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ORIGINAL PAPER

Should the septum be included in the assessment of right ventricular longitudinal strain? An ultrasound two-dimensional speckle-tracking stress study

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Abstract

Right ventricular longitudinal strain (RVLS) by 2D speckle-tracking echocardiography (2D-STE) is a useful parameter for assessing systolic function. However, the exact method to perform it is not well defined as some authors evaluate only free wall (FW) segments while others include all six RV segments. To compare the assessment of RVLS at rest and during exercise by these two approaches. Echocardiography was performed on 80 healthy subjects at rest and during exercise. The analysis consisted of standard and 2D-STE assessment of RV global and segmental strain tracing only RVFW and also tracing all six RV segments. At rest, RVLS could be assessed in 78 (feasibility 97.5%) subjects by both methods. However, during exercise, RVLS by RVFW method was feasible in 67 (83.8%) as compared to 74 (92.5%) by RV6S approach. Both at rest and during exercise, RVLS values by the two methods showed excellent correlation ($r = > 0.90$). However, RVLS values assessed by RV6S were lower (absolute values) than those by RVFW approach (RV6S vs. RVFW; rest: -27.0 ± 3.9 vs. -9.5 ± 3.9, $p < 0.001$ and exercise: -30.7 ± 5.2 vs. -33.3 ± 5.1, $p < 0.001$). Furthermore, basal strain was higher and apical strain lower (absolute values) by RV6S approach. At rest, reproducibility for RVLS was excellent and similar for the two methods. However, during exercise, reproducibility for RVFW method was poorer, especially at the apex. The two currently described methods for RVLS assessment by 2D-STE demonstrated excellent agreement. However, the RV6S approach seemed to be more feasible and reproducible, particularly during exercise. Moreover, global and segmental strain values are different with both methods and should not be interchanged.

Keywords Longitudinal strain · Right ventricle · Exercise echocardiography

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Introduction

Echocardiographic evaluation of right ventricular (RV) systolic function is essential in a variety of clinical scenarios, but remains challenging due to its unique geometry and thin wall [1, 2]. In addition, standard echo-derived RV function parameters are limited by their load- and view-dependency [3]. Myocardial deformation imaging using 2D speckle-tracking echocardiography (2D-STE) may help in functional evaluation by allowing the assessment of the different components of deformation (longitudinal shortening versus overall change) and differentiate regional changes. Assessment of RV longitudinal strain (RVLS) has proven its utility for diagnosis and prognosis in congenital cardiomyopathies [4], pulmonary arterial hypertension (PAH) [5, 6], heart failure [7, 8] and arrhytmogenic cardiomyopathy [9]. Indeed, current international guidelines describe RVLS as an accurate tool for RV function evaluation and recommend its use in clinical practice [1, 2]. However, the exact method to perform RVLS analysis is not well established as some authors include in the region of interest (ROI) just only the segments of the RV free wall [7, 9] while others include all six RV segments (free wall and septal segments) [5, 10]. The lack of uniformity has hindered its applicability in clinical practice and has made the interpretation of data difficult due to various research groups using different methods of RVLS estimation. A recent study by Muraru et al. [11] compared these two different approaches for RVLS assessment at rest and showed that using a 6-segment ROI for RV free wall strain analysis was more feasible and reproducible than tracing just the 3 segments of the RV free wall.

RVLS analysis has been recently applied for exercise stress echocardiography offering an excellent tool to non-invasively evaluate the real-time RV response to exercise and thus, making it useful for the estimation of RV functional reserve [12, 13]; which has demonstrated to be superior to echocardiographic RVLS analysis at rest for the diagnosis of arrhythmogenic cardiomyopathy [14] and hypertrophic cardiomyopathy [15] at early stages and to unmask potential deleterious effects of extreme endurance exercise on RV performance [16]. To our knowledge, no studies have compared the assessment of RVLS by these two methods during exercise.

Accordingly, this exploratory study was designed: (1) to evaluate the agreement between RVLS values assessed by the two methods and (2) to compare the feasibility and reproducibility of both approaches at rest and during exercise. We hypothesized that using a 6-segment ROI for RVLS analysis would be more feasible and reproducible than a 3-segment ROI evaluation at rest but particularly during exercise when imaging quality is known to worsen.

