Research of the normal reference values of right ventricular longitudinal strain indices in healthy adults using 2D speckle-tracking echocardiography

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Abstract

Background: Although right ventricular strain indices obtained from speckle-tracking echocardiography have prognostic value in cardiovascular diseases, normal reference values remain unclear and vary between different manufacturers and software. In Vietnam, there have been no studies addressing this issue. This study aims to determine the reference values of the two strain indices, RVFWLS and RVGLS, and to explore their relationship with age and gender. **Method**: A total of 132 healthy adults (>18 age) with no medical history of cardiovascular diseases and other internal diseases, who met all inclusion criteria were fully assessed, including clinical assessment, laboratory measurements, and ECG examination. In addition, all participants in our study underwent transthoracic echocardiographic examination, including both conventional parameters and right ventricular strains. **Results:** The reference values for right ventricular free wall longitudinal strain (RVFWLS) and right ventricular four-chamber longitudinal strain (RV4CLS) are -28.09 ± 3.47 and -24.90 ± 3.05, respectively. The absolute values of RVFWLS and RV4CLS are higher in females than in males, with values of -29.35 ± 3.37 and -26.10 ± 3.04 for females, compared to -26.58 ± 2.97 and -23.47 ± 2.39 for males, respectively, which are statistically significant (p<0.001). Age shows a positive correlation with both RVFWLS and RV4CLS, with correlation coefficients of r = 0.218 and r=0.237, respectively, and statistical significance of p<0.05 and p<0.01. **Conclusion:** The index RVFWLS and RV4CLS using speckle-tracking echocardiography are significantly higher in females than in males (p<0.001). Therefore, caution should be exercised when using these values in clinical practice.

Keywords: *right ventricular strain, Reference values, Speckle tracking echocardiography.*

1. INTRODUCTION

Right ventricular function was previously overlooked, and research on the right ventricle was limited. However, in recent years, with advancements in interventional cardiology and imaging diagnostics, the structure and function of the right ventricle have received increased attention [1-2].

The assessment of right ventricular systolic function plays a crucial role in the diagnosis, prognosis, and treatment of various cardiovascular diseases. Common parameters used to evaluate right ventricular function, such as right ventricular strain (RVS), right ventricular fractional area change (RV FAC), tricuspid annular plane systolic excursion (TAPSE), and pulmonary artery systolic pressure (PAPs), measured by 2D echocardiography and Doppler tissue imaging, are influenced by right ventricular overload pathologies and are dependent on the imaging angle, which can lead to inaccuracies [1-3]. Speckle-tracking echocardiography (STE) can mitigate these limitations by being less affected by imaging angles and right ventricular load abnormalities. It also helps overcome the challenges posed by the right ventricle's complex structure and passive movement.

Strain is a dimensionless parameter calculated from the change in length between two points before and after movement. With some technical advancements, myocardial strain can be measured using ultrasound imaging and has been integrated into clinical practice to provide a non-invasive and objective indicator of myocardial contractility. Myocardial strain reflects both the regional and global systolic function of the myocardium. Estimated strain values from 2D echocardiography are strong prognostic factors for various cardiovascular diseases. They can detect subclinical myocardial changes at an early stage and may serve as prognostic indicators for multiple cardiovascular conditions [2].

Numerous studies have demonstrated that longitudinal strain indices of the right ventricle are crucial for diagnosing and prognosticating cardiovascular conditions such as pulmonary hypertension, arrhythmogenic right ventricular

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cardiomyopathy, congenital heart disease, and heart failure. Research has observed that in heart failure patients, impaired right ventricular longitudinal strain (RVLS) correlates with myocardial fibrosis and decreased cardiac function [3-5]. The European Association of Cardiovascular Imaging (EACVI) and the American Society of Echocardiography (ASE) (2018) recommend that the Right Ventricular Free Wall Longitudinal Strain (RVFWLS) and Right Ventricular Four-Chamber Longitudinal Strain (RV4CLS) are essential indices for assessing right ventricular function with high sensitivity and flexibility [5].

