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Normal range and usefulness of right ventricular systolic strain to detect subtle right ventricular systolic abnormalities in patients with heart failure: a multicentre study

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Aims The aim of the present multicentre study was to analyse a large cohort of healthy subjects and patients with a common condition such as heart failure (HF) with the purpose of determining the normal range and the usefulness of right ventricular (RV) systolic strain to detect subtle RV systolic abnormalities using 2D speckle-tracking echocardiography.

Methods and results We analysed 238 healthy subjects and a cohort of 642 patients characterized by asymptomatic patients ($n = 216$) and patients with HF with preserved (HFpEF) and reduced (HFrEF) ejection fraction ($n = 218$ and $n = 208$, respectively) prospectively included in 10 centres. The normal range of RV systolic strain analysing the healthy subjects was as follows: RV global strain -24.5 ± 3.8 and RV free wall strain -28.5 ± 4.8 (lowest expected value -17 and -19%, respectively). Concerning the ability of these myocardial parameters to detect subtle RV systolic abnormalities, RV global and free wall systolic strain were able to detect subtle RV longitudinal systolic abnormalities in a significant proportion of patients with HFrEF and to a lesser extent in HFpEF despite preserved tricuspid annular plane systolic excursion, tricuspid lateral annular peak systolic velocity by pulsed tissue Doppler imaging, and RV fractional area change. In addition, RV global and free wall systolic strain were significantly linked to the symptomatic status of the patients.

Conclusions The findings from this study provide important data regarding the normal range of RV global and free wall systolic strain and highlight the clinical relevance of these RV myocardial parameters to detect subtle RV systolic abnormalities in patients with HF.

Keywords speckle tracking • echocardiography • right ventricular • strain

Introduction

Conventional right ventricular (RV) systolic parameters such as tricuspid annular plane systolic excursion (TAPSE) and tricuspid lateral annular peak systolic velocity by pulsed tissue Doppler imaging (S′) remain recommended measurements to assess RV systolic function.[1,2] Nonetheless, these parameters have some limitations such as load and angle dependence and inaccuracy to evaluate a global RV systolic function because they represent only the displacement or function of a single RV segment.[1–7] In view of that, the most

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recent guidelines on RV measurements highlighted that these limitations should be taken into consideration when using these RV parameters.[1,2] In addition, recent studies showed that conventional RV measurements such as TAPSE, S′, and fractional area change (FAC) had a significantly lower correlation with RV ejection fraction (RVEF) using magnetic resonance imaging (MRI) than new myocardial parameters such as RV systolic strain.[8–13] Notwithstanding this, the ability of RV global and free wall systolic strain to detect subtle RV systolic abnormalities, when conventional RV measurements are normal, remains poorly understood. In addition, the definition of a normal RV longitudinal systolic function using RV global and free wall systolic strain is lacking. Some studies analysing healthy subjects with 2D speckle-tracking echocardiography (2DSTE) have reported the values of RV systolic strain in this population.[14–17] However, these studies were limited to determine the normal range of RV global and free wall systolic strain because of the small number of patients analysed (<80 women or men).[14–17]

Therefore, on the basis of the weak evidence regarding the normal range and the ability of RV systolic strain to detect subtle RV systolic abnormalities, the aim of the present multicentre study was to analyse a large cohort of healthy subjects and patients with a common condition such as heart failure (HF) with the purpose of determining the normal range and the usefulness of RV systolic strain to detect subtle RV systolic abnormalities.

Methods

Study population

In order to determine the normal range of RV systolic strain using 2DSTE, we enrolled healthy subjects ≥18 years of age prospectively included in 10 centres from Japan and Germany. These subjects were part of the Japanese Ultrasound Speckle Tracking of the Left Ventricle Research Project which enrolled consecutively healthy volunteer subjects in different university hospitals and was endorsed by the Japanese Society of Echocardiography.[18–20] Healthy subjects were defined as those individuals with the absence of any disease and cardiovascular risk factors such as obesity [body mass index (BMI) ≥ 30 kg/m^2], diabetes (fasting plasma glucose ≥ 126 mg/dl), hypertension (systolic and diastolic blood pressures ≥ 140/90 mmHg), hypercholesterolaemia (fasting plasma LDL cholesterol ≥ 160 mg/dl), no medication, and normal findings in transthoracic echocardiography according to the diagnostic criteria of the European Association of Cardiovascular Imaging (EACVI).[2,21] The ethics committees from each of the hospitals approved this research project, and informed consent was obtained from all subjects.

With the purpose of evaluating the ability of RV systolic strain to detect subtle RV systolic abnormalities in common conditions in the clinical practice, we analysed patients with HF with preserved (HFpEF) and reduced (HFrEF) left ventricular (LV) ejection fraction (LVEF) and a group of asymptomatic patients consecutively included between November 2012 and November 2014 (some of these patients were enrolled in previous studies of our research group).[19,20] HFpEF was defined according to the diagnostic criteria of the European Society of Cardiology (ESC) and the American College of Cardiology (ACC): (a) clinical signs or symptoms of HF (i.e. dyspnoea NYHA functional class ≥ 2), (b) evidence of preserved or normal LVEF (i.e. LVEF > 50%), and (c) evidence of abnormal LV diastolic dysfunction determined by Doppler echocardiography or cardiac catheterization.[22,23] LV diastolic dysfunction was determined by echocardiography according to the diagnostic criteria of the EACVI: i.e. septal or lateral mitral annular early-diastolic (e′) peak velocity <8 or <10 cm/s using TDI, respectively, or maximal LA volume index (LAVI) ≥34 mL/m^2.[21] HFrEF was defined in accordance with the guidelines on HF of the ESC: (a) clinical signs or symptoms of HF (i.e. dyspnoea NYHA functional class ≥ 2) and (b) evidence of reduced LV systolic function (i.e. LVEF < 50%).[22] The group of asymptomatic patients was determined as those with NYHA functional class I, evidence of preserved LVEF (LVEF > 50%), and the presence of some cardiovascular disease or risk factor (such as obesity, diabetes, hypertension, or coronary artery disease). With the purpose of excluding non-cardiac causes of dyspnoea in patients with HF, we excluded subjects with (a) severe pulmonary disease defined as pulmonary pathology with requirement of supplemental oxygen or need of treatment with corticoids, (b) severe kidney disease defined as estimated glomerular filtration rate (GFR) <15 mL/min/1.73 m^2 for at least 3 months or dialysis requirement, and (c) severe chronic liver disease. Moreover, patients with severe valvular heart disease were excluded as well. In addition, to avoid underestimations of RV myocardial analyses, patients with inadequate 2D imaging quality in ≥1 myocardial segments of the RV were also excluded.

RV and LV measurements using conventional transthoracic echocardiography

All patients were examined at rest using a Vivid 7 or E9 (GE Healthcare) ultrasound system. RV and LV conventional measurements such as diameter, volume, LVEF, TAPSE, FAC, and S′ were assessed as recommended by the EACVI.[1,2,21] All these measurements were calculated as the average of three measurements and performed at conditions of respiratory (<20 breaths/min), haemodynamic (90–160 mmHg of systolic blood pressure), and electrical (60–99 bpm) stabilities.

RV and LV measurements using 2D speckle-tracking echocardiography

The myocardial analyses of the RV and LV were performed offline using 2DSTE (Echo-Pac 113, GE) in a central echocardiography laboratory at Charité University Hospital and blinded to the clinical characteristics of the subjects. The myocardial systolic function of the RV was evaluated by means of the average value of the longitudinal systolic strain peak from all segments of the free and septal wall (i.e. RV global systolic strain) and only from the free wall of the RV (i.e. RV free wall systolic strain) in the apical four-chamber view focused in the RV (see *Figure 1* and Supplementary data, *Videos S1 –S5*).[8–10] Furthermore, we analysed the myocardial systolic function of the LV by means of the global longitudinal systolic strain which was derived from the analysis of the LV from the apical four-chamber, two-chamber, and long-axis views.[19,20]

Statistical analysis

Continuous data were presented as mean ± standard deviation (SD) and dichotomous data in percentage. Differences in continuous variables between two groups were analysed using Student's *t*-test. Categorical variables were compared by χ^2 test and Fisher's exact test as appropriate. Comparisons between three or more groups were analysed using a one-way analysis of variance (ANOVA). The relationship of RV systolic strain with continuous variables was analysed using a simple linear regression analysis. In addition, in order to identify the variables with the strongest association with RV global and free wall systolic strain, a multivariate stepwise forward linear regression analysis was performed. Moreover, we analysed the link between RV systolic parameters and the symptomatic status using a logistic regression analysis.