Methods

Study population

Eighty volunteers (50% women) were prospectively recruited among hospital employees. Criteria for recruitment were: 20–45 years old, no history or symptoms of cardiovascular or lung disease, no cardiovascular risk factors, normal physical examination, normal ECG and being capable to perform a maximal exercise test on a cycle-ergometer.

The study protocol complied with the declaration of Helsinki and was approved by the Ethics Committee of our institution. All participants provided written informed consent.

Echocardiography

All subjects underwent an exercise stress echocardiogram with an increment in workload of 25 W every 2 min until they reached 85% of maximum theoretical heart rate (HR). Exercise was performed on a semisupine cycle-ergometer (EE e-bike; GE Medical; Milwaukee, USA) with simultaneous 12-lead electrocardiographic recording. An echocardiogram was performed after at least 20 min of rest in preprandial condition and again during maximum effort. All echocardiographic images were acquired with a commercially available ultrasound system (Vivid Q; GE Medical; Milwaukee, USA). Images were acquired from the parasternal (long- and short-axis) and apical (RV-focused 4-, 4-, 3- and 2-chamber) views. Three consecutive cardiac cycles for each acquisition were digitally stored in a cine loop format for off-line 2D-STE analysis with available software from one of the most commonly used vendors, General Eletric (EchoPac, version 202.41.0, Milwaukee, WI, USA). Cardiac chamber dimensions were measured according to international recommendations [1] and indexed for body surface area according to the DuBois formula. RV end-diastolic area and end-systolic area were estimated by tracing the endocardium from a RV-focused apical 4-chamber view. Ventricular and atrial volumes and LV ejection fraction were derived using the biplane Simpson method. LV and RV diastolic function were assessed by peak early (E) flow velocity and lateral annular velocities of the mitral and tricuspid valves [1]. Stroke volume (SV) was calculated with quantitative Doppler as the product of RV outflow tract area and velocity time integral of flow at that level [17].

Myocardial deformation imaging

Myocardial deformation of right ventricle was evaluated by 2D-STE (2Dstrain, Echo Pac, version 202.41.0, General Electric Healthcare, Milwaukee, WI, USA). RVLS was assessed from a RV-focused apical 4-chamber view [2] by

two methodologies. The first method consisted of manually tracing the entire RV endocardial border (lateral and septal walls) which automatically generated a region of interest (ROI) that included RV free wall segments and septal segments (RV6S method, Fig. 1a). The second method consisted of manually tracing the RV endocardial border along the lateral wall which generated a ROI that included the three segments of the RV free wall only (RVFW method, Fig. 1b). In both cases, the width and the position of the automatically generated ROI was manually adjusted to assure an accurate assessment of the entire myocardium. In addition, RV segmental strains were assessed in the basal (inlet), mid and apical segments of the RV free wall by the two methodologies. Special care was taken to acquire zoomed images of the RV in apical views (60–80 frames per second) to ensure an adequate ratio of spatial/temporal resolution. Both at rest and during exercise, the quality of the tracking was evaluated by the software automatically and visually by a single investigator. When more than one segment showed inadequate tracking despite repetitive assays readjusting the ROI width and position, RVLS was excluded from analysis.

Statistical analysis

Data were analyzed with SPSS Software for Windows (V.21.0, SPSS Inc., Chicago, New York, USA). All continuous variables were analyzed for normality of distribution using a Shapiro–Wilk test. Subsequently, differences between reference values obtained using the two methods for RV strain analysis were tested by a paired T-student test and Bland–Altman plots. If normality was not confirmed, Wilcoxon signed rank test was applied. Fisher's exact test was used to compare feasibility of RVLS assessment based on gender. Correlations between the different parameters were assessed with the Pearson test. RV global and segmental longitudinal strains were assessed in 10 random subjects by a second investigator, as well as by the same primary investigator at least 1 month after the first analysis for inter- and intraobserver reproducibility evaluation and it was expressed as intraclass correlation coefficient. A p-value < 0.05 was considered for significance in all analyses.

Results

Baseline population characteristics

Table 1 summarizes population characteristics and echocardiographic parameters at rest in our study population. None of the participants had personal or family history of cardiovascular diseases. Resting heart rate, blood pressure and body surface area were within normal limits. All subjects had normal electrocardiograms at rest, with sinus rhythm and showed not pathological changes during exercise (data not shown). Functional and structural parameters of both ventricles were within normal range [1].