However, the normal values for right ventricular longitudinal strain indices remain limited due to the focus of studies on left ventricular longitudinal strain indices and the lack of standardization across different echocardiographic software platforms [1-2], [5], This impacts the assessment of right ventricular dysfunction. In Vietnam, there is a lack of research on normal values for right ventricular longitudinal strain. Therefore, we conducted a study titled ***"Research of the normal reference values of right ventricular longitudinal strain indices in healthy adults using 2D speckle-tracking echocardiography"*** to determine reference values for the two indices, RVFWLS and RVGLS, and their relationship with age and gender.

2. MATERIALS AND METHODS

2.1. Study population

- **Inclusion criteria**

All healthy subjects (healthcare staff and their relatives) undergoing routine health check-ups at Ba Ria Hospital from December 2023 to August 2024, with no history or symptoms of cardiovascular or pulmonary disease, and with normal health assessments and ECGs, will be included. Participants must be aged 18 or older and consent to participate in the study.

- **Exclusion criteria**

Smoking, hypertension, diagnosed diabetes or fasting blood glucose levels >100 mg/dl, body mass index >30 kg/m², creatinine >1.3 mg/dl, glomerular filtration rate <60 ml/min/1.73 m², and a history of dyslipidemia.

Abnormal findings on echocardiography (such as abnormal myocardial motion, any degree of valvular stenosis, or more than mild valvular regurgitation, congenital heart disease, acquired left and right heart disease); acute and chronic lung disease, professional sports activity, pregnancy, and arrhythmias.

Subjects with unclear echocardiographic images.

Individuals who decline to participate in the study will be excluded.

2.2. Study method

- **Study Design**: cross-sectional descriptive study.
- **Sample Size and Sampling Method**: the sample size is 132, selected using a convenience sampling method from individuals undergoing routine health check-ups at Ba Ria Hospital.
- **Specific Research Methods**:

Conventional 2D echocardiography was performed using a Philips Affinity 70G machine (USA) by an experienced echocardiographer. All subjects underwent echocardiographic assessment of left and right ventricular morphology and function. This process was used to exclude individuals who did not meet the study criteria.

Subsequently, a 2D echocardiographic four-chamber view focusing on the right ventricle was performed and measured across three consecutive cardiac cycles. The image depth and sector width were adjusted to ensure resolution and 50-80 frames per second (fps) [1-2], [5].

Right ventricular strain indices were assessed using 2D myocardial strain echocardiography. The four-chamber view focusing on the right ventricle was used to measure longitudinal strain indices of the right ventricle. These indices were calculated semi-automatically using the Autostrain RV software (version 15.0, Philips Healthcare, Andover, MA, USA) (Figure 1) [5]. The right ventricular free wall and the interventricular septum were divided into three segments (basal, mid, and apical). RV4CLS represents the average value obtained from all six segments, while RVFWLS is the average value from the three segments of the right ventricular free wall.

The automated analysis software divides the right ventricle free wall and interventricular septum into three regions (basal, mid, and apical) [2-5]. The tracking quality is confirmed by the software and visually verified using 2D images. Right ventricular free wall strain and RV4CLS are measured fully automatically. The software will process the image and calculate, the recorded results will be displayed, and can be adjusted.

Subjects with more than two segments showing incomplete tracking, despite attempts to adjust the position and width of the ROI, will be excluded from the analysis.

The analysis results will record the longitudinal strain of the entire right ventricle four-chamber view (RV4CLS) and the longitudinal strain of the right ventricular free wall (RVFWLS). These two indices will be collected and used for the study data.