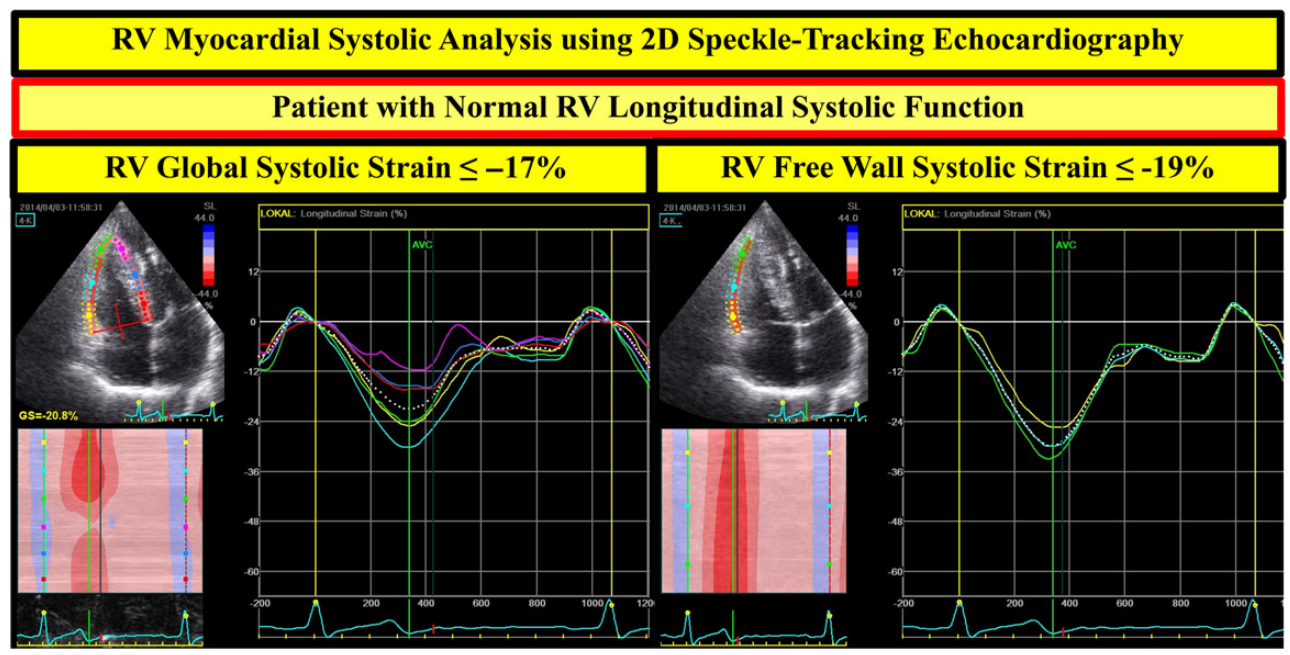

Figure 1 RV global systolic strain and RV free wall systolic strain using 2DSTE. RV global systolic strain represents the longitudinal systolic function of the septal and free wall of the RV. RV free wall systolic strain analyses only the longitudinal systolic function of the free wall of the RV. RV global and free wall systolic strain were analysed in a RV-focused four-chamber view tracing a specific region of interest including only the free wall to obtain RV free wall strain and tracing other specific region of interest including the septal and free wall to obtain RV global strain, as it is shown in this figure and in Supplementary data, *Videos S1–S4*. This figure shows a patient with normal RV longitudinal systolic function determined by a RV global systolic strain $\leq -17\%$ and a RV free wall systolic strain $\leq -19\%$. See also Supplementary data, *Videos S1–S5* illustrating the characteristics of a normal RV longitudinal systolic function determined by RV global and free wall systolic strain.

In accordance with the recent guidelines on chamber quantification of the EACVI,[2] a normal RV systolic function using conventional RV measurements was defined as TAPSE $\geq$ 17 mm, S′ $\geq$ 9.5 cm/s, and FAC $\geq$ 35%.[2] In this regard, subtle RV systolic abnormalities were defined as those detected when conventional RV systolic measurements were normal. In line, the lowest expected cut-off value of RV global and free wall systolic strain in the healthy population (calculated as -1.96 SD from the mean) was used to determine a normal or abnormal RV longitudinal systolic strain.

The adequate reproducibility of RV systolic strain has been previously confirmed in several studies of our and other laboratories.[6–17,24] In effect, when we analysed the intra- and interobserver variability on 20 randomly selected subjects in the present study, both RV global systolic strain and RV free wall systolic strain had low intra- and interobserver variability, with absolute mean differences lower than 1% (RV global systolic strain 0.83 $\pm$ 0.59 and 0.91 $\pm$ 0.73%; RV free wall systolic strain 0.82 $\pm$ 0.59 and 0.89 $\pm$ 0.63%; respectively).

All statistical analyses were performed with Statview 5.0 (SAS Institute) and SPSS 22.0 (IBM). Differences were considered statistically significant when $P < 0.05$.

Results

Clinical characteristics of the study population

A total of 256 healthy subjects met the eligibility criteria during the study period. However, in this group of individuals, RV global and free wall systolic strain could not be analysed in 18 subjects because of an inadequate 2D imaging quality of the RV (feasibility 93%). Thus, 238 healthy adult subjects (117 Japanese and 121 Germans subjects) with adequate imaging quality for an analysis by 2DSTE were finally studied and analysed. Clinical characteristics and conventional RV and LV measurements of these subjects are shown in *Table 1*. Concerning the asymptomatic and HF population, a total of 710 patients were initially included. Nevertheless, 68 patients had inadequate 2D imaging quality for an analysis by RV global and free wall systolic strain (feasibility 90.4%). Accordingly, 642 patients were finally analysed (218 with HFpEF, 208 with HFrEF, and 216 asymptomatics). Clinical and LV characteristics of these patients are shown in *Table 1*.

Normal range of RV global and free wall systolic strain

The normal range of RV global and free wall systolic strain analysing the healthy subjects was as follows: RV global strain -24.5 ± 3.8 and RV free wall strain -28.5 ± 4.8 (lowest expected value -17 and -19%, respectively) (see *Table 2*). Regarding age and gender distribution of these RV myocardial parameters, there were no significant differences in RV global and free wall systolic strain between younger and older subjects and small differences between women and men (*Table 2*). In addition, with the purpose of evaluating a possible race variation in RV global and free wall systolic strain, we analysed a subgroup of healthy Asians ($n = 100$ Japanese; age 37.3 $\pm$ 11.1 years) and healthy European subjects ($n = 100$ Germans; age

