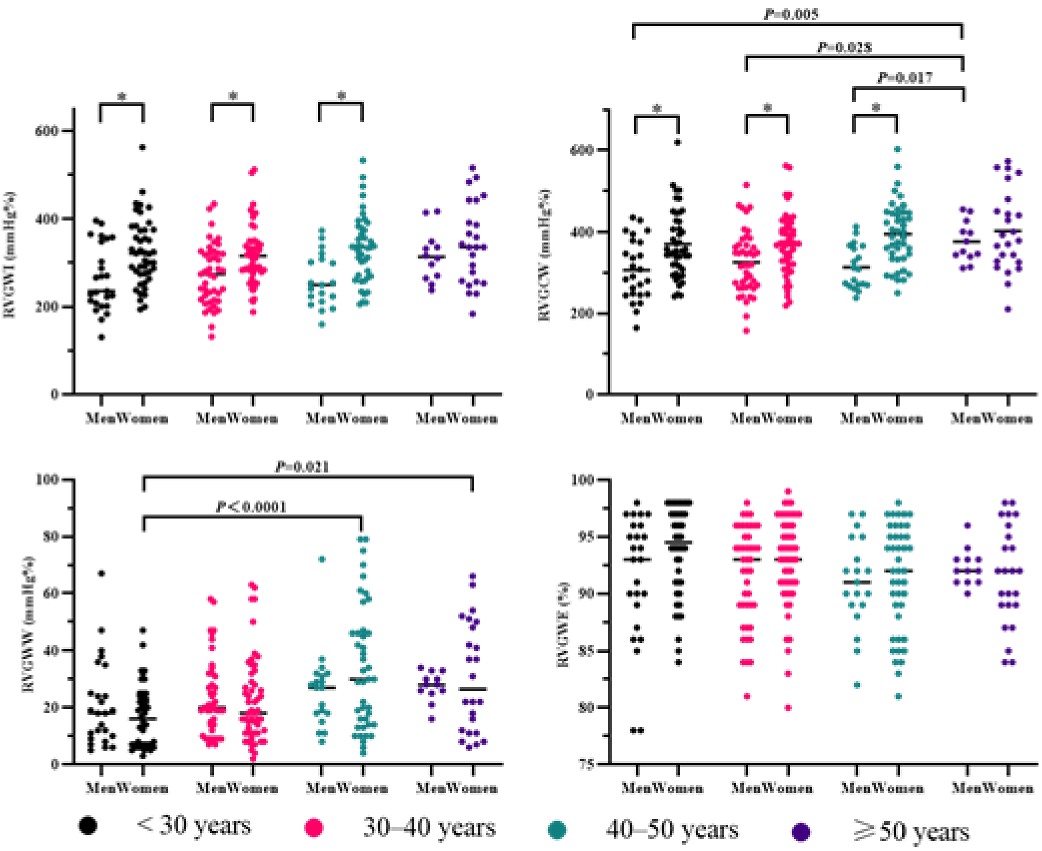

Figure 2

Individual values of right ventricular global work index (RVGWI), right ventricular global constructive work (RVGCW), right ventricular global wasted work (RVGWW), and right ventricular global work efficiency (RVGWE) according to gender and age categories. Horizontal lines represent median values or mean values. **P*-value <0.05 between genders.