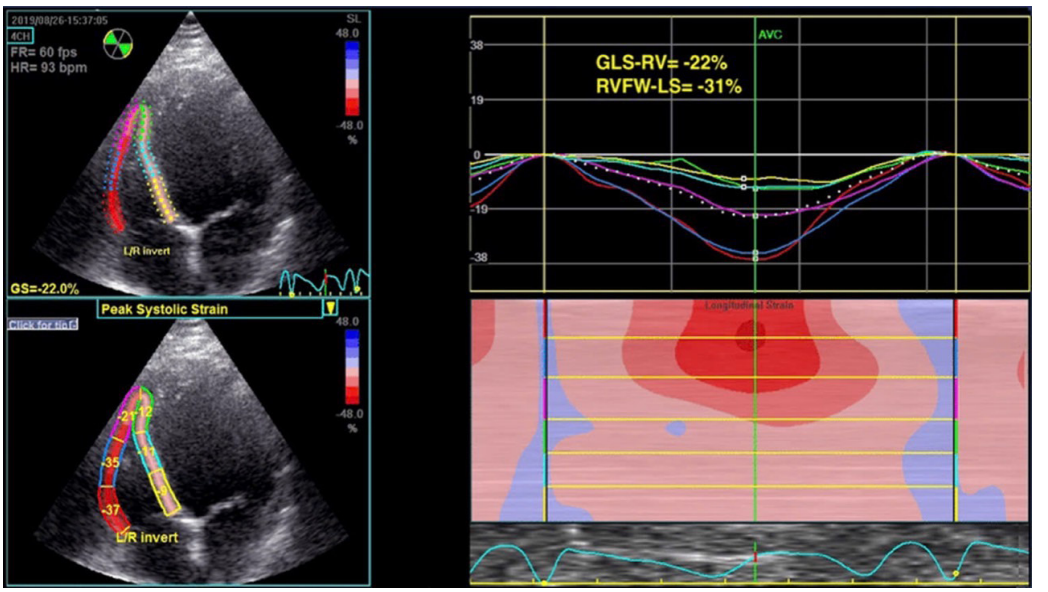

Figure 1. Right ventricular longitudinal strain indices using Autostrain RV software, QLAB version 15.0 (Philips Healthcare, Andover, MA, USA) [5]

Other variables, such as age and gender, were also recorded and analyzed for their relationship and correlation with the right ventricular longitudinal strain indices measured by 2D speckle-tracking echocardiography.

2.3. Statistical analysis

All collected data were processed using medical statistical algorithms on a computer with SPSS version 20.0 data analysis software.

3. RESULTS

3.1. Baseline characteristics of research participants

Table 1. Baseline characteristics

Characteristics	n (%)	Median (Quartiles)
Male	60 (45.5%)	
Female	72 (54.5%)	
Age (year)	43.29 ± 15.02	Minimum: 24; Maximum:83
Age ≥ 60	23 (17.4%)	
Body Surface Area (BSA, m^2)	1.62 ± 0.19	1.59 (1.49-1.78)

The table shows that males constitute 45.5% and females 54.5%. The average age is 43.29 ± 15.02 years, with the youngest being 24 years old and the oldest 83 years old, only 17.4% (23 subjects) were in the 60-85 age group. The average body surface area (BSA) is 1.62 m^2 ± 0.19.

3.2. Reference values for the two strain indices, RVFWLS and RVGLS

Table 2. Values of the right ventricular strain indices

Index	Mean (%)	Median (Quartiles)
Right Ventricular Free Wall Longitudinal Strain (RV-FWLS)	-28.09 ± 3.47	-27.65 (-30.45-25.30)
Right Ventricular Four-Chamber Longitudinal Strain (RV-4CLS)	-24.90 ± 3.05	-24.45 (-27.10-22.80)

The mean value of RVFWLS is -28.09% ± 3.47, and the mean value of RV4CLS is 24.90% ± 3.05.

Table 3. Values of the right ventricular strain indices when grouped by gender

	Males (n = 60)	Females (n = 72)	p
Right Ventricular Free Wall Longitudinal Strain (RVFWLS) (%)	-26.58 ± 2.97	-29.35 ± 3.37	<0.001
Right Ventricular Free Wall Longitudinal Strain (RVFWLS), (Median, Quartiles)	-26.20 (-28.60-24.45)	-29.30 (-32.05-27.05)	<0.001
Right Ventricular Four-Chamber Longitudinal Strain (RV4CLS) (%)	-23.47 ± 2.39	-26.10 ± 3.04	<0.001
Right Ventricular Four-Chamber Longitudinal Strain (RV4CLS), (Median, Quartiles)	-23.25 (-24.65-21.70)	-26.20 (-27.80-24.00)	<0.001

Quartiles 25% and 75%.