Table 1 Clinical characteristics and conventional LV and RV measurements

	Healthy subjects ($n = 238$)	Asymptomatic patients ($n = 216$)	HFpEF patients ($n = 218$)	HFrEF patients ($n = 208$)
Clinical characteristics				
Age, years	36.5 ± 12.6	59.9 ± 14.4	72.0 ± 10.5	67.4 ± 14.1
Women, %	50	39.4	52.3	22.1
BMI, kg/m^2	22.5 ± 2.4	25.8 ± 3.9	28.3 ± 5.3	26.4 ± 4.8
Systolic blood pressure, mmHg	118.9 ± 9.8	132.2 ± 14.8	137.6 ± 13.9	124.4 ± 17.9
Diastolic blood pressure, mmHg	70.9 ± 8.6	78.5 ± 11.2	80.1 ± 11.7	74.7 ± 11.9
Hypertension, %	0	81	93.1	75
Diabetes, %	0	13.4	35.8	27.4
Coronary artery disease, %	0	16.2	39	57.7
Obesity, %	0	16.2	29.4	21.2
Atrial fibrillation, %	0	0	9.6	29.8
Conventional LV measurements				
LVEF, %	63.1 ± 5.5	61.3 ± 3.9	61.9 ± 6.1	35.4 ± 9.6
LV Mass, g/m^2	75.6 ± 16.4	95.3 ± 22.8	105.6 ± 26.3	141.0 ± 40.8
Septal e′ mitral annular velocity by TDI, cm/s	11.2 ± 2.1	6.4 ± 2.2	4.8 ± 1.6	4.1 ± 1.6
Lateral e′ mitral annular velocity by TDI, cm/s	14.2 ± 2.9	9.0 ± 2.9	7.0 ± 2.2	5.8 ± 2.6
Mitral early-diastolic inflow velocity (E), cm/s	76.9 ± 15.9	66.0 ± 18.9	82.9 ± 25.7	81.8 ± 28.3
Mitral E/e′ septal–lateral ratio	6.3 ± 1.4	9.3 ± 4.1	15.2 ± 5.8	18.3 ± 8.0
LV global longitudinal systolic strain, %	−21.0 ± 2.2	−19.2 ± 2.3	−17.7 ± 3.3	−9.8 ± 3.7
Conventional RV measurements				
FAC, %	49.4 ± 7.6	47.4 ± 5.8	45.4 ± 8.7	39.1 ± 9.8
TAPSE, mm	20.2 ± 2.7	19.0 ± 1.9	19.2 ± 2.9	16.2 ± 3.3
Tricuspid annular systolic velocity (S′), cm/s	12.6 ± 1.7	12.3 ± 2.1	12.3 ± 2.6	9.8 ± 2.5
RV basal end-diastolic diameter, mm	30.5 ± 5.0	35.6 ± 4.6	33.7 ± 6.2	39.1 ± 6.5
Tricuspid regurgitation jet peak velocity, m/s	1.86 ± 0.34	1.99 ± 0.33	2.38 ± 0.54	2.41 ± 0.62
Tricuspid regurgitation jet peak velocity >2.9 m/s, %	0	0.9	17.9	22.5
Severe tricuspid regurgitation, %	0	0	0	0

Data are expressed as mean ± SD or percentages. e′ indicates early diastolic. S′ indicates tricuspid lateral annular peak systolic velocity by TDI. TDI indicates pulsed tissue Doppler imaging.

36.9 ± 12.1 years) of similar age. In this regard, there were no significant differences between Asians and Europeans in RV global and free wall systolic strain (RV global systolic strain −24.9 ± 3.6 vs. −24.1 ± 3.5%, *P*-value 0.108; and RV free wall systolic strain −28.7 ± 4.1 vs. −28.1 ± 4.5%, *P*-value 0.342, respectively).

Ability of RV systolic strain to detect subtle RV systolic abnormalities

Concerning the ability of RV systolic strain to detect subtle RV systolic abnormalities, RV global and free wall systolic strain were able to detect subtle RV longitudinal systolic abnormalities in a significant proportion of patients with HFrEF and to a lesser extent in HFpEF despite preserved RV conventional measurements such as TAPSE, S′, and FAC (see *Figures 2–4* and Supplementary data, *Videos S6 –S10* as well as Supplementary data, *Figures S1 to S4*). In line, RV global and free wall systolic strain detected a significantly higher rate of RV systolic abnormalities in HFrEF and to a lesser extent in HFpEF in comparison with conventional RV measurements (see *Figure 5* and Supplementary data, *Figures S5 and S6*). In addition, in these patients, the symptomatic status was significantly linked to both RV global and free wall systolic strain (see *Tables 3* and *4*). In agreement, patients with more impaired RV global and free wall systolic strain had worse functional class (dyspnoea—NYHA classification) than those with less altered RV systolic strain (see *Tables 3* and *4*).

On the other hand, the incremental clinical value of adding RV systolic strain to conventional RV measurements to detect subtle RV systolic abnormalities was not important in asymptomatic patients (see *Figure 6*). In this regard, RV global and free wall systolic strain did not detect a high rate of RV longitudinal systolic abnormalities in asymptomatic patients when conventional RV measurements such as TAPSE, FAC, or S′ were preserved (see *Figure 6*).

Clinical and cardiac factors linked to RV global and free wall systolic strain

Between the clinical and cardiac factors related to RV systolic strain, principally LV systolic strain and to a lesser extent LVEF and RV free wall thickness were significantly linked to RV global and free wall systolic strain (see *Table 5*). Consistent with these findings, patients with HFpEF with abnormal RV global and free wall systolic strain had a concomitant rate of abnormal LV longitudinal systolic strain

Table 2 Myocardial RV systolic parameters using 2DSTE

	Healthy subjects ($n = 238$)	Asymptomatic patients ($n = 216$)	HFpEF patients ($n = 218$)	HFrEF patients ($n = 208$)
RV global (septal and free wall) systolic strain, %				
All patients	-24.5 ± 3.8	-22.4 ± 3.5	-20.7 ± 4.0	-15.3 ± 4.7
Lowest expected value	-17.0	n/a	n/a	n/a
Women	-25.0 ± 4.0	-22.9 ± 3.6	-21.0 ± 4.0	-15.5 ± 5.4
Lowest expected value	-17.1	n/a	n/a	n/a
Men	-23.9 ± 3.5[a]	-22.0 ± 3.5	-20.5 ± 4.1	-15.2 ± 4.5
Lowest expected value	-17.0	n/a	n/a	n/a
Younger than 50 years	-24.3 ± 3.7	-22.2 ± 3.9	-20.6 ± 3.5	-15.9 ± 5.1
Lowest expected value	-17.0	n/a	n/a	n/a
Older than 50 years	-24.8 ± 3.9	-22.4 ± 3.4	-20.7 ± 4.1	-15.2 ± 4.6
Lowest expected value	-17.1	n/a	n/a	n/a
RV free wall systolic strain, %				
All patients	-28.5 ± 4.8	-26.7 ± 5.1	-24.6 ± 5.1	-19.0 ± 5.8
Lowest expected value	-19.0	n/a	n/a	n/a
Women	-29.0 ± 5.0	-27.3 ± 5.1	-24.6 ± 5.1	-19.6 ± 6.7
Lowest expected value	-19.2	n/a	n/a	n/a
Men	-27.9 ± 4.7	-26.3 ± 5.1	-24.7 ± 5.1	-18.9 ± 5.6
Lowest expected value	-18.7	n/a	n/a	n/a
Younger than 50 years	-28.4 ± 4.9	-26.8 ± 6.0	-25.0 ± 4.4	-20.6 ± 7.0
Lowest expected value	-18.8	n/a	n/a	n/a
Older than 50 years	-28.8 ± 4.5	-26.7 ± 4.8	-24.6 ± 5.1	-18.9 ± 5.7
Lowest expected value	-19.9	n/a	n/a	n/a

Data are expressed as mean $\pm$ SD. [a]indicates significant statistical differences ($P < 0.05$); in this case, between men and women in RV global systolic strain in healthy subjects. In HFpEF, HFrEF, and asymptomatic patients, there were no significant statistical differences between men and women or between younger and older than 50 years of age. n/a, not applicable.