Ventricular performance and hemodynamic parameters during exercise

Table 2 shows hemodynamic and echocardiographic parameters during peak exercise in the study population. The increase in cardiac output during this acute maximum exercise was mainly achieved by an increase in heart rate and to a lesser extent by an increase in stroke volume. Exercise

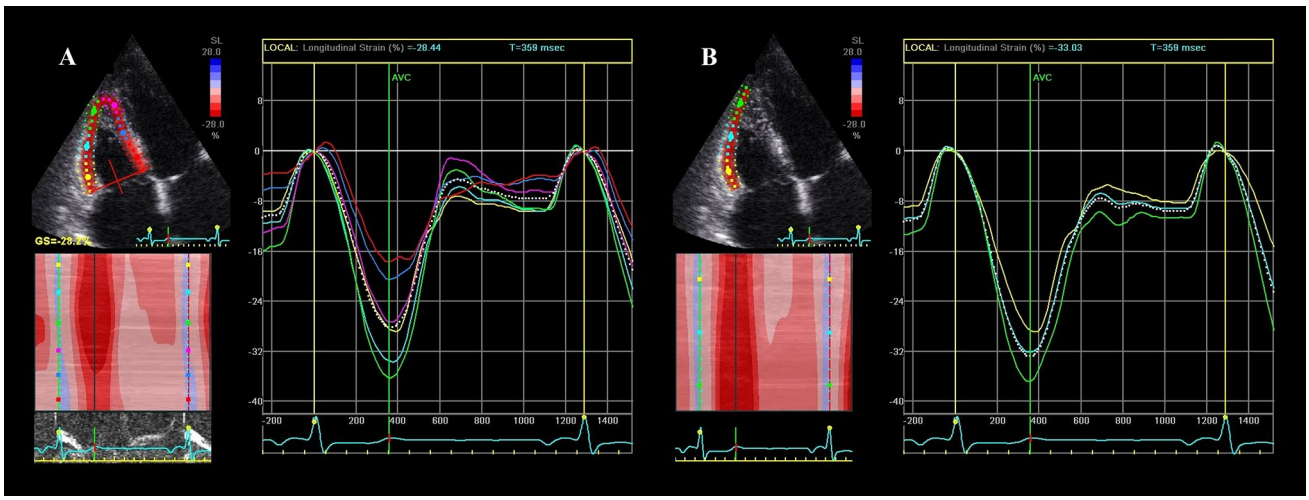

Fig. 1 Illustration of the two currently accepted methods for right ventricular longitudinal strain (RVLS) evaluation: **a** RVLS is obtained from measuring RV free wall and interventricular septum using a 6-segment region of interest (ROI), **b** RVLS is estimated by tracing 3-segments ROI along the RV free wall

Table 1 Population characteristics and baseline echocardiographic parameters in the study population

	Study population
Age (years)	37.1 ± 4.5
BSA (m^2)	1.76 ± 0.19
RVOT (mm/m^2)	19.1 ± 1.9
RAV (ml/m^2)	22.3 ± 6.5
LVEDV (ml/m^2)	56.1 ± 12.4
LVESV (ml/m^2)	24.3 ± 7.9
LVEF (%)	57.0 ± 4.6
Septal S' mitral (cm/s)	7.2 ± 1.2
Septal e' mitral (cm/s)	9.1 ± 1.7
E mitral (m/s)	0.81 ± 0.11
Septal E/e' mitral	11.3 ± 0.7
Lateral S' mitral (cm/s)	9.5 ± 1.2
Lateral e' mitral (cm/s)	12.7 ± 1.6
Lateral E/e' mitral	6.4 ± 0.7
LAV (ml/m^2)	21.8 ± 5.7

RVOT right ventricular outflow tract, *RAV* right atrial maximum volume, *LVEDV* left ventricular end-diastolic volume, *LVESV* left ventricular end-systolic volume, *LVEF* left ventricular ejection fraction, *LAV* left atrial volume

Table 2 Hemodynamic and echocardiographic parameters during peak exercise in the study population