There is a statistically significant difference between males and females in the free wall strain and overall longitudinal strain indices of the right ventricle, with p<0.001.

3.3. Relationship between these indices

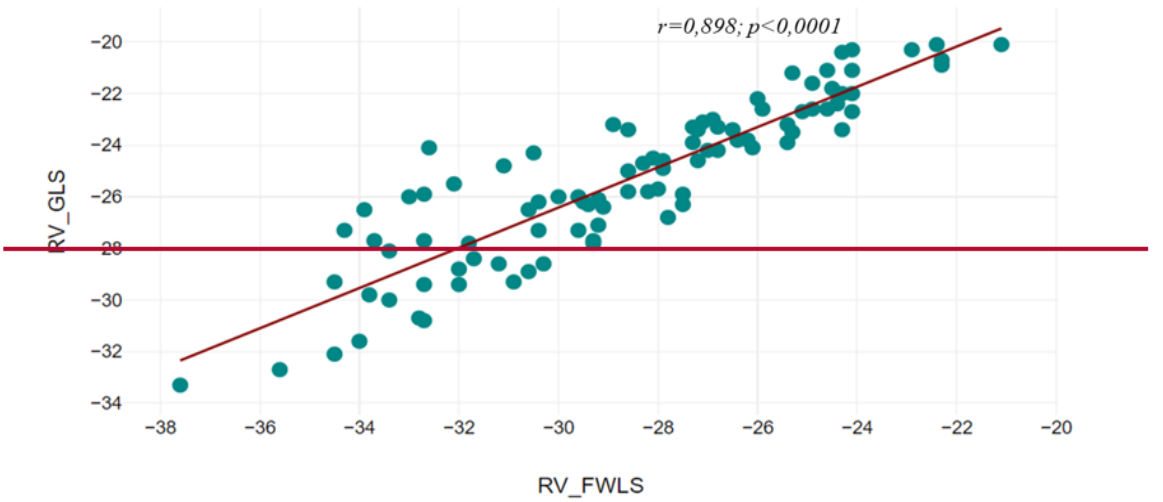

Figure 2. Correlation between the right ventricular free wall longitudinal strain (RV-FWLS) and the right ventricle global longitudinal strain (RV-GLS)

There is a strong correlation between RV-FWLS and RV-GLS, with a correlation coefficient of r=0.898, p<0.0001.

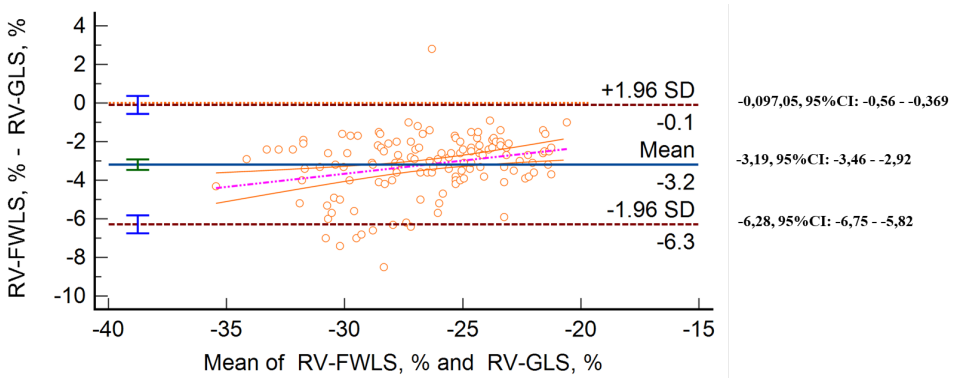

Figure 3. Agreement between RV-FWLS and RV-GLS

There is a high level of agreement between the two strain indices, with a mean difference of -3.19 and a 95% confidence interval of -3.46 to -2.92.