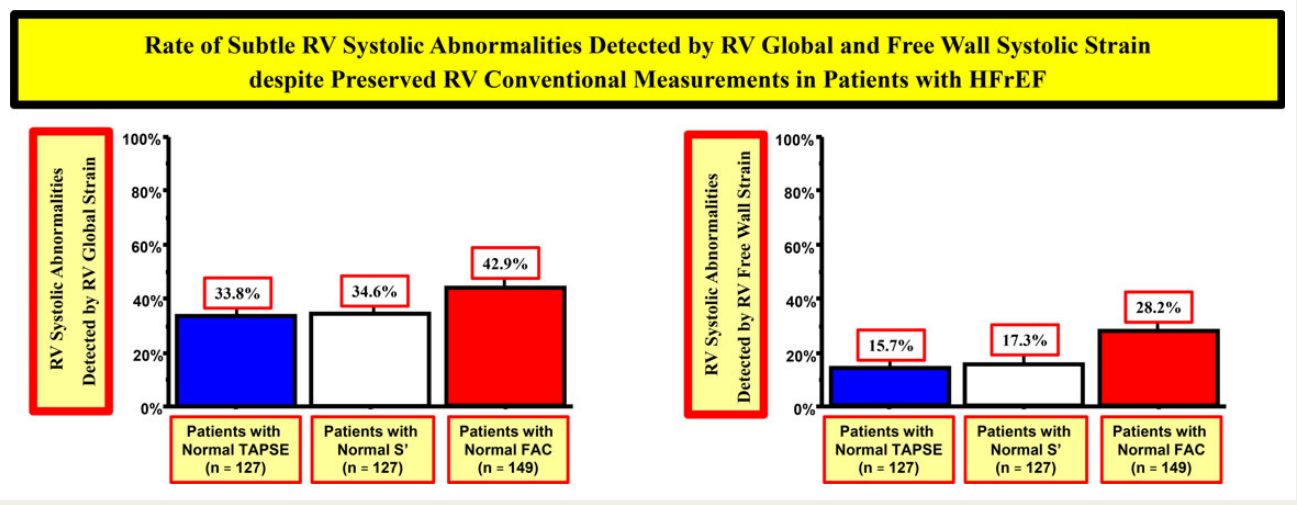

Figure 2 Subtle RV systolic abnormalities detected by RV global and free wall systolic strain despite preserved RV conventional measurements in patients with HFrEF. Preserved RV conventional measurements were determined according to the recommendations for chamber quantification of the EACVI (i.e. FAC $\geq$ 35%, TAPSE $\geq$ 17 mm, and S′ $\geq$ 9.5 cm/s). RV systolic abnormalities using RV systolic strain were determined as RV global and free wall systolic strain > -17 and > -19%, respectively (according to the lowest expected value of these measurements in healthy subjects). See also in the Supplementary data online a subgroup analysis showing the ability of RV global and free wall systolic strain to detect subtle RV systolic abnormalities in the subgroups of HFrEF patients with atrial fibrillation and sinus rhythm (see Supplementary data, *Figures S1* and *S2*).

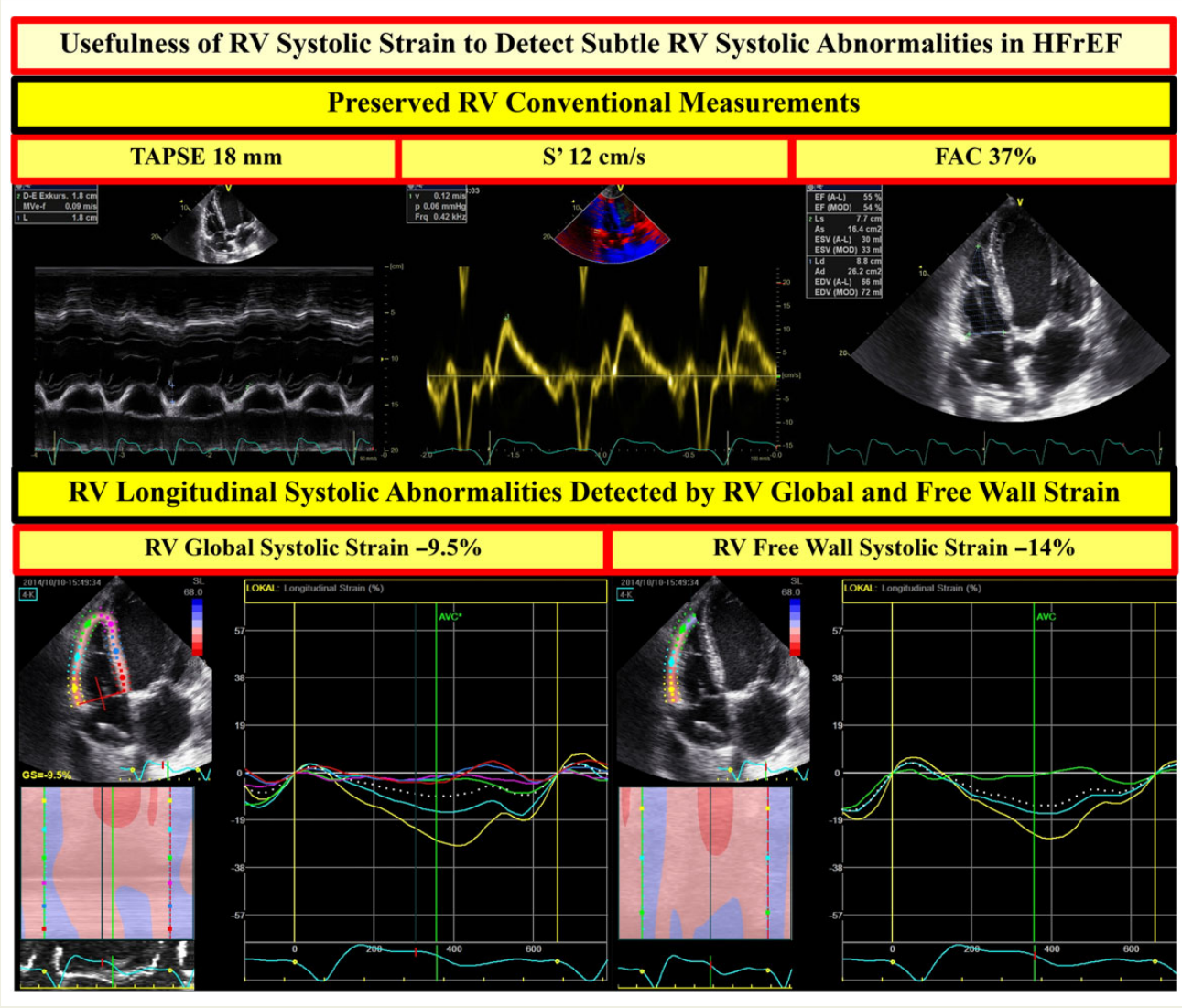

Figure 3 Usefulness of RV global and free wall systolic strain to detect subtle RV systolic abnormalities in HFrEF. This figure shows the ability of RV global and free wall systolic strain to detect subtle RV systolic abnormalities in a patient with HFrEF. Likewise, in the same patient, Supplementary data, *Videos S6 –S10*, show the usefulness of RV global and free wall systolic strain to detect subtle RV systolic abnormalities despite preserved systolic motion in the basal segment of the free wall of the RV.

(LV strain $\geq -16\%$) at 88% and a rate of RV hypertrophy (RV free wall > 5 mm) at 60%. In line, patients with HFrEF with impaired RV global and free wall systolic strain had also an altered LV longitudinal systolic strain at 99.2% and a RV hypertrophy at 33.6%. In contrast, RV global and free wall systolic strain were moderately linked to the mitral E/e′ ratio, tricuspid regurgitation velocity, and to the age of the patients (see *Table 5*).

Discussion

In the present multicentre study analysing a large cohort of healthy subjects and patients with HF, we have determined the normal range and the usefulness of RV global and free wall systolic strain to detect subtle RV systolic abnormalities.