	Baseline	Peak exercise	% Change
Workload (Watts)	NA	170.7 ± 46.9	NA
HR (b.p.m)	64.9 ± 10.2	160.5 ± 10.0*	+ 149.5
SBP (mmHg)	116.6 ± 12.1	188.2 ± 16.7*	+ 62.4
DBP (mmHg)	75.4 ± 7.6	74.3 ± 4.9	− 2.6
RV.SV (ml/m^2)	44.2 ± 6.4	55.5 ± 8.7*	+ 25.4
RV.CO (l/m^2)	2.8 ± 0.4	8.9 ± 1.5*	+ 219.7
RVEDA (cm^2/m^2)	11.9 ± 3.2	11.6 ± 2.9	+ 1.2
RVESA (cm^2/m^2)	6.1 ± 1.9	5.4 ± 1.7*	− 11.5
RVFAC (%)	48.3 ± 5.6	53.5 ± 5.8*	+ 11.0
RVEF (%)	60.3 ± 6.3	66.3 ± 7.2*	+ 10.0
TAPSE (mm)	22.7 ± 2.8	29.8 ± 3.7*	+ 32.8
S' tricuspid (cm/s)	10.0 ± 1.3	17.2 ± 3.1*	+ 73.5
e' tricuspid (cm/s)	10.7 ± 2.0	22.9 ± 5.4*	+ 114.5
E tricuspid (m/s)	0.52 ± 0.26	0.96 ± 0.29*	+ 85.2
E/e'	4.9 ± 1.2	4.2 ± 3.8	− 14.3

HR heart rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *SV* stroke volume, *CO* cardiac output, *RVEDA* right ventricular end-diastolic area, *RVESA* right ventricular end-systolic area, *RVFAC* right ventricular fractional area change, *RVEF* right ventricular ejection fraction, *TAPSE* Tricuspid annular plane systolic excursion, *NA* not applicable

*$p < 0.05$ versus baseline by Student *T* test

induced a significant rise of all RV systolic and diastolic parameters while it induced no changes in RV size. Blood pressure response to exercise was in all subjects within normal range [18].

Right ventricle longitudinal strain at rest and during exercise

At rest, RVLS could be assessed in 78 of 80 subjects (feasibility 97.5%) by both methods. However, at peak exercise, RVLS by the RVFW was feasible in 67 out of 80 (83.8%) as compared to 74 out of 80 by RV6S (92.5%). When both methods failed to estimate RVLS strain, it was in most cases due to poor imaging quality (5 of 6, 83%). However, when the FW method was inaccurate in analysing RVLS, it was mostly due to an inadequate tracking of the apical and mid segments (6 of 7, 86%). The feasibility of RVLS analysis at rest was equivalent in men and women. However, during exercise, the feasibility of RVLS assessment by RV6S showed a trend to be worse in women than in men (Table 3). The maximum HR achieved during exercise was significantly higher in women when compared with men (HR women vs. men: 166.4 ± 6.9 vs. 154.8 ± 9.2 b.p.m, $p < 0.05$). In addition, HR during peak exercise showed a trend to be higher in those individuals in which RVLS assessment was not feasible by the RV6S method during exercise as compared to the individuals in which it could be analysed (168.6 ± 8.9 vs. 159.8 ± 9.8 b.p.m respectively, $p = 0.06$).

Table 4 shows RVLS values at rest and during peak exercise evaluated by the two methods. Figure 2 depicts Bland–Altman analysis for RV global and segmental longitudinal strain at rest and during exercise. RVLS assessment by both approaches, and both at rest and during exercise demonstrated excellent correlation (Table 4). However, at rest, basal mean RVLS was slightly higher and apical mean RVLS slightly lower (absolute values) by RV6S as compared to RVFW (Table 4 and Fig. 2). During exercise, variability between RV6S and RVFW segmental deformation

Table 3 Feasibility of right ventricular longitudinal strain assessment of the two methods based on gender

Feasibility of RVLS assessment	Men	Women	P
Rest			
RVLS by RV6S (n, %)	(40, 100)	(38, 95)	0.15
RVLS by RVFW (n, %)	(40, 100)	(38, 95)	0.15
Exercise			
RVLS by RV6S (n, %)	(40, 100)	(35, 88)	0.06
RVLS by RVFW (n, %)	(35, 88)	(32, 80)	0.28

Underlined values signify $p > 0.05$ and < 0.10 by Fisher's exact test

RVLS right ventricular longitudinal strain. *RV6S* RVLS assessed by a 6 segments ROI (free wall plus septal RV segments), *RVFW* RVLS assessed by 3-segments ROI traced along the RV free wall

Table 4 Right ventricle global and segmental longitudinal strain values at rest and during exercise assessed by the two methods