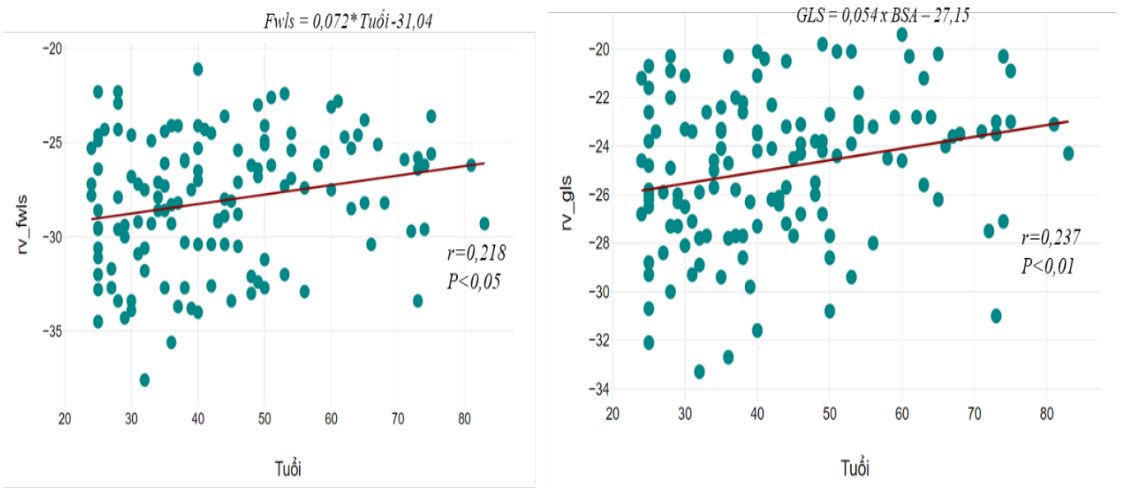

Figure 4. Linear regression equations between age and the two right ventricular strain indices

Age is positively correlated with RVFWLS and RV4CLS, with correlation coefficients of r = 0.218 (p = 0.0121) and r = 0.237 (p = 0.0062), respectively (negative value decrease).

4. DISCUSSION

4.1. Baseline characteristics of research participants

From November 2023 to August 2024, we collected a total of 132 eligible subjects for inclusion in the study, of which 54.5% were female and 45.5% were male, with a mean age of 43.29 ± 15.02 years. The NORMAL study (2018) reported a mean age of 47 years in its study population, with females accounting for 53% [6]; The study by Fine NM et al. (2014) is a meta-analysis of 10 studies, involving a total of 486 healthy subjects with a mean age ranging from 43 to 57 years, of whom 59% were female [7]; The WASE (2021) study by the World Alliance of Societies of Echocardiography on right ventricular function reported a mean age of 47 years, with females accounting for 49% of the study population [8]. Although the proportion of females in these studies is quite similar to our study, it is evident that the mean age of our study population is considerably lower. This can be explained by the fact that individuals aged 60 and above often suffer from cardiovascular conditions, leading to a significant portion of this age group not meeting the selection criteria. As a result, in our study, only 17.4% (23 subjects) were in the 60-85 age group. Similarly, other authors have also noted that older age groups are affected by comorbidities, and advanced age may influence right ventricular strain values [5].

4.2. Reference values for the two strain indices, RVFWLS and RVGLS

Our study reported mean values of right ventricular free wall longitudinal strain (RVFWLS) at -28.09 ± 3.47% and right ventricular global longitudinal strain (RV4CLS) at -24.90 ± 3.05%. In contrast, the NORMAL study (2018) found mean RVFWLS values of -26.4% ± 4.2 and RV4CLS values of -21.5% ± 3.2 [6]; The WASE study (2021) reported RVFWLS and RV4CLS values of -28.3 ± 4.3 and -25.4 ± 3.8, respectively [8]. It can be seen that the results from our study are quite similar to those of the WASE study (2021) and higher than those reported in the NORMAL study (2018) [6-8]. This can be explained by the fact that the studies used ultrasound machines from different manufacturers and corresponding processing software. Specifically, our study and the WASE study (2021) used Philips echocardiography machines with Auto Strain RV QLAB 15.0 software, while the NORMAL study (2018) used GE machines and EchoPAC software [6]. Therefore, when referencing these parameters in research, it is important to consider the software used. Alternatively, a control group could be employed in studies involving patients to obtain more reliable results.