Normal range and definition of normal RV systolic strain

Some studies analysing healthy subjects with 2DSTE have reported the values of RV systolic strain in this population.[14–17] However, these studies were limited to determine the normal range of RV global and free wall systolic strain because of the small number of patients analysed (<80 women or men).[14–17] For these reasons, one of the objectives of the present study was to analyse a large cohort of healthy subjects with the purpose of establishing the normal range of RV global and free wall systolic strain which could help to define a normal RV longitudinal systolic function using these myocardial parameters. In effect, analysing a healthy population of 238 subjects, the normal range of RV global and free wall systolic strain was -24.5 ± 3.8 and -28.5 ± 4.8 (lowest expected cut-off

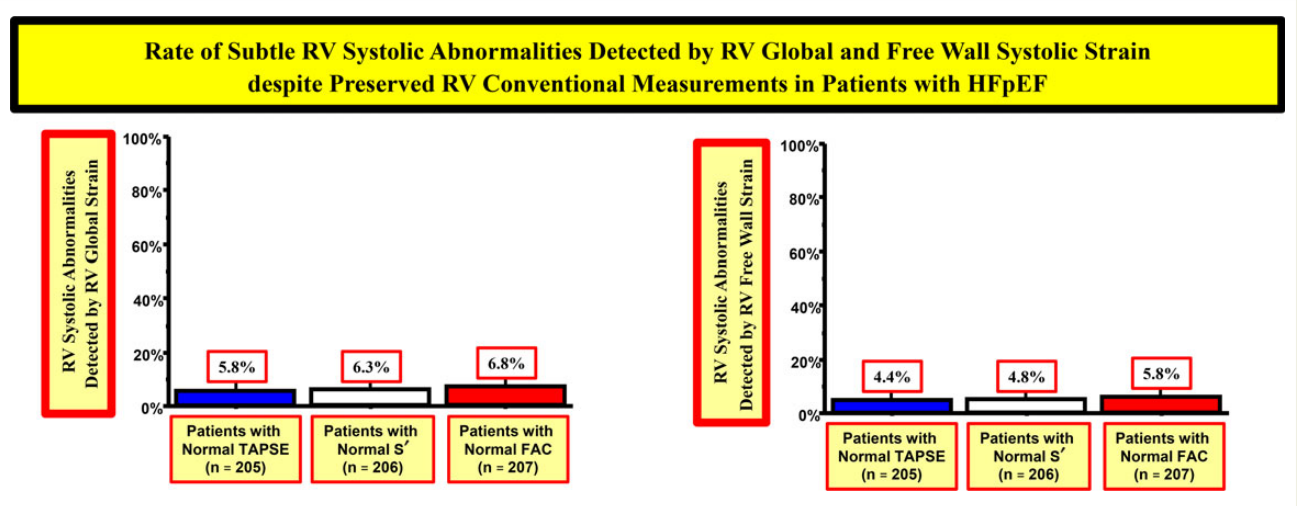

Figure 4 Subtle RV systolic abnormalities detected by RV global and free wall systolic strain despite preserved RV conventional measurements in patients with HFpEF. Preserved RV conventional measurements were determined according to the recommendations for chamber quantification of the EACVI (i.e. FAC ≥ 35%, TAPSE ≥ 17 mm, and S′ ≥ 9.5 cm/s). RV systolic abnormalities using RV systolic strain were determined as RV global and free wall systolic strain > −17 and > −19%, respectively (according to the lowest expected value of these measurements in healthy subjects). See also in the Supplementary data online a subgroups analysis showing the ability of RV global and free wall systolic strain to detect subtle RV systolic abnormalities in the subgroups of HFpEF patients with atrial fibrillation and sinus rhythm (see Supplementary data, *Figures S3* and *S4*).

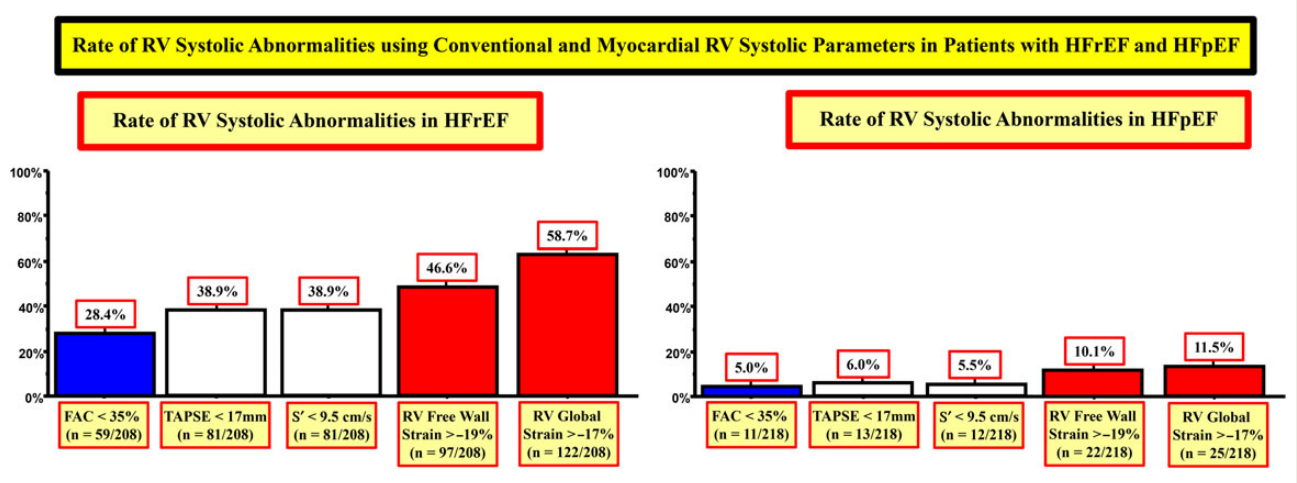

Figure 5 Rate of RV systolic abnormalities using conventional and new RV systolic parameters in patients with HFrEF and HFpEF. RV systolic abnormalities using conventional RV measurements were determined according to the recommendations for chamber quantification of the EACVI (i.e. FAC < 35%, TAPSE < 17 mm, and S′ <9.5 cm/s). RV systolic abnormalities using RV systolic strain were determined as RV global and free wall systolic strain > −17 and > −19%, respectively (according to the lowest expected value of these measurements in healthy subjects). There were statistical differences in the rate of RV systolic abnormalities using new (RV global and free wall systolic strain) vs. conventional (FAC, TAPSE, and S′) RV systolic parameters in patients with HFrEF and HFpEF ($P < 0.01$). See also in the Supplementary data online a subgroup analysis showing the rate of RV systolic abnormalities using conventional and new RV systolic parameters in the subgroups of HFrEF and HFpEF patients with atrial fibrillation and sinus rhythm (see Supplementary data, *Figures S5* and *S6*).

values −17 and −19%, respectively), with minimal differences between younger and older subjects and between women and men. In accordance with these findings, previous studies have found similar cut-offs of RV global and free wall systolic strain to differentiate a normal from an abnormal RVEF by MRI as well as to determine outcomes in patients with HF and cardiovascular diseases.[8,11,13,16,25,26] In line, the most recent guidelines on chamber quantification of the EACVI suggested that a cut-off of RV free wall systolic strain > −20% could be considered as abnormal.[2]

Table 3 Correlation of symptomatic status with conventional and myocardial RV systolic parameters