RVLS	RV6S	RVFW	RVFW versus RV6S (p)	Correlation (r)
At rest				
Basal	− 25.1 ± 3.5	− 24.5 ± 3.4	<u>< 0.001</u>	0.97
Mid	− 30.1 ± 4.6	− 30.2 ± 4.3	0.35	0.97
Apical	− 33.0 ± 5.0	− 33.9 ± 5.0	<u>< 0.001</u>	0.98
Global	− 27.0 ± 3.9	− 29.5 ± 3.9	<u>< 0.001</u>	0.93
Peak exercise				
Basal	− 30.5 ± 4.6	− 30.7 ± 4.2	0.15	0.96
Mid	− 33.3 ± 5.4	− 33.5 ± 4.9	0.56	0.95
Apical	− 34.4 ± 7.4	− 35.6 ± 6.9	<u>< 0.001</u>	0.94
Global	− 30.7 ± 5.2	− 33.3 ± 5.1	<u>< 0.001</u>	0.92

Underlined values signify $p < 0.05$ by paired T-student test or Wilcoxon signed rank test. Significant correlations and their magnitude (r) by Pearson rank test

RVLS right ventricular longitudinal strain, *RV6S* RVLS assessed by a 6 segments ROI (free wall plus septal RV segments), *RVFW* RVLS assessed by 3-segments ROI traced along the RV free wall

was greater (Fig. 2). RV apical strain values were still significantly higher by the RVFW method but the difference between basal strain values was lost, probably due to the greater variability. Both at rest and during exercise, RV global strain by RV6S was lower (Table 4 and Fig. 2) and showed poor, but significant, correlation with RV ejection fraction (at rest: $r = +0.36$; at peak exercise: $r = +0.34$, $p < 0.05$), while no correlation was observed between RV volumetric function and RVFW strain. At rest, RVLS assessed by both methods demonstrated modest correlation with tricuspid annular plane systolic excursion (TAPSE, RV6S/RVFW: +0.32/+0.31, respectively, $p < 0.05$ for both) and S' of tricuspid annulus (RV6S/RVFW: +0.35/+0.36, respectively, $p < 0.05$ for both). Interestingly, at effort, this correlation was maintained for the RV6S method but was lost for the RVFW method.

At rest, RVLS reproducibility was excellent by both methods. However, during exercise, reproducibility for RVFW was poorer, especially for the apical segment (Table 5).

Discussion

The evaluation of right ventricular function by 2D-STE at rest and during exercise has been demonstrated to be a useful diagnostic [5, 14, 15, 19] and prognostic tool [4, 7, 20] for different cardiovascular and lung diseases as well as a useful instrument for monitoring RV functional changes induced by cardiac resynchronization therapy [21]. Accordingly, its use in clinical practice has been recommended in recent guidelines [1, 2]. However, the exact approach to perform