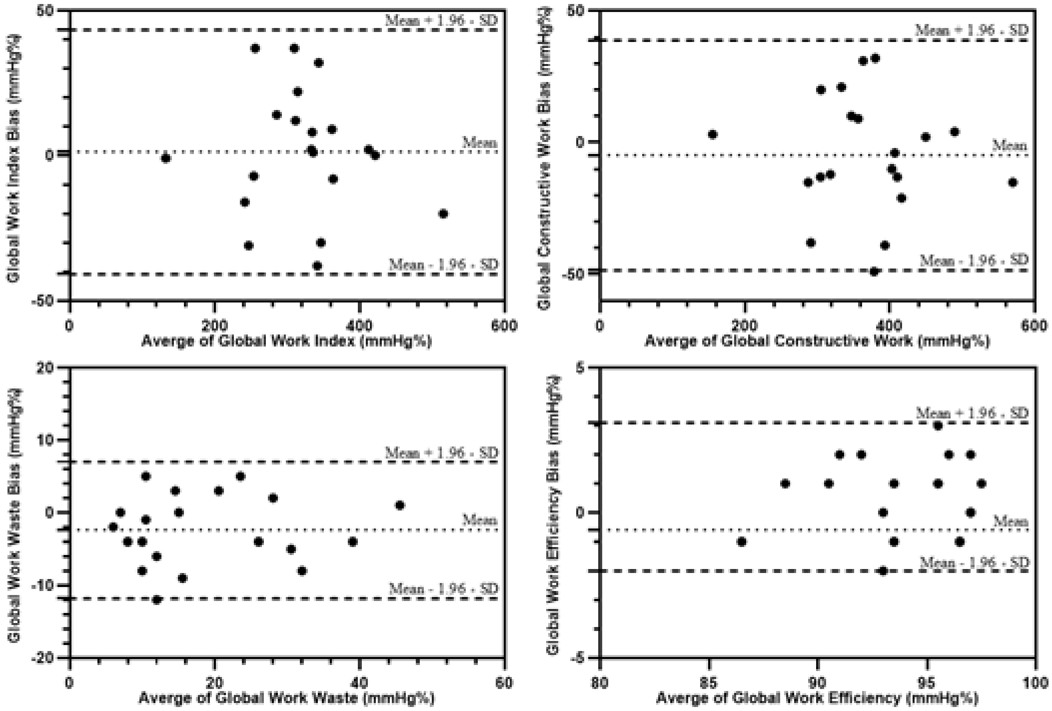

Figure 3

The Bland–Altman analysis for assessing intraobserver variability of right ventricular global work index, right ventricular global constructive work, right ventricular global wasted work, and right ventricular global work efficiency.

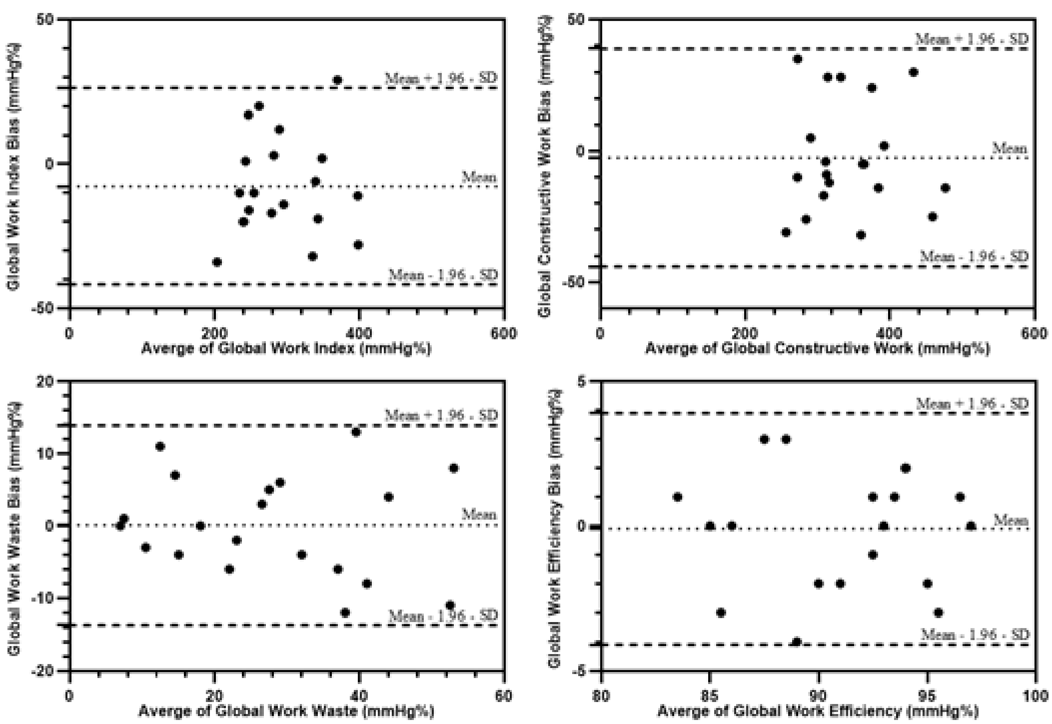

Figure 4

The Bland–Altman analysis for assessing interobserver variability of right ventricular global work index, right ventricular global constructive work, right ventricular global wasted work, and right ventricular global work efficiency.

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table3.docx