	Asymptomatic and HFrEF patients				
	Symptomatic status		NYHA functional class		
	Asymptomatic ($n = 216$)	HFrEF ($n = 208$)	Class I ($n = 216$)	Class II ($n = 122$)	Classes III–IV ($n = 86$)
Myocardial RV systolic parameters					
RV global (septal-free wall) systolic strain, %	-22.4 ± 3.5	-15.3 ± 4.7*	-22.4 ± 3.5	$-17.1 \pm 4.0^{\dagger}$	$-12.8 \pm 4.4^{\ddagger}$
RV free wall systolic strain, %	-26.7 ± 5.1	-19.0 ± 5.8*	-26.7 ± 5.1	$-21.1 \pm 5.2^{\dagger}$	$-16.0 \pm 5.4^{\ddagger}$
Conventional RV systolic parameters					
TAPSE, mm	19.0 ± 1.9	16.2 ± 3.3*	19.0 ± 1.9	$17.1 \pm 3.1^{\dagger}$	$14.9 \pm 3.1^{\ddagger}$
Tricuspid annular systolic velocity (S′), cm/s	12.3 ± 2.1	9.8 ± 2.5*	12.3 ± 2.1	$10.3 \pm 2.2^{\dagger}$	$9.0 \pm 2.7^{\ddagger}$
FAC, %	47.4 ± 5.8	39.1 ± 9.8*	47.4 ± 5.8	$41.9 \pm 8.8^{\dagger}$	$35.0 \pm 9.7^{\ddagger}$
	Asymptomatic and HFpEF patients				
	Symptomatic status		**NYHA functional class**		
	Asymptomatic ($n = 216$)	**HFpEF ($n = 218$)**	**Class I ($n = 216$)**	**Class II ($n = 153$)**	**Classes III–IV ($n = 65$)**
Myocardial RV systolic parameters					
RV global (septal-free wall) systolic strain, %	-22.4 ± 3.5	-20.7 ± 4.0*	-22.4 ± 3.5	$-21.6 \pm 3.5^{\dagger}$	$-18.7 \pm 4.6^{\ddagger}$
RV free wall systolic strain, %	-26.7 ± 5.1	-24.6 ± 5.1*	-26.7 ± 5.1	-25.7 ± 4.5	$-22.1 \pm 5.4^{\ddagger}$
Conventional RV systolic parameters					
TAPSE, mm	19.0 ± 1.9	19.2 ± 2.9	19.0 ± 1.9	19.8 ± 2.7	$17.8 \pm 2.8^{\ddagger}$
Tricuspid annular systolic velocity (S′), cm/s	12.3 ± 2.1	12.3 ± 2.6	12.3 ± 2.1	12.6 ± 2.4	$11.4 \pm 2.8^{\ddagger}$
FAC, %	47.4 ± 5.8	45.4 ± 8.7*	47.4 ± 5.8	47.4 ± 8.0	$40.6 \pm 8.5^{\ddagger}$

Data are expressed as mean $\pm$ SD. *indicates significant statistical differences ($P < 0.05$) between symptomatic and asymptomatic patients. †indicates significant statistical differences ($P < 0.05$) between patients with NYHA Class II vs. Class I. ‡indicates significant statistical differences ($P < 0.05$) between patients with NYHA Classes III–IV vs. Class II or I. It is important to highlight that there were no significant statistical differences in TAPSE and S′ in asymptomatic vs. HFpEF patients. S′ indicates tricuspid lateral annular peak systolic velocity by pulsed tissue Doppler imaging.

Table 4 Association of symptomatic status with conventional and myocardial RV systolic parameters

	Asymptomatic and HFrEF patients			
	OR for HF symptoms (dyspnoea)		OR for NYHA functional class ≥3	
	OR [95% CI]	*P*-value	OR [95% CI]	*P*-value
Myocardial RV systolic parameters				
RV global systolic strain > −17%	>75 [31.1–>75]	<0.001	20.4 [11.1–37.3]	<0.001
RV free wall systolic strain > −19%	62.0 [19.2–>75]	<0.001	18.7 [10.5–33.1]	<0.001
Conventional RV systolic parameters				
TAPSE <17 mm	68.2 [16.4–>75]	<0.001	12.8 [7.3–22.4]	<0.001
Tricuspid annular systolic velocity (S′) <9.5 cm/s	68.2 [16.4–>75]	<0.001	10.9 [6.3–18.9]	<0.001
FAC <35%	42.3 [10.1–>75]	<0.001	16.0 [8.5–30.0]	<0.001
	Asymptomatic and HFpEF patients			
Myocardial RV systolic parameters				
RV global systolic strain > −17%	9.1 [2.7–30.9]	<0.001	20.0 [8.3–48.2]	<0.001
RV free wall systolic strain > −19%	7.9 [2.3–27.0]	<0.001	24.9 [9.4–65.7]	<0.001
Conventional RV systolic parameters				
TAPSE <17 mm	6.7 [1.5–30.4]	0.012	27.6 [7.5–>75]	<0.001
Tricuspid annular systolic velocity (S′) <9.5 cm/s	6.2 [1.3–28.1]	0.017	24.8 [6.7–>75]	<0.001
FAC <35%	5.6 [1.2–25.9]	0.024	22.1 [5.9–>75]	<0.001

OR indicates odds ratio. CI indicates confidence interval.

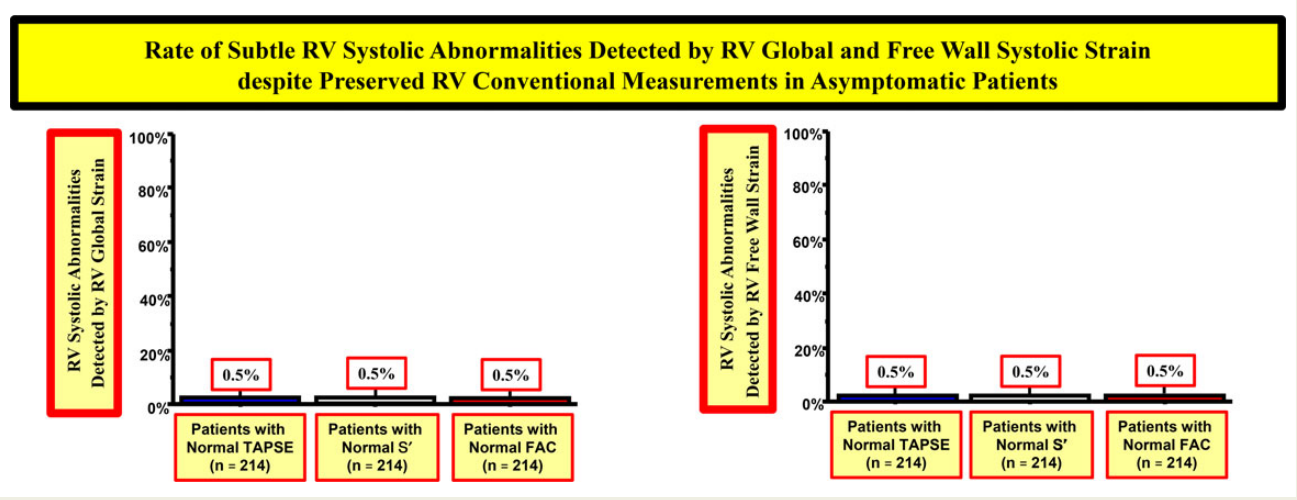

Figure 6 Rate of subtle RV systolic abnormalities detected by RV global and free wall systolic strain despite preserved RV conventional measurements in asymptomatic patients. Preserved RV conventional measurements were determined according to the recommendations for chamber quantification of the EACVI (i.e. FAC ≥ 35%, TAPSE ≥ 17 mm, and S′ ≥ 9.5 cm/s). RV systolic abnormalities using RV systolic strain were determined as RV global and free wall systolic strain > −17 and > −19%, respectively (according to the lowest expected value of these measurements in healthy subjects).