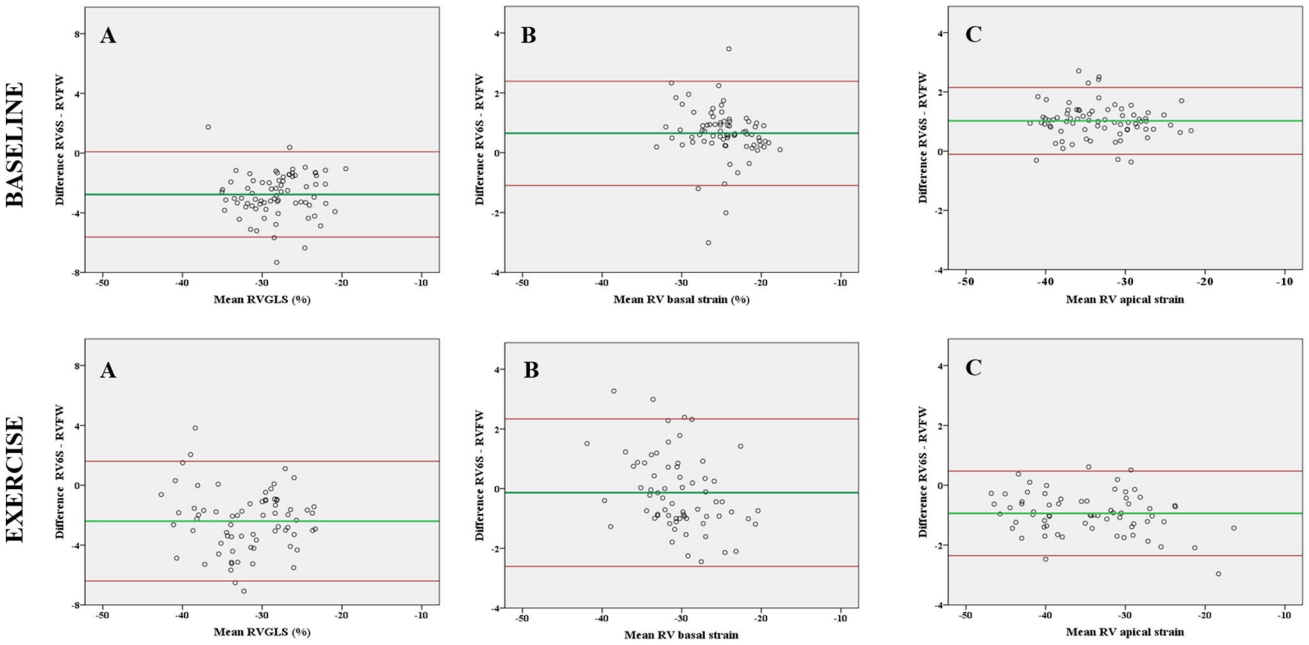

Fig. 2 Bland–Altman plot of right ventricular longitudinal (RVLS) global (**a**) and segmental (**b**, **c**) strain assessed by the two methods at rest and during exercise. At rest, the agreement between the two methodologies was good, but poorer during exercise. Global and apical RVLS values assessed by RV free wall approach were significantly higher as compared to RV six segments method. At rest, basal RVLS values by RV free wall method were lower, but this difference was lost during exercise

Table 5 Reproducibility of right ventricular longitudinal strain parameters by the two methods

RVLS (intra/inter-observer variability)	Baseline		Peak exercise	
	RV6S	RVFW	RV6S	RVFW
Basal	0.93/0.87	0.92/0.87	0.91/0.84	0.90/0.83
Mid	0.95/0.93	0.93/0.92	0.93/0.90	0.91/0.85
Apical	0.96/0.90	0.95/0.89	0.92/0.89	0.89/0.80
Global	0.95/0.90	0.94/0.90	0.92/0.89	0.90/0.84

RVLS right ventricular longitudinal strain, *RV6S* RVLS assessed by a 6 segments ROI (free wall plus septal RV segments), *RVFW* RVLS assessed by 3 segments ROI along the RV free wall

RVLS analysis is not well defined, with two methods currently being used: evaluation of RVLS by tracing a 3-segments ROI along the RVFW or by tracing a 6-segments ROI including the free wall and the interventricular septum [1, 2]. Recent data suggest that the last would be a more feasible and reproducible approach for RVLS assessment at rest [11] and thus, the recent international recommendations for RVLS assessment support this approach [2]. However, data is lacking comparing them and evaluating its agreement, reproducibility and feasibility during exercise.

In the current exploratory study we provide a comprehensive evaluation of the two methods in use for RVLS assessment by 2D-STE both at rest and during exercise. The key findings of our study can be summarized as follows: (a) RVLS segmental and global values obtained measuring free wall RVLS using a 3-segment ROI, or a 6-segment ROI (free wall and septal segments) demonstrated excellent consistency; (b) however, absolute values obtained by the two methods are different and should not be interchangeable; (c) the RV6S approach demonstrated to be more feasible and reproducible than the RVFW method during exercise.

RVFW and RV6S approaches have been indistinctly used for RV function evaluation in different studies, assuming that they should be equivalent. As previously established and in agreement with Muraru and colleagues data [11] we showed that RVGLS assessed by the RVFW is markedly higher (absolute values) than RVGLS obtained by the RV6S method. However, in contrast with their results [11], we observed that the two methods yielded also to slightly different mean longitudinal strain values at the inlet and at the apex of the RV. Our findings underscore even more that the two approaches should not be interchanged and the exact method applied for RVLS evaluation should always be specified.