4.3. Relationship between these indices

Our study recorded gender and age differences in right ventricular strain values. Specifically, the RV4CLS in males was -23.47 ± 2.39, while in females it was -26.10 ± 3.04. The RVFWLS in males was -26.58 ± 2.97, compared to -29.35 ± 3.37 in females. These differences were statistically significant with $p < 0.001$. In other words, the absolute values of right ventricular strain indices (RVFWLS and RV4CLS) were higher in females than in males. Similarly, several other studies have also shown statistically significant gender

differences in right ventricular strain indices, the 5th Copenhagen City Heart Study (2024) involving 1.297 participants without cardiovascular disease or risk factors indicates that the absolute values of RVFWLS and RV4CLS are higher in females compared to males (-27.5 ± 55 vs. -25.4 ± 4.5, p < 0.001 and -22.3 ± 35 vs. -20.6 ± 3, p < 0.001, respectively) [9]. The study by Park J-H et al. (NORMAL) reported that females have higher absolute values of RV4CLS compared to males (-22.3 ± 3.3 vs. -20.7 ± 2.9%, p < 0.001).

The study by Muraru D et al. (2016) involving 276 healthy volunteers (55% women; age range 18-76) found that the absolute values of both RVFWLS and RV4CLS are consistently higher in females compared to males, regardless of whether the average RVLS was considered over 6 segments or 3 segments [10]. Therefore, reference values in studies should be analyzed by sex. An RV4CLS value > -19% was used as a threshold for detecting right ventricular dysfunction in a study conducted using Echo PAC software. However, this value should be used with caution in different study populations. Current ultrasound guidelines recommend -20% as the abnormal threshold for RVFWLS, but acknowledge that this threshold is based on consensus from limited data and may vary depending on factors such as the provider's software [11].

Additionally, our study showed a strong correlation between the two indices, RVFWLS and RV4CLS, with r=0.898, p<0.0001, and a high agreement in RVFWLS and RV4CLS strain indices, with a mean difference of -3.19 and a 95% confidence interval of -3.46 to -2.92. Thus, both indices can be used to assess right ventricular function.

Our study results indicate that the indices RVFWLS and RV4CLS are positively correlated with age, with correlation coefficients of r=0.218, p=0.0121 and r=0.237, p=0.0062, respectively. According to the study, changes in right ventricular strain indices are not significant in individuals under 60 years of age, whereas in those over 60 years, these indices tend to decrease, similar to findings in studies by Addetia K and Chia EM [8], [12].

The study by Landzaat JWD (2023) is a meta-analysis of 28 studies on right ventricular strain values in healthy individuals. It found that there is no clear reference value for right ventricular strain that can be derived from the studies due to statistical heterogeneity between them. However, based on all the analytical results, the authors recommend that a reference value lower than -20% for right ventricular strain should be considered indicative of reduced function [13].

Like all the studies analyzed, our study has several limitations. The accuracy of measuring right ventricular systolic strain may vary depending on the subject and the study, depending on the experience of the operator and the quality of the imaging. In particular, strain values are also dependent on the software used, which suggests that separate reference ranges may be needed for different vendors. Further research is required to understand the variability in average strain values across studies, especially as sensitivity analyses of subgroups indicate that these differences are not solely due to the vendor's software [14].

5. CONCLUSIONS

This study provides gender-specific reference values and specific methods for right ventricular longitudinal strain obtained by 2D speckle-tracking echocardiography from a group of healthy volunteers. Absolute right ventricular strain values are higher in females compared to males (p<0.001). Age is positively correlated with both RVFWLS and RV4CLS, with correlation coefficients of r=0.218 and r=0.237, respectively, and p-values of <0.05 and <0.01. Further studies with larger samples in healthy subjects are needed to establish normal reference values for right ventricular strain.

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