Conventional vs. new RV systolic parameters to evaluate RV systolic function

Conventional RV systolic parameters such as TAPSE and S′ are adequate measurements of RV systolic function.[1,2] However, these conventional RV analyses have some limitations such as load and angle dependence and inaccuracy to evaluate a global RV systolic function because they represent only the displacement or function of a single RV segment.[1–7] Despite these limitations, the incremental clinical value of new angle-independent and global RV analyses such as RV systolic strain over conventional RV measurements remains poorly understood. In effect, the ability of RV systolic strain to detect subtle RV systolic abnormalities, when conventional RV

Table 5 Clinical and cardiac variables linked to RV global and free wall systolic strain

	Healthy subjects (n = 238)		Asymptomatic patients (n = 216)		HFpEF patients (n = 218)		HFrEF patients (n = 208)	
	r	p	r	p	r	p	r	p
RV global (septal and free wall) systolic strain								
Age, years	0.03	0.560	−0.03	0.592	0.08	0.211	−0.03	0.580
LV global longitudinal systolic strain, %	0.31	<0.001	0.31[a]	<0.001	0.51[a]	<0.001	0.62[a]	<0.001
Tricuspid regurgitation jet peak velocity, m/s	−0.01	0.977	−0.01	0.969	−0.07	0.281	−0.26	<0.001
RV free wall thickness, mm	0.12	0.177	−0.03	0.671	−0.38[a]	<0.001	−0.32	<0.001
RV septal wall thickness, mm	−0.21[a]	<0.001	−0.09	0.179	−0.18	0.007	−0.01	0.894
LVEF, %	0.10	0.127	0.23[a]	<0.001	0.08	0.219	0.56	<0.001
Mitral E/e′ septal–lateral ratio	0.16	0.014	−0.07	0.249	−0.15	0.019	−0.31	<0.001
Systolic blood pressure, mmHg	−0.09	0.148	−0.07	0.275	−0.01	0.798	0.15	0.024
Body surface area, m^2	−0.29	<0.001	−0.12	0.067	−0.08	0.234	−0.05	0.404
BMI, kg/m^2	−0.19	0.002	−0.07	0.291	−0.01	0.887	−0.09	0.183
RV free wall systolic strain								
Age, years	0.01	0.989	−0.03	0.628	0.10	0.122	−0.04	0.479
LV global longitudinal systolic strain, %	0.19	0.003	0.13	0.053	0.41[a]	<0.001	0.49[a]	<0.001
Tricuspid regurgitation jet peak velocity, m/s	−0.01	0.994	0.04	0.518	−0.07	0.280	−0.24	<0.001
RV free wall thickness, mm	0.01	0.980	−0.08	0.224	−0.31[a]	<0.001	−0.29	<0.001
RV septal wall thickness, mm	−0.17	0.009	−0.02	0.785	−0.08	0.192	−0.01	0.885
LVEF, %	0.07	0.235	0.13	0.051	0.02	0.728	0.48	<0.001
Mitral E/e′ septal–lateral ratio	0.09	0.143	0.05	0.427	−0.11	0.092	−0.20	0.002
Systolic blood pressure, mm Hg	−0.02	0.738	−0.10	0.137	0.05	0.396	0.13	0.049
Body surface area, m^2	−0.23	<0.001	−0.10	0.112	−0.07	0.270	−0.02	0.778
BMI, kg/m^2	−0.16	0.010	−0.03	0.630	−0.09	0.175	−0.01	0.969

[a]Identified variable with the strongest association with RV global and free wall systolic strain in a multivariate stepwise forward linear regression analysis (all variables were included in the analysis). No variable had significant association with RV free wall systolic strain in a multivariate stepwise forward linear regression analysis in healthy subjects and in asymptomatic patients.

parameters are normal, is not known. In the present study analysing a large cohort of patients with HF, RV global and free wall systolic strain were able to detect subtle RV longitudinal systolic abnormalities in a significant proportion of patients with HFrEF and to a lesser extent in HFpEF despite preserved RV conventional measurements such as TAPSE, S′, and FAC. In addition, we evidenced that in these patients the symptomatic status was significantly linked to RV global and free wall systolic strain. In agreement with these findings, recent studies in patients with HF showed that new RV myocardial parameters such as RV systolic strain had a significantly better correlation with RVEF by MRI than conventional RV analyses and a strong correlation with the functional class of the patients.[8,11,12,24,26–29] Therefore, on the basis of our findings, we consider that RV global and free wall systolic strain could be considered important methods to assess the myocardial systolic function of the RV in patients with HF.

Clinical and cardiac factors linked to RV global and free wall systolic strain

In the analysis of the factors that could influence on RV global and free wall systolic strain, we found that these RV myocardial parameters were principally linked to the longitudinal systolic function of the LV. These findings are in agreement with several previous studies that also found a significant interrelationship between the longitudinal systolic function of the RV and LV.[30–34] Furthermore, another point to take into consideration is the possible influence of the vendor's software package on RV global and free wall strain. Recent studies evidenced that 2DSTE values of the LV vary between different software packages such as GE, Philips, and Toshiba.[18,35–37] Thus, while there are no data showing a variability between different ultrasound software packages regarding RV strain, we consider that the normal range and cut-off values of RV global and free wall systolic strain reported in this study should be considered according to the ultrasound software package utilized (i.e. Echo-Pac from GE), which so far is the most extensively validated software to analyse the RV with 2DSTE.[8–10,13,15,16,24–34]

Limitations

Some limitations from this study should be considered. One point to take into consideration is the experience of the operator to perform RV myocardial analyses with 2DSTE, particularly for RV free wall strain. Unlike RV or LV global systolic strain, whose analyses are similar in four-chamber view, RV free wall strain requires a high experience in 2DSTE because this isolated wall analysis is different from the conventional LV or RV global strain analysis. In line, it is important taking into account that the 2DSTE software to analyse the

LV is the same used to analyse the RV. Furthermore, it is worth noting that we did not compare the echocardiographic strain analyses with those performed by cardiac MRI. Nonetheless, several previous studies have demonstrated a strong correlation of RV global and free wall systolic strain with RVEF by MRI.[8–13,26]

Conclusions

In the present multicentre study analysing a large cohort of healthy subjects and patients with HF, we have determined the normal range and the usefulness of RV global and free wall systolic strain to detect subtle RV systolic abnormalities. Therefore, we consider that these findings could help to define a normal RV longitudinal systolic function using RV global and free wall systolic strain and highlight the clinical relevance of adding these new RV myocardial parameters to the conventional RV measurements in patients with HF.

Supplementary material

Supplementary Material is available at *European Journal of Echocardiography* online.