In the literature, some authors used only free wall RVLS [7, 9, 22] based on the fact that most of the interventricular septum (IVS) belongs to the LV. However, although in less magnitude, contraction of the interventricular septum and hence of the LV, contribute with at least 20% to the RV systolic performance [23, 24]. Indeed, in heart failure (HF) patients with reduced ejection fraction, RVLS calculated as the average of all six RV segments demonstrated to add significant prognosis information to LV function [25]. In addition, it was found to be the best tool to differentiate hypertensive LV hypertrophy from hypertrophic cardiomyopathy [26]. Nevertheless, RVLS calculated as the average of just the three FW segments was the most accurate functional parameter that correlated with the extent of RV myocardial fibrosis in patients with advanced HF. In addition, there is large evidence on its utility for diagnosis and prognosis purposes in PAH [27, 28]. Therefore, it seems that the most accurate RVLS value to use is dependent on the disease for which it is applied and thus, for clinical and research purposes both RVLS values (FW and 6-segments) should be provided.

Evaluation of the increase in RV function during exercise (RV contractile reserve) has demonstrated to be superior to resting analysis for the differential diagnosis of various cardiomyopathies [14-16]. Combination of 2D exercise echocardiography and 2D-STE provides real time evaluation of RV myocardial function during exercise [29, 30]. However, the quality of the images acquired during exercise are known to partially hinder its feasibility [31]. As expected, in our study, the reproducibility and feasibility of RVLS analysis decreased significantly during exercise, but this fall was substantially more marked for the RVFW method. Myocardial deformation analysis was designed for assessment of function of an ellipsoid, the LV [32]. The same technology has been successfully applied for two other spherical shapes, the crescent RV [2, 10] and the round atria [2, 33]. While the algorithm was designed to also allow the assessment of a single LV wall, the more complex shape of the RV apex compared to the LV one could make the tracking of the RV apex more challenging when no continuation towards the septum is present and thus could be less precise, and, as confirmed in our study, this inaccuracy could be especially important during exercise when image quality is already more challenging and limited [34]. Our findings point out the need for the development of a myocardial deformation analysis software specifically designed for the complex RV geometry. This would provide a more a feasible and reproducible RVLS assessment which would be crucial in situations in which the image quality is known to worsen such as during exercise.

On the other hand, we showed that feasibility of RVLS analysis showed a trend to be poorer in women than men; this could be in relation with the higher peak HR achieved during exercise and consequently the worse global imaging quality.

In accordance with Teske et al. [35] we observed a modest correlation between RVLS and TAPSE and S' of the tricuspid annulus at rest. However, at exercise, this correlation

was only maintained for the RV6S method. TAPSE and tricuspid S' are known to mostly reflect the function of the RV inlet [3], and as expected, both parameters showed a moderate correlation with RV basal strain assessed by the two approaches at rest and during exercise (RV6S/RVFW at rest: $r = +0.46/0.42$ respectively and at peak exercise: $r = +0.48/0.41$, respectively, $p < 0.05$ for all). In agreement with previous report from Lord et al. [34], the assessment of the RV segmental strain by the RVFW approach during exercise was specially challenging at the apex. This led to a greater variability between RV apical strain values assessed by the two methodologies and could explain the lack of association between the above parameters during exercise.

Limitations

This observational study was carried out in a relatively small sample of participants, limiting its statistical power. Furthermore, our population included middle age healthy and active subjects which are expected to have good acoustic windows at rest and even during exercise. This could explain our excellent reproducibility for the RVLS assessment, but might limit its generalization for the usual clinical population. In addition, we analysed myocardial deformation derived only from speckle tracking; potentially, Doppler Tissue Imaging (DTI) techniques with proven higher temporal resolution [34] would allow a more accurate analysis at higher heart rates such as the case during exercise; however, angle dependency of DTI does not allow for the assessment of apical segments.

Clinical implications

According to our results, we suggest that the best current available approach to determine RVLS would be to apply the RV6S method and describe global (including FW and 3-septal segments) and free wall strain (3-lateral segments) values. Additionally, until a consensus is established, we consider that it should be mandatory to specify the method applied for RVLS evaluation in any research or clinical study. Furthermore, our findings claim the need of a strain analysis software dedicated for the RV in order to assure feasibility, reproducibility an accuracy of RVLS assessment in particular during exercise.

Conclusion

The two currently accepted methods for RVLS assessment by 2D-STE demonstrated excellent agreement and reproducibility at rest. However, absolute global and segmental strain values obtained for the two methods were slightly different and are thus not interchangeable. Importantly, during exercise, both methods showed similar increase in RVLS; however, the RV6S method was more reproducible and feasible than the RVFW one.

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Conflict of interest The authors declare that they have no conflict of interest.

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