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References

1. 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**:685–713.
2. 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. *Eur Heart J Cardiovasc Imaging.* 2015;**16**:233–70.
3. Kucukdurmaz Z, Karapinar H, Karavelioğlu Y, Açar G, Gul I, Emiroglu MY *et al.* Effect of blood donation mediated volume reduction on right ventricular function parameters in healthy subjects. *Echocardiography* 2012;**29**:451–4.
4. Pavelescu A, Naeije R. Effects of epoprostenol and sildenafil on right ventricular function in hypoxic volunteers: a tissue Doppler imaging study. *Eur J Appl Physiol.* 2012;**112**:1285–94.
5. Cameli M, Ballo P, Garzia A, Lisi M, Bocelli A, Mondillo S. Acute effects of low doses of ethanol on left and right ventricular function in young healthy subjects. *Alcohol Clin Exp Res.* 2011;**35**:1860–5.
6. Giusca S, Dambrauskaite V, Scheurwegs C, D'hooge J, Claus P, Herbots L *et al.* Deformation imaging describes right ventricular function better than longitudinal displacement of the tricuspid ring. *Heart.* 2010;**96**:281–8.
7. Mercer-Rosa L, Parnell A, Forfia PR, Yang W, Goldmuntz E, Kawut SM. Tricuspid annular plane systolic excursion in the assessment of right ventricular function in children and adolescents after repair of Tetralogy of Fallot. *J Am Soc Echocardiogr.* 2013;**26**:1322–9.
8. Leong DP, Grover S, Molaee P, Chakrabarty A, Shirazi M, Cheng YH *et al.* Nonvolumetric echocardiographic indices of right ventricular systolic function: validation with cardiovascular magnetic resonance and relationship with functional capacity. *Echocardiography.* 2012;**29**:455–63.
9. Li Y, Xie M, Wang X, Lu Q, Fu M. Right ventricular regional and global systolic function is diminished in patients with pulmonary arterial hypertension: a 2-dimensional ultrasound speckle tracking echocardiography study. *Int J Cardiovasc Imaging.* 2013;**29**:545–51.
10. Bernard Y, Morel M, Descotes-Genon V, Jehl J, Meneveau N, Schiele F. Value of speckle tracking for the assessment of right ventricular function in patients operated on for tetralogy of fallot. Comparison with magnetic resonance imaging. *Echocardiography.* 2014;**31**:474–82.
11. Lu KJ, Chen JX, Profitis K, Kearney LG, DeSilva D, Smith G *et al.* Right ventricular global longitudinal strain is an independent predictor of right ventricular function: a multimodality study of cardiac magnetic resonance imaging, real time three-dimensional echocardiography and speckle tracking echocardiography. *Echocardiography.* 2015;**32**:966–74.
12. Park JH, Negishi K, Kwon DH, Popovic ZB, Grimm RA, Marwick TH. Validation of global longitudinal strain and strain rate as reliable markers of right ventricular dysfunction: comparison with cardiac magnetic resonance and outcome. *J Cardiovasc Ultrasound.* 2014;**22**:113–20.
13. Focardi M, Cameli M, Carbone SF, Massoni A, De Vito R, Lisi M *et al.* Traditional and innovative echocardiographic parameters for the analysis of right ventricular performance in comparison with cardiac magnetic resonance. *Eur Heart J Cardiovasc Imaging.* 2015;**16**:47–52.
14. Tong C, Li C, Song J, Liu H, Deng Y. Assessment of right ventricular free wall longitudinal myocardial deformation using speckle tracking imaging in normal subjects. *J Huazhong Univ Sci Technolog Med Sci.* 2008;**28**:194–6.
15. Meris A, Faletra F, Conca C, Klersy C, Regoli F, Klimusina J *et al.* Timing and magnitude of regional right ventricular function: a speckle tracking-derived strain study of normal subjects and patients with right ventricular dysfunction. *J Am Soc Echocardiogr.* 2010;**23**:823–31.
16. Guendouz S, Rappeneau S, Nahum J, Dubois-Randé JL, Gueret P, Monin JL *et al.* Prognostic significance and normal values of 2D strain to assess right ventricular systolic function in chronic heart failure. *Circ J.* 2012;**76**:127–36.
17. Fine NM, Chen L, Bastiansen PM, Frantz RP, Pellikka PA, Oh JK *et al.* Reference values for right ventricular strain in patients without cardiopulmonary disease: a prospective evaluation and meta-analysis. *Echocardiography* 2015;**32**:787–96.
18. Takigiku K, Takeuchi M, Izumi C, Yuda S, Sakata K, Ohte N *et al.* Normal range of left ventricular 2-dimensional strain: Japanese Ultrasound Speckle Tracking of the Left Ventricle (JUSTICE) study. *Circ J.* 2012;**76**:2623–32.
19. Morris DA, Otani K, Bekfani T, Takigiku K, Izumi C, Yuda S *et al.* Multidirectional global left ventricular systolic function in normal subjects and patients with hypertension: multicenter evaluation. *J Am Soc Echocardiogr.* 2014;**27**:493–500.
20. Morris DA, Takeuchi M, Krisper M, Köhncke C, Bekfani T, Carstensen T *et al.* Normal values and clinical relevance of left atrial myocardial function analysed by speckle-tracking echocardiography: multicentre study. *Eur Heart J Cardiovasc Imaging.* 2015;**16**:364–72.
21. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA *et al.* Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *Eur J Echocardiogr.* 2009;**10**:165–93.
22. McMurray JJ, Adamopoulos S, Anker SD, Auricchio A, Böhm M, Dickstein K *et al.* ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure Association (HFA) of the ESC. *Eur Heart J.* 2012;**33**:1787–47.
23. Yancy CW, Jessup M, Bozkurt B, Butler J, Casey DE Jr, Drazner MH *et al.* 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol.* 2013;**62**:e147–239.
24. Morris DA, Gailani M, Vaz Pérez A, Blaschke F, Dietz R, Haverkamp W *et al.* Right ventricular myocardial systolic and diastolic dysfunction in heart failure with normal left ventricular ejection fraction. *J Am Soc Echocardiogr.* 2011;**24**:886–97.
25. Ternacle J, Berry M, Cognet T, Kloeckner M, Damy T, Monin JL *et al.* Prognostic value of right ventricular two-dimensional global strain in patients referred for cardiac surgery. *J Am Soc Echocardiogr.* 2013;**26**:721–6.
26. Lemarié J, Huttin O, Girerd N, Mandry D, Juillière Y, Moulin F *et al.* Usefulness of speckle-tracking imaging for right ventricular assessment after acute myocardial infarction: a magnetic resonance imaging/echocardiographic comparison within the relation between aldosterone and cardiac remodeling after myocardial infarction study. *J Am Soc Echocardiogr.* 2015;**28**:818–27.
27. Salerno G, D'Andrea A, Bossone E, Scarafile R, Riegler L, Di Salvo G *et al.* Association between right ventricular two-dimensional strain and exercise capacity in

patients with either idiopathic or ischemic dilated cardiomyopathy. *J Cardiovasc Med (Hagerstown)*. 2011;**12**:625–34.
28. Cameli M, Righini FM, Lisi M, Bennati E, Navarri R, Lunghetti S *et al.* Comparison of right versus left ventricular strain analysis as a predictor of outcome in patients with systolic heart failure referred for heart transplantation. *Am J Cardiol*. 2013;**112**: 1778–84.
29. Cameli M, Lisi M, Righini FM, Focardi M, Lunghetti S, Bernazzali S *et al.* Speckle tracking echocardiography as a new technique to evaluate right ventricular function in patients with left ventricular assist device therapy. *J Heart Lung Transplant.* 2013; **32**:424–30.
30. van der Hulst AE, Delgado V, Holman ER, Kroft LJ, de Roos A, Hazekamp MG *et al.* Relation of left ventricular twist and global strain with right ventricular dysfunction in patients after operative 'correction' of Tetralogy of Fallot. *Am J Cardiol.* 2010;**106**: 723–9.
31. Prinz C, van Buuren F, Faber L, Bitter T, Bogunovic N, Burchert W *et al.* Myocardial fibrosis is associated with biventricular dysfunction in patients with hypertrophic cardiomyopathy. *Echocardiography.* 2012;**29**:438–44.
32. Kempny A, Diller GP, Orwat S, Kaleschke G, Kerckhoff G, Bunck Ach *et al.* Right ventricular-left ventricular interaction in adults with Tetralogy of Fallot: a combined cardiac magnetic resonance and echocardiographic speckle tracking study. *Int J Cardiol.* 2012;**154**:259–64.
33. Konishi K, Dohi K, Tanimura M, Sato Y, Watanabe K, Sugiura E *et al.* Quantifying longitudinal right ventricular dysfunction in patients with old myocardial infarction by using speckle-tracking strain echocardiography. *Cardiovasc Ultrasound.* 2013;**11**:23.
34. Haeck ML, Höke U, Marsan NA, Holman ER, Wolterbeek R, Bax JJ *et al.* Impact of right ventricular dyssynchrony on left ventricular performance in patients with pulmonary hypertension. *Int J Cardiovasc Imaging.* 2014;**30**:713–20.
35. Biaggi P, Carasso S, Garceau P, Greutmann M, Gruner C, Tsang W *et al.* Comparison of two different speckle tracking software systems: does the method matter? *Echocardiography.* 2011;**28**:539–47.
36. Risum N, Ali S, Olsen NT, Jons C, Khouri MG, Lauridsen TK *et al.* Variability of global left ventricular deformation analysis using vendor dependent and independent two-dimensional speckle-tracking software in adults. *J Am Soc Echocardiogr.* 2012; **25**:1195–203.
37. Negishi K, Lucas S, Negishi T, Hamilton J, Marwick TH. What is the primary source of discordance in strain measurement between vendors: imaging or analysis? *Ultrasound Med Biol.* 2013;**39**:714